The Catnip Response

A thesis presented
by
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to
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IMPORTANT NOTICE

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Thanks are due to Mr. Frederick A. Ulmer, curator of mammals at the Philadelphia Zoological Gardens who cooperated in the testing of catnip on many of his "big cats." The photographs of lions, leopards and jaguars in Chapter 5 are of animals in the collection at the Philadelphia Zoo. The author is also grateful to the authorities of the National Zoo, Washington, D.C., The Bronx Zoo and The Staten Island Zoo, New York, The Franklin Park Zoo, Boston and The Ringling Brothers Circus for the opportunity to utilize their animals in this study.

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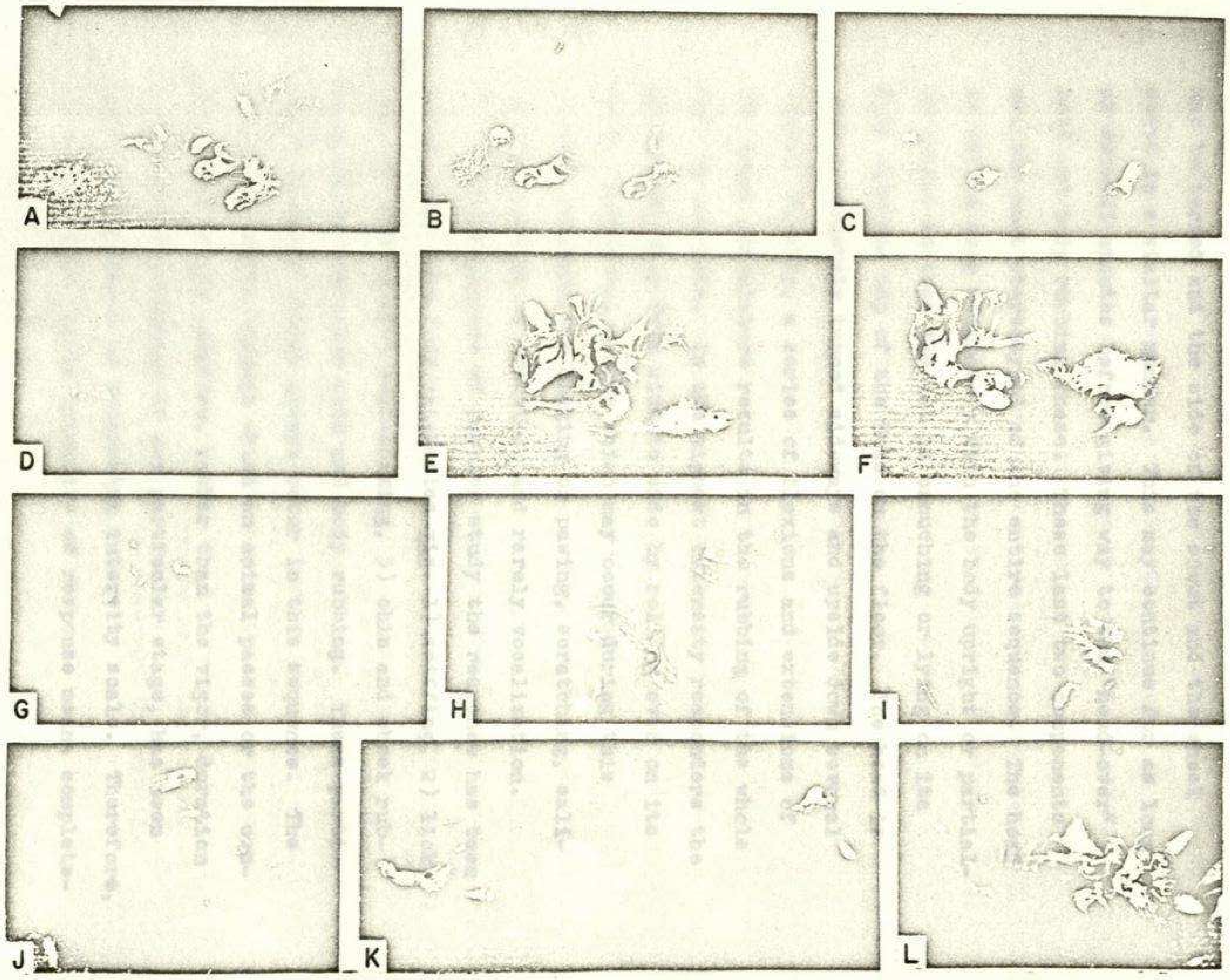
General Introduction:

The catnip response, given by some but not all cats, consists of a series of stereotyped actions (Figure 1) releases by an essential oil of the plant Nepeta cataria. The presence of this oil results in an alerting response by the animal which then orients towards the source and attempts to localize it. The animal approaches the source, usually dried leaves of the catnip plant, sniffing regularly. The sniffing may be short or prolonged, depending upon the individual and the circumstances, but seldom lasts more than a minute. Upon reaching the source the animal commences to lick and/or chew the leaves. This is often interrupted by shaking the head from side to side and momentarily gazing vacantly in no particular direction. This phase may be absent, short or prolonged up to five minutes, and some animals give no further response in which case it is ordinarily most extended. The components thus far mentioned have been designated low intensity responses, and cats which terminate the response at this point as low intensity responders.

The next level in the response sequence consists of chin and cheek rubbing. The animal is usually oriented toward the source, often in a crouched position. The neck is extended and withdrawn repeatedly, the chin being pushed and drawn through, over or toward the source. The head

Figure 1. The catnip response of a domestic cat. A. Sniffing and localization of leaves; B - C. Crouching, licking and chewing; D. Licking and pawing; E - J. Rubbing and rolling; K. Extension; L. Flexion.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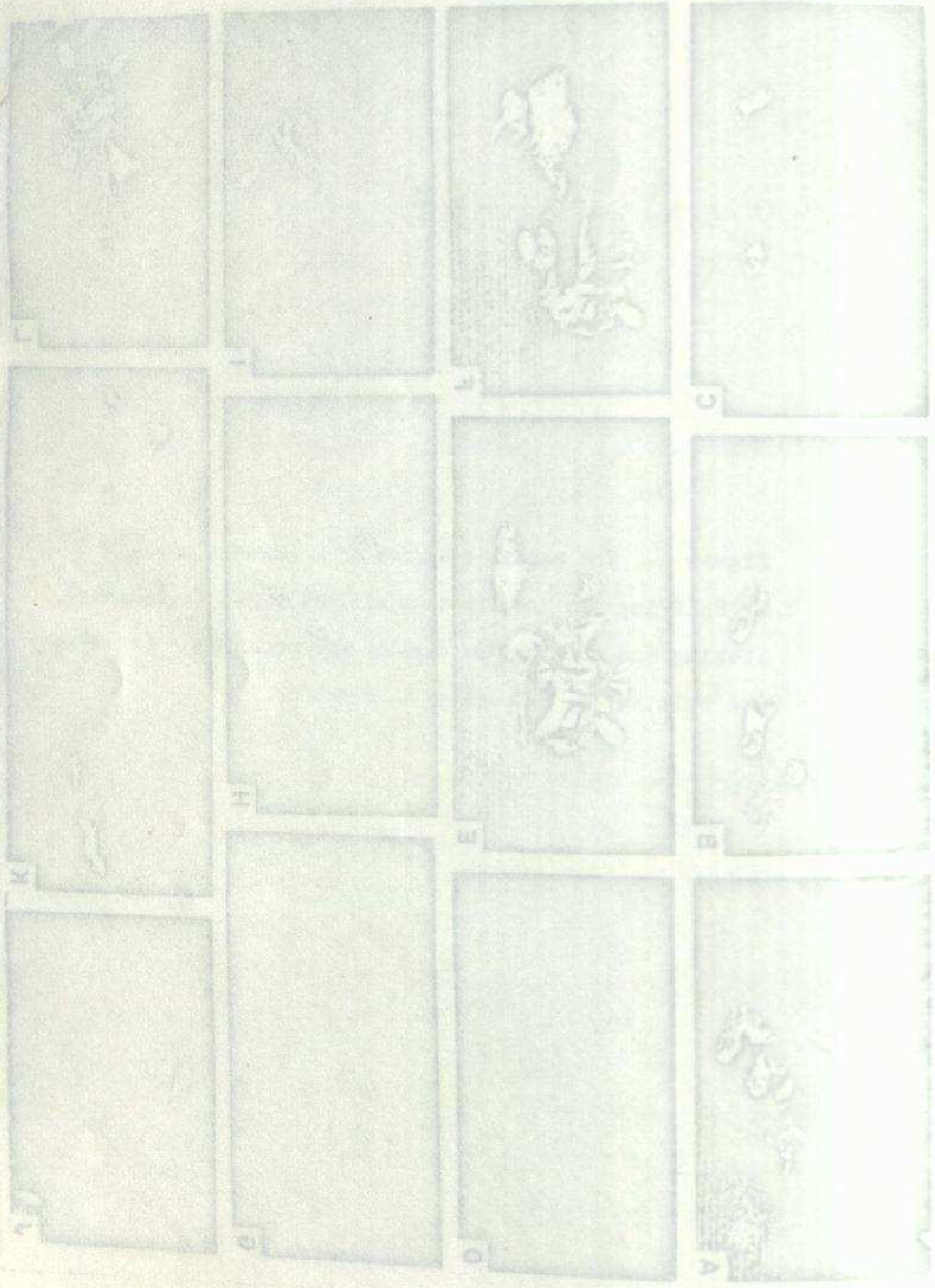

may be turned and the side of the snout and the cheek moved in a similar manner. This may continue for as long as several minutes before giving way to the "head-over" roll and body rubbing phase. These last two components are the most stereotyped of the entire sequence. The head is rolled over completely with the body upright or partially turned so that the cat is crouching or lying on its side with the top of the head on the floor. The head is then alternately turned sideways and upside down several times. Finally, a series of flexions and extensions of the trunk musculature results in the rubbing of the whole body on one side. In the highest intensity responders the animal may flip from side to side by rolling over on its back. Additional action which may occur during this general sequence are digging or pawing, scratching, salivating, washing or grooming, and rarely vocalization.

For the purpose of further study the response has been broken down into four categories <u>viz</u>. 1) sniffing, 2) licking and chewing with head-shaking, 3) chin and cheek rubbing and 4) head-over roll and body rubbing. These particular patterns almost always occur in this sequence. The number of stages through which an animal passes or the completeness of the response, rather than the vigor, duration or any other parameter of any particular stage, has been taken to represent an increasing intensity scale. Therefore, throughout this thesis intensity of response means completeness of response. Each succeeding stage generally, although not necessarily, requires a considerable increase in motor effort. There also appears to be an increased motivational requirement, for the transition from one phase to the next is often preceded by intention movements which are characteristic pf an effort to overcome inhibition. Further discussion of the behavior will be given later.

A number of compounds have been identified which elicit a catnip-like response (Figure 2). These are nepetalactone (I) (McElvain, <u>et</u>. <u>al</u>., 1941, 1942, 1955; Meinwald, 1954); matatabilactone* (Sakan, <u>et</u>. <u>al</u>., 1959, 1960); a recemic mixture of iridomyrmecin† (II) and isoiridomyrmecin (IIa) (Dolejs, <u>et</u>. <u>al</u>., 1960) which would have the enol intermediate of the structure IIb; and actinidine (III) (Sakan, <u>et</u>. <u>al</u>., 1959, 1960). Since the

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* The response of Felids to matatabilactone was kindly described to me with the aid of a moving picture by Dr. Akira Fujino and by Dr. Hiroshi Kaneto, Department of Pharmacology, Osaka University, in a letter of 12 September 1962. According to these authorities, actinidine is somewhat more effective than matatabilactone in eliciting a response which is identical to the catnip response except that <u>flehmen</u> (see Chapter 3) occurs. This latter pattern is absent in domestic cats reacting to nepetalactone but is frequently elicited in lions, leopards and jaguars by catnip. The domestic cat showed this response to ether extracts of tomcat urine.

† A sample of iridomyrmecin from the laboratory of Dr. M. Pavan, Instituto di Anatomia Comparata dell' Universita di Pavia, Pavia, Italy, was kindly supplied to me by Dr. E. O. Wilson, The Biological Laboratories, Harvard University.

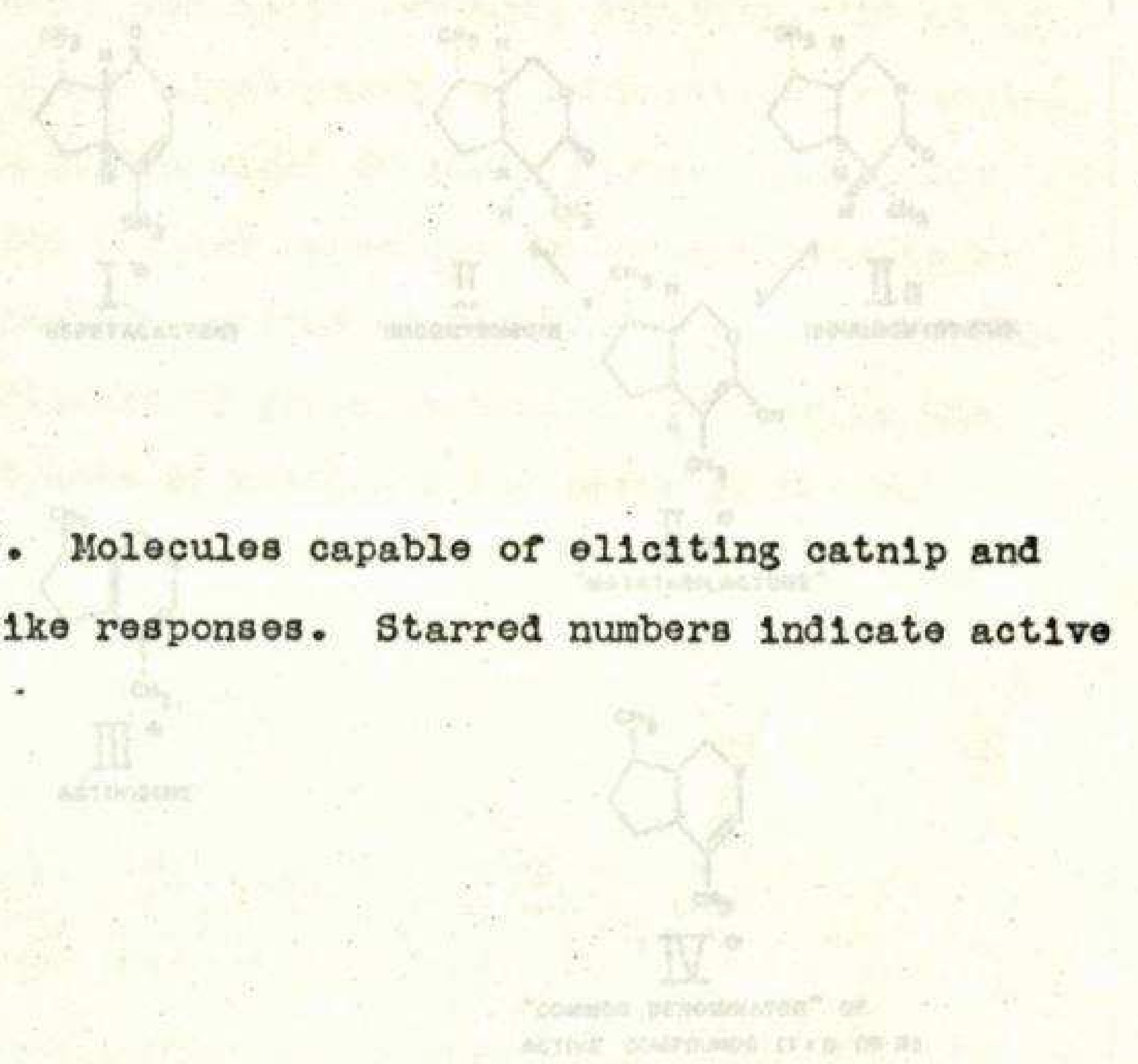

Figure 2. Molecules capable of eliciting catnip and catnip-like responses. Starred numbers indicate active forms.

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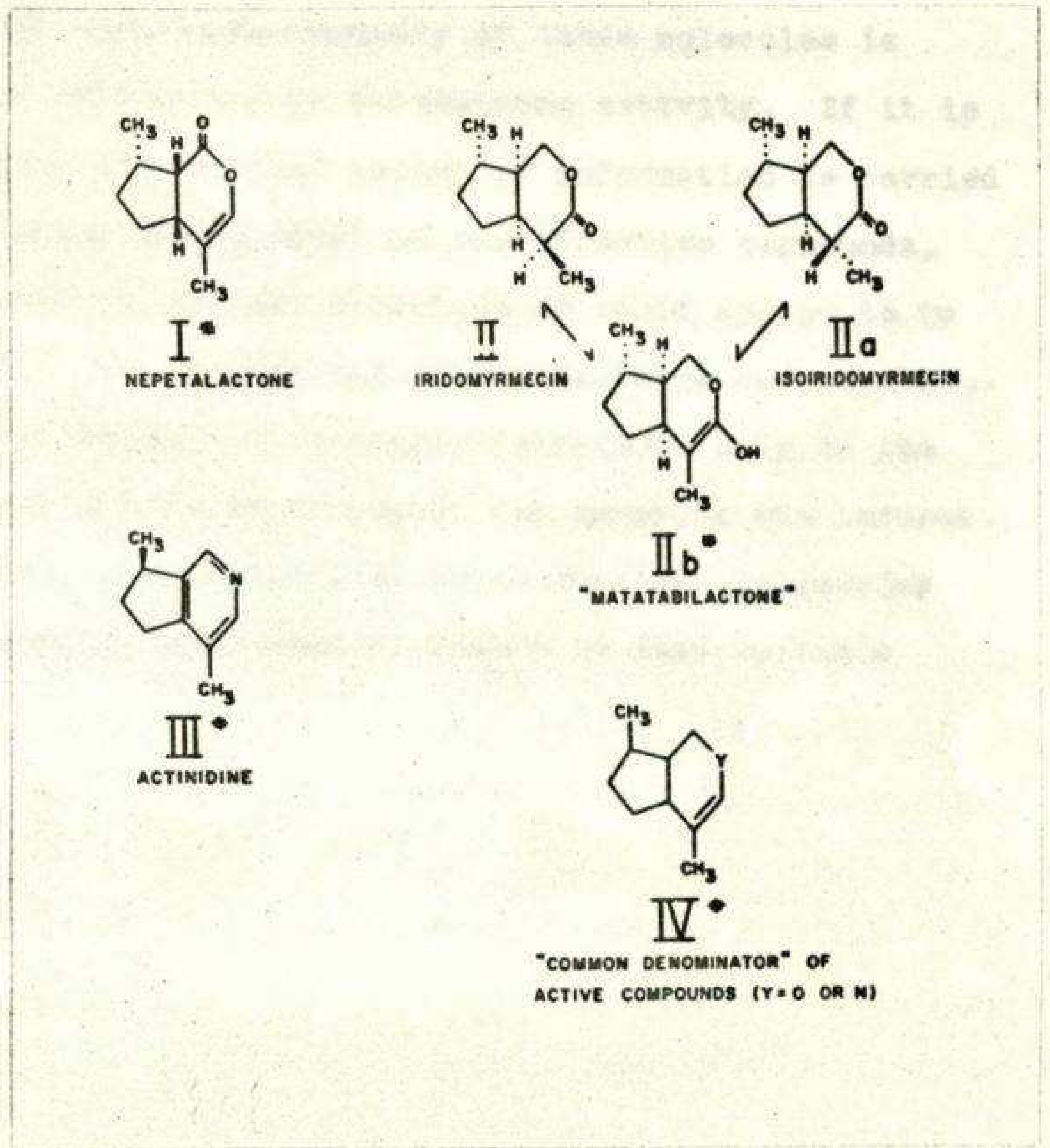

I*
NEPETALACTONE
II
IRIDOMYRMECIN
IIa
ISOIRIDOMYRMECIN
IIb*
"MATATABILACTONE"
III*
ACTINIDINE
IV*
"COMMON DENOMINATOR" OF ACTIVE COMPOUNDS (Y=O OR N)

ring juncture of these compounds can be either of two possible cis configurations or planar, and the asymmetric methyl group of the cyclopentane ring can vary, it would appear that the stereochemistry of these molecules is relatively unimportant in determining activity. If it is assumed that the critical amount of information is carried by the "common denominator" of the effective compounds, then at most the partial structure IV would appear to be sufficient. The unspecified stereochemistry and substituents of the molecule(s) probably contribute only to the extent that it acts as a vehicle for carrying the information portion, i.e. determines those physical properties of the molecule which make it a more or less suitable odorant.

Chapter 1. Inheritance of the Catnip Response in Domestic Cats

A. Introduction

Since cats were divisible into two groups according to whether or not they responded to catnip it was deemed important to determine as soon as possible if any genetic basis for this difference could be discovered. This not only appeared to be a simple approach under the circumstances, but also it was apparent that such knowledge would greatly facilitate further study by bringing one important variable more or less under control.

In the present consideration the response has been broken down into the four components 1) sniffing, 2) licking and chewing with head shaking, 3) chin and cheek rubbing and 4) head-over roll and body rubbing. As previously mentioned these components almost invariably appear in the above sequence. In fact, among 58 responding cats, only three individuals deviated from this sequence and omitted the licking and chewing with head shaking. These animals went immediately into the rolling phase. Among responding animals the response may be inhibited for various reasons, necessitating repeated testing of non-responders before any conclusion may be drawn as to their status. Also, the response is not manifested in kittens under six to eight weeks of age and may not develop fully until three or more months of age.

B. Methods

The first step taken in this investigation was to tabulate responders and non-responders among the related cats in the colony and to extend the pedigree to include animals outside the colony which were occasionally used as studs. In this instance it was possible to gather information on many other animals sired by these studs since they were Siamese cats mated under strict supervision.* It was from this pedigree (Figure 3) that the genetic basis was originally determined, but further crosses of both related and unrelated cats have confirmed the initial conclusions. As yet there is insufficient data for a statistical analysis.

Administration of catnip has usually been effected by presenting dried leaves to the cat. Some animals were tested with nepetalactone-containing atmospheres in an olfactometer, the details of which will be reported more fully below (Chapter 2).

C. Results and Discussion

From the pedigree, the significant crosses will be seen to be those of animals No. 1 X No. 4 and No. 8 X No. 9. In both cases two responders produced a non-responder, indicating a dominant factor controlling the

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* I am indebted to Mrs. Carl F. Muckenhoupt of Newton Highlands, Massachusetts, for her invaluable assistance in procuring information, testing many cats and permitting the use of her animals for stud service.

Figure 3. Pedigree of the catnip response. Solid forms represent catnip sensitive cats, open forms non-sensitive cats and question marks sensitivity of cats not tested. Squares indicate males, circles indicate females. See text for discussion of numbered individuals.

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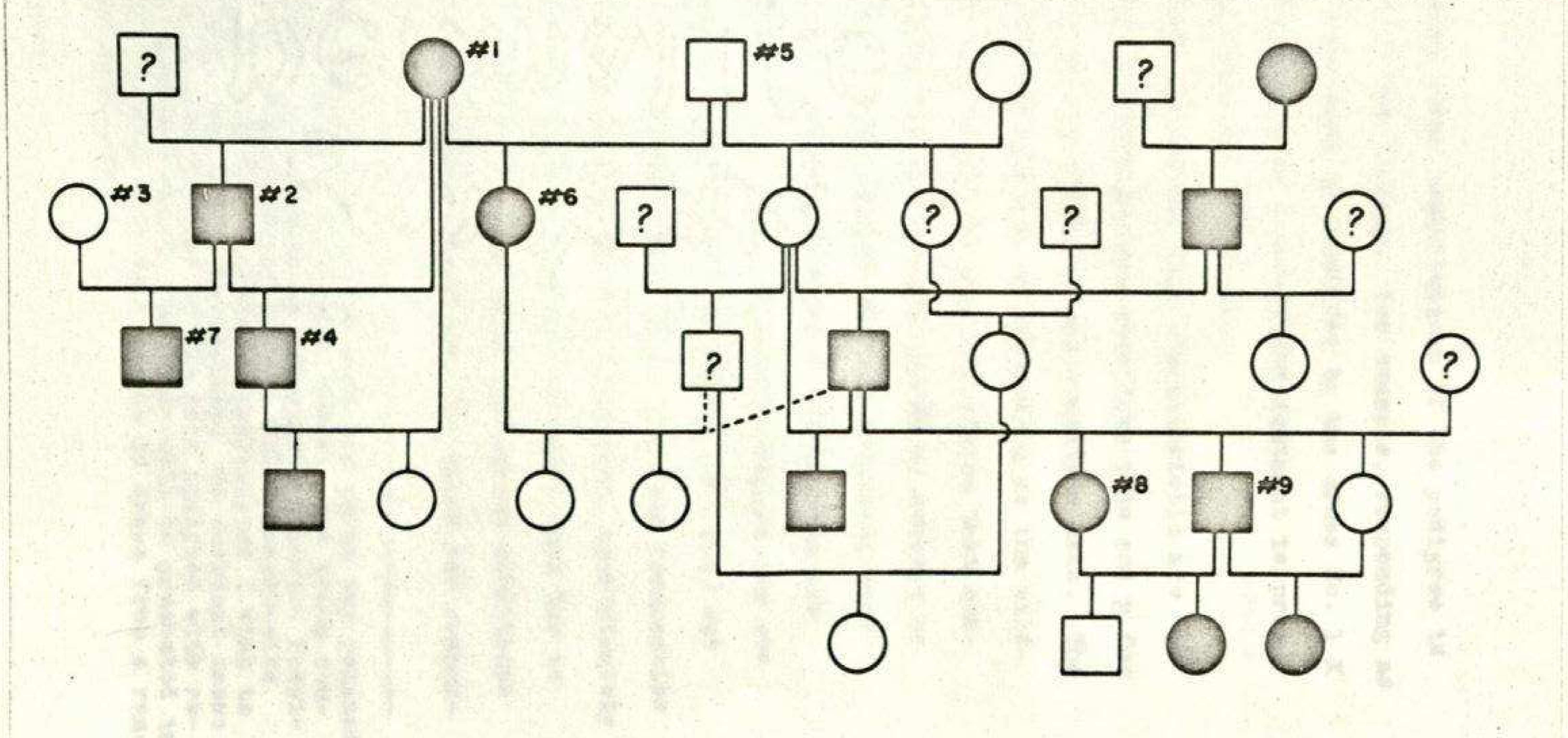

response. Among other contributions of the pedigree is the exclusion of sex linkage. For example, responding as a sex-linked recessive is precluded by the cross No. 1 X No. 5, and responding as a sex-linked dominant is precluded by the cross No. 3 X No. 2.

The symbols chosen for this characteristic are $+^{\underline{n}}$ for responders or nepetalactone-sensitive cats and n for non-responders or non-nepetalactone-sensitive cats. The rather arbitrary designation of responding as the wild-type is based principally on the supposition that non-responding is the absence of some undefined sensory or neural function. With respect to gene frequency some introductory work has been started.* These data are summarized in Table 1. The combination frequencies are approximately .69 (58/84) for responders ($p^2 + 2pq$) and .31 (26/84) for non-responders (q^2). The gene frequencies calculated from these figures are, therefore, approximately .45 ($p\,+^{\underline{n}}$) and .55 ($q\underline{n}$). It should be noted that due to an inability to test all cats under equivalent conditions and to repeat the testing procedure, the value for respon-

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* The animals used in this survey work are in no way related to those in the pedigree discussion above. The group consisted of strays, etc. housed at the Angell Memorial Hospital, M.S.P.C.A., Animal Rescue League, and Massachusetts General Hospital, Boston, to which organizations I wish to express my thanks for their cooperation. No surgical cases or diseased cats are included in the data analyzed with respect to the catnip response. Evidence will be presented in a future paper to show that this sample is drawn from a random breeding population.

Maximum stage of response	Females	Males	Totals
Sniffing	5	3	8
Licking and chewing	13 (2)	18 (1)	31
Chin and cheek rubbing	1	0	1
Head-over roll, etc.	7*	11 (1)	18
Total responders	26	32	58
Non-responders	15 (1)	11 (2)	26
Totals	41 (3)	43 (4)	84

* Three animals from this group omitted licking and chewing.

Table 1. Response category distribution in 84 cats tested with catnip. Bracketed figures indicate the number of castrated animals included in the figure preceding the brackets.

ders must be taken as a minimum. It is tentatively assumed that some partial responses are due to various inhibiting factors resulting from the temporary and recent caging of these animals in strange surroundings and in the vicinity of strange cats.

The eight animals grouped under sniffing (Table 1) are considered responders on the basis of the rather compulsive and prolonged sniffing which they displayed. In testing a number of cats with tea leaves no extensive sniffing was observed. Further work is necessary to clarify the rather unusual observation that only a single cat which failed to give a total response did manifest chin and cheek rubbing. There appear to be two classes of responders (Figure 4), partial (low intensity) and total (high intensity), but it is impossible to separate a possible genetic basis for this from environmental factors without a uniform testing situation. With the exception of the three individuals noted, all cats passed through the stages preceding their maximum stage of response. The degree of responding does not correlate with the homozygous and heterozygous condition as judged from the pedigree since heterozygotes, No. 6 and No. 7, gave total responses. Thus, polygenic modifiers may be indicated, i.e. expressivity. Expressivity occurs when other loci modify the action of a gene in a non-epistatic manner. The present data do not warrant any conclusions as to the degree of penetrance.

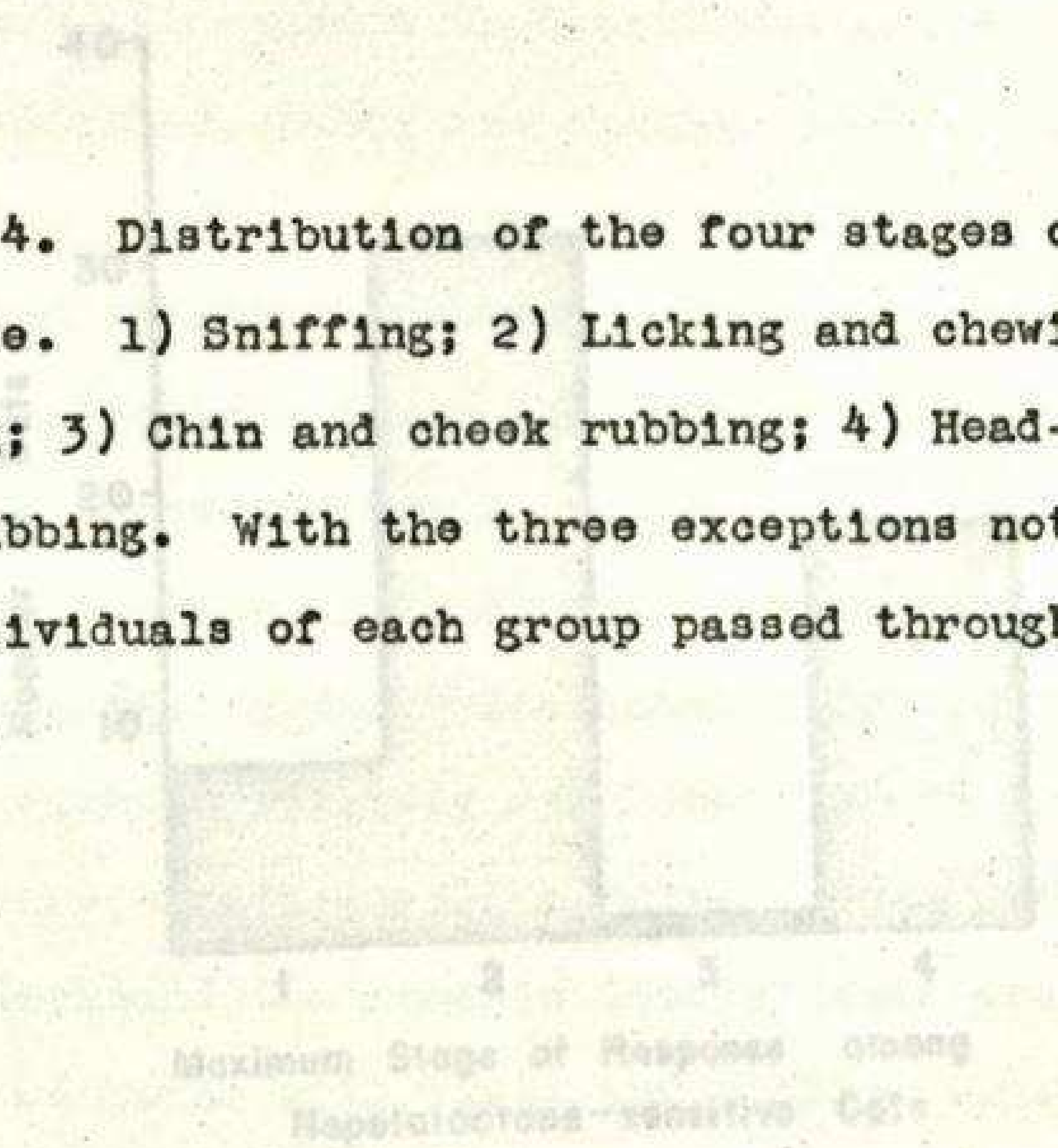

Figure 4. Distribution of the four stages of the catnip response. 1) Sniffing; 2) Licking and chewing with head shaking; 3) Chin and cheek rubbing; 4) Head-over roll and body rubbing. With the three exceptions noted in the text, the individuals of each group passed through the preceding stages.

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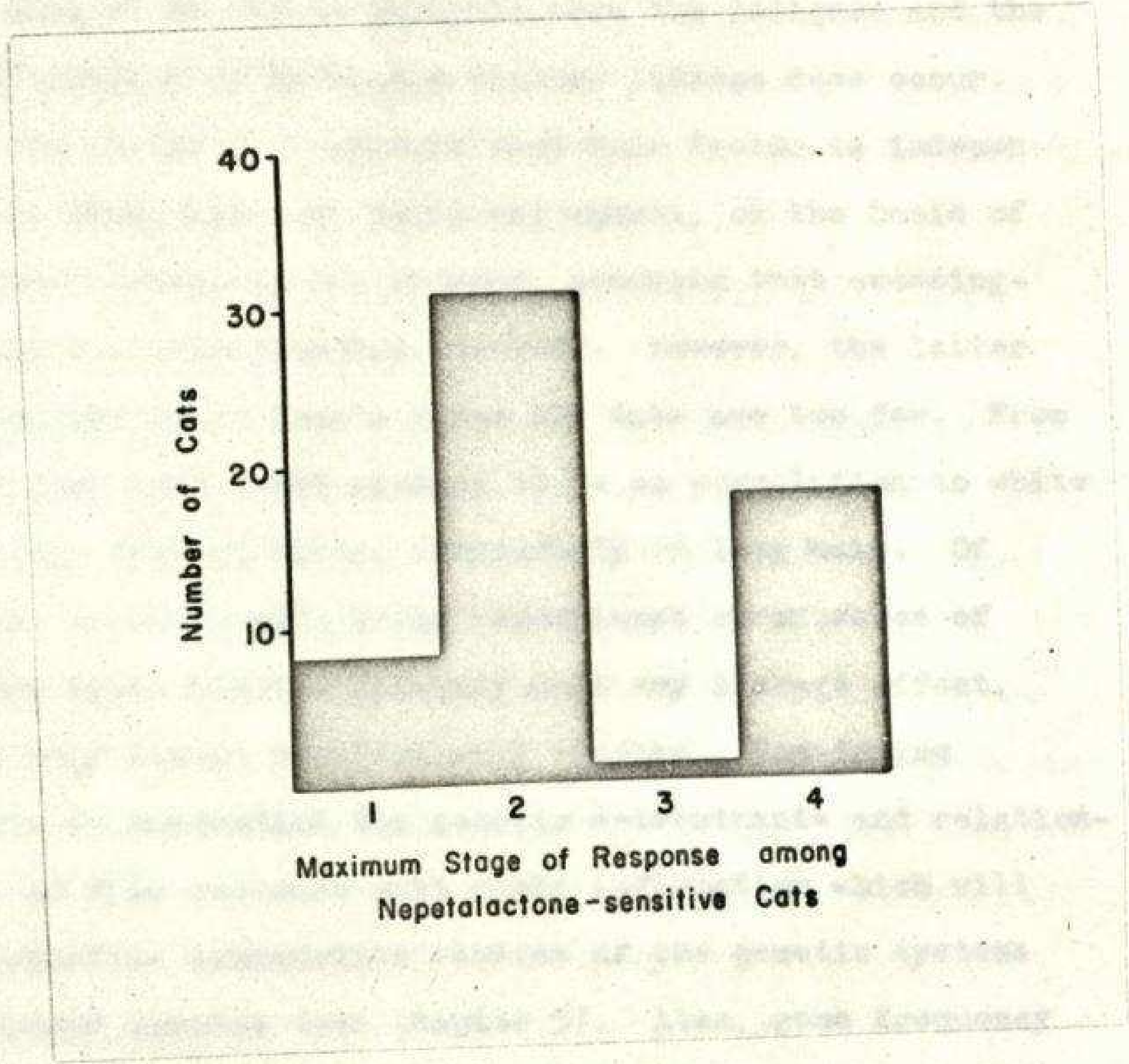


There is no significant differance between males and females as determined by a χ^2 homogeneity test ($\chi^2 = 1.18$, $P =$ ca. .70).

Finally, the behavior of the alternatives $+^{n}$ and n with respect to several other known loci in the cat has been studied as far as possible from the pedigree and the survey animals to determine whether linkage does occur. From the pedigree it appears that this factor is independent of Manx, Siamese, tabby and agouti, on the basis of its distribution in the progeny, assuming that crossing-over is not significantly involved. However, the latter possibility still exists since the data are too few. From the survey cats there appears to be no correlation to white spotting, blue dilution, polydactyly or long hair. Of course, in this small group recombinant chromosomes of various types might completely mask any linkage effect, which only future breeding will resolve. Continuing efforts to understand the genetic determinants and relationships of this response will yield information which will make possible comparative studies of the genetic systems in related species (see Chapter 5). Also, gene frequency studies on different populations of domestic cats should produce data which have a bearing on the adaptive significance of the characteristic.

Chapter 2. Behavioral Aspects of the Catnip Response

A. Introduction

A general description of the catnip response was given in the introduction to this work. It will be the purpose of this chapter to expand this description and to consider such matters as the ontogeny and stability of the response and to describe experiments which differentiate between sensory and central aspects of the response.

B. Observations on Catnip-like Responses and Courtship Display

Extensive personal observations of both catnip responding and courting cats have revealed the striking similarity of parts of these two behavior patterns. The chin and cheek rubbing, head-over roll and body rubbing components of the catnip response are virtually identical to certain courtship patterns of the estrus female (descriptions of which may be found in Green, et. al., 1951; Leyhausen, 1960; Michael, 1961) although posturing (lordosis), treading and tail deviation never occur and vocalization occurs only rarely. The proestrus or estrus female will interrupt a period of quiescence with a sudden alerting reaction. This is then often followed by what might be fairly described as a "vacuum catnip response." That is, the female commences to rub her chin and cheek on any available object and to turn her head over and roll (Figure 5).

These actions may be punctuated with occasional grooming activity. If these displays do not succeed in attracting a tomcat they give way to more intense courtship patterns such as vigorous and loud vocalization.

The tomcat is persistent and aggressive, but ordinarily quite gentle, in his courtship of the female. He will as a rule sit in an upright position a few feet from the female and observe her display. He will make attempts to secure a neck-bite and mount the female when in the course of her rolling she presents herself in an advantageous position. If mounting is tolerated by the female and copulation occurs, the tomcat will do little more than sit around waiting for every opportunity to remate. If, however, the female continuously rejects the male while she persists in her display, he will commence to display in a similar manner. This appears to excite the female and she often approaches the male and commences rubbing against him or rolling beside him. Leyhausen (1960) describes the chin and cheek rubbing of the sexually aroused male (Figure 6). Finally, personal observations suggest that this display of the male may be used as a general advertisement of his willingness to mate and that the proximity of an estrus female is not necessary to provoke it. This conclusion was reached when it was noted that a tomcat which had established his territory in a residential neighborhood, often gave this display at points which he marked with his urine. He was

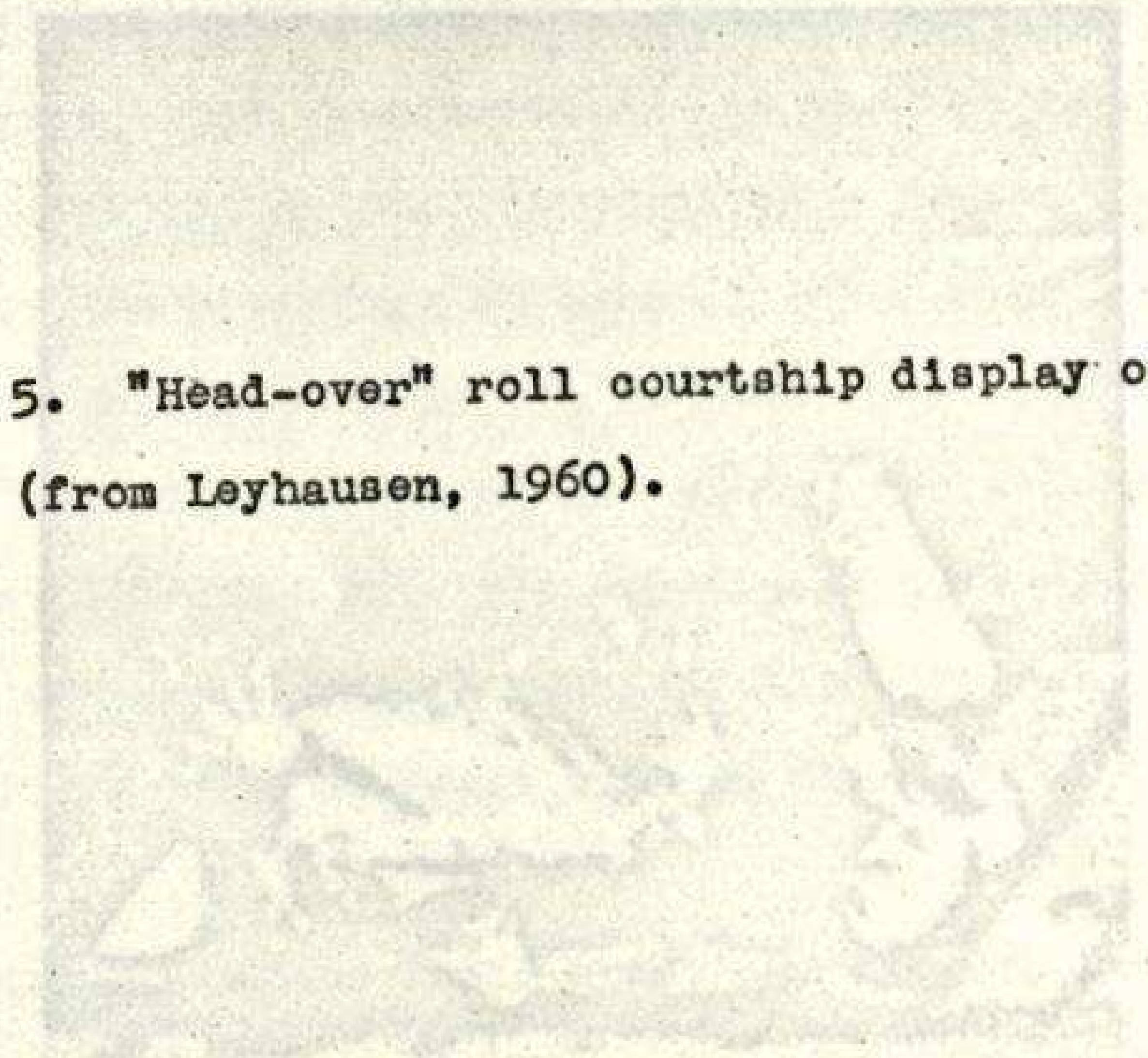


Figure 5. "Head-over" roll courtship display of an estrus female (from Leyhausen, 1960).

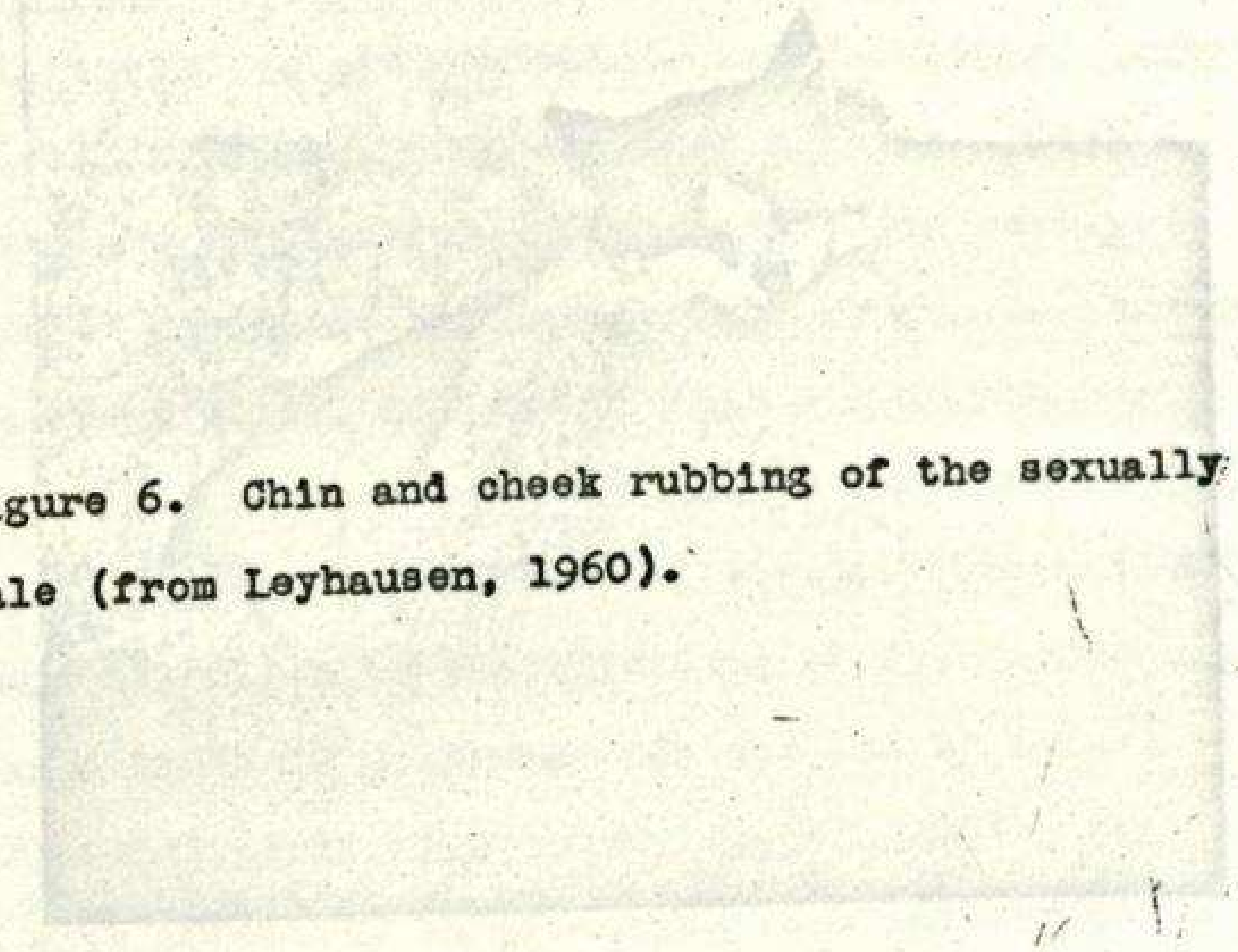
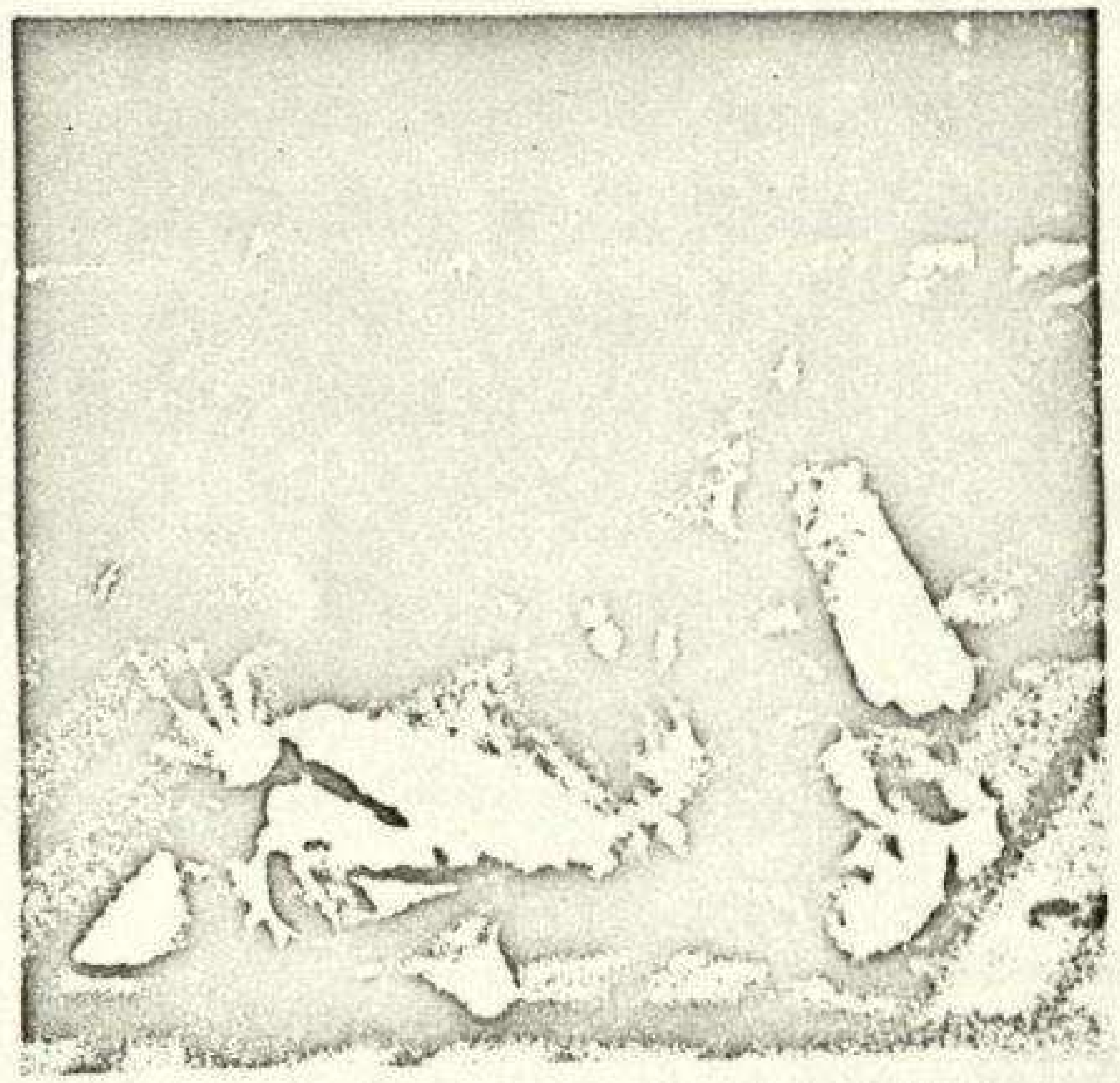


Figure 6. Chin and cheek rubbing of the sexually aroused male (from Leyhausen, 1960).



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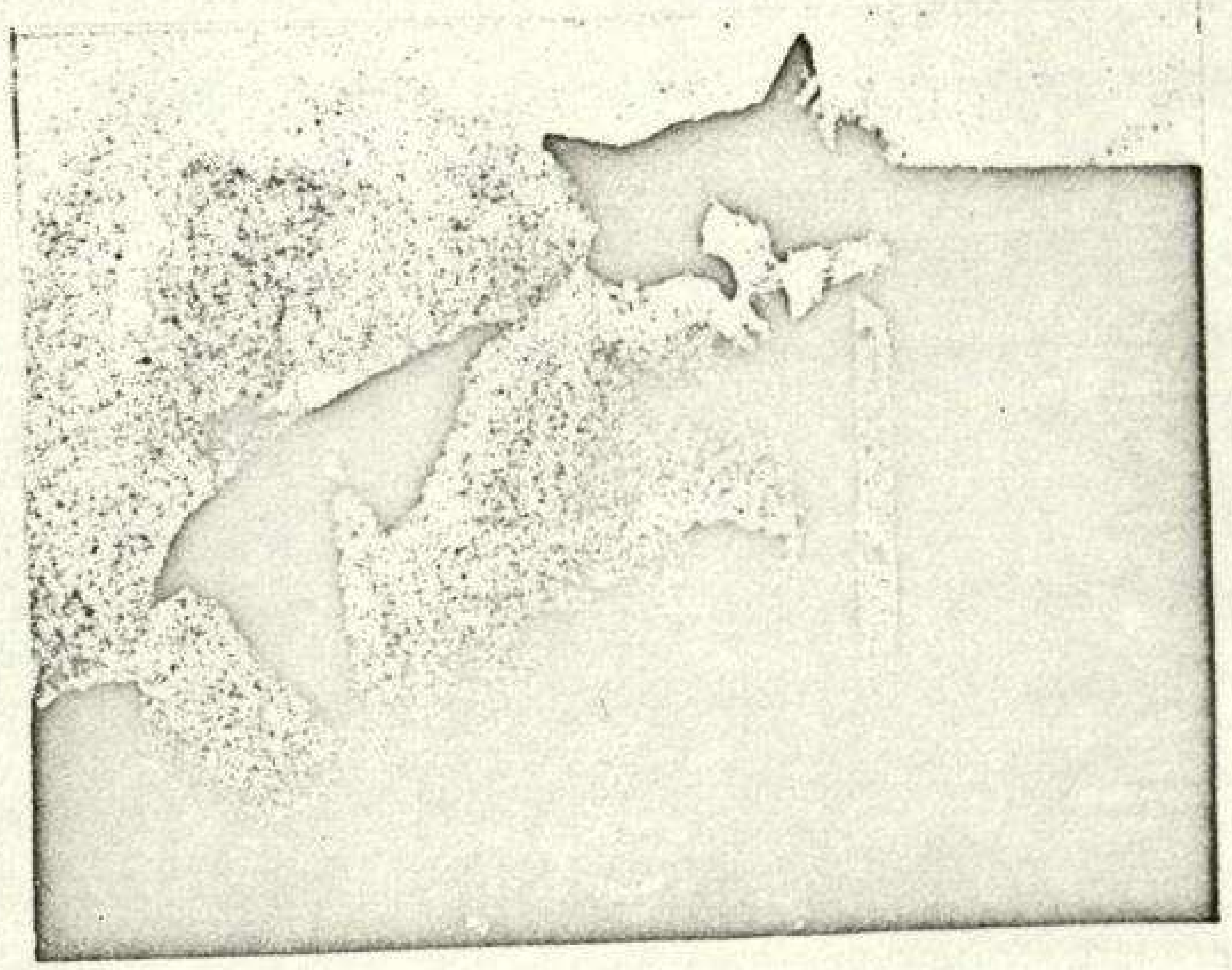
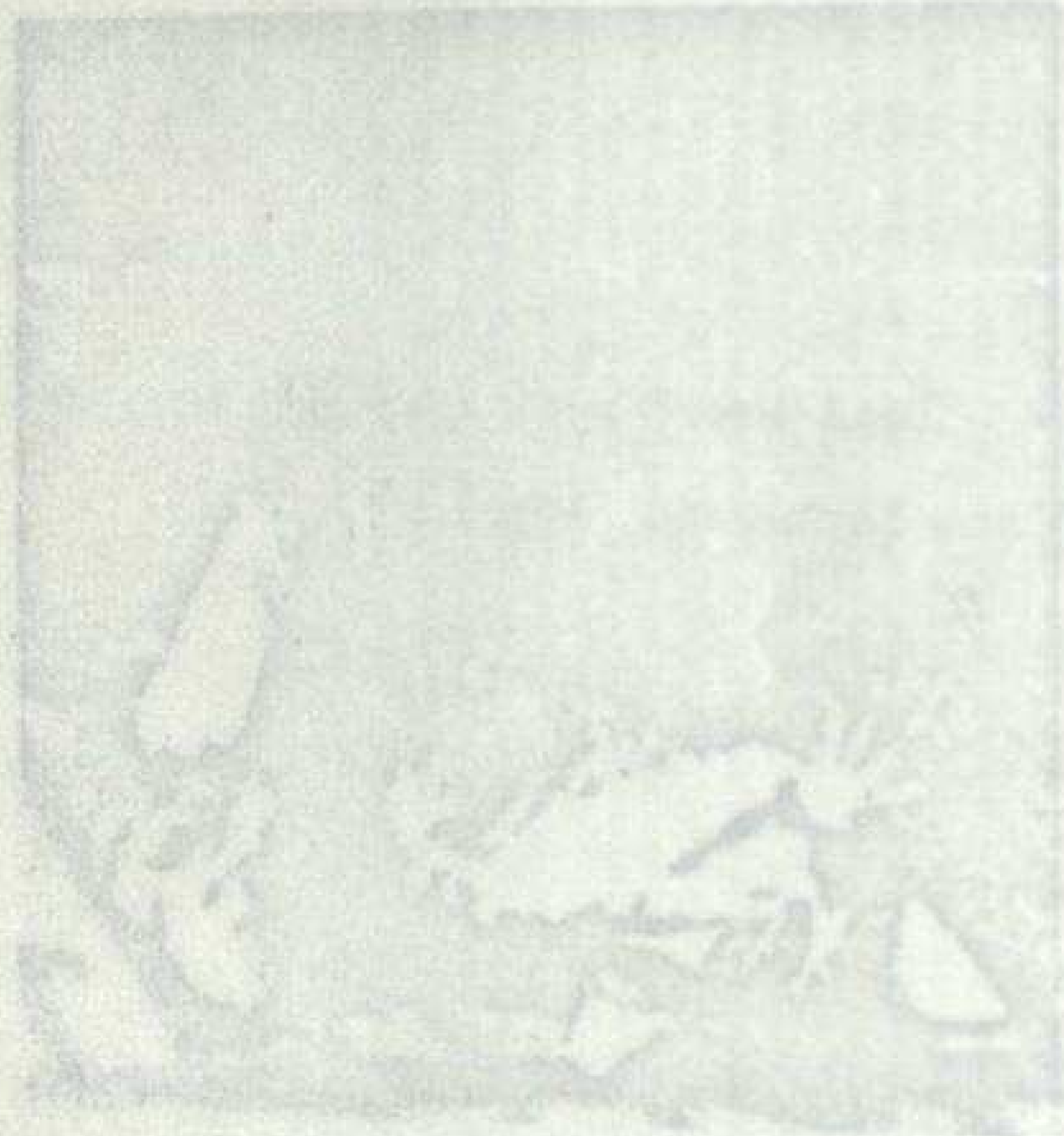


ly aroused



seen on numerous occasions to give a "vacuum catnip response" at a given spot on a sidewalk and then to spray a nearby bush with his urine. He would then depart this area and repeat the procedure at several other places in his territory. Female cats in the neighborhood would locate these "advertising sites" and often give catnip-like responses at them. This was especially true if the female was in estrus. Further considerations related to these observations will be dealt with in Chapter 3.

C. Ontogeny

Young kittens, before their eyes have opened, invariably spit and withdraw from catnip. However, the same response is noted upon the presentation of many strange olfactory stimuli. More important is the fact that a kitten of several weeks of age shows an even more pronounced withdrawal, including eye squinting, ear flattening, spitting and occasionally piloerection and back arching. Such a reaction appears to diminish in intensity upon repeated presentation. These are similar to fear responses (Leyhausen, 1960), but importantly, kittens of this age do not react in this way to other strange odorants unless they are obviously noxious (e.g. ammonia, formaldehyde, etc.). Thorpe (1958) devotes some attention to the eliciting of fear responses by familiar stimuli in a strange context and by normal stimuli of inordinately high intensity, concluding that these are more effective in provoking fear and avoidance than completely alien stimuli regardless of intensity. Arguing backwards, it might be suggested that catnip simulates some familiar stimulus in a strange context and/or at an unusually high intensity (see the response of tiger cubs described in Chapter 5). It should be mentioned that an occasional adult cat shows typical avoidance-withdrawal reactions to catnip. Those animals which are genetically destined to become responders show a heightened curiosity towards catnip while those that are genetically non-responders become indifferent to it. The fact that all kittens show a fear-avoidance response which can be attributed to catnip although as adults they may or may not be responders, suggests that the genetic difference between responders and non-responders is not due to a sensory difference. However, there is conflicting evidence on this point which will be discussed below. Finally, of 39 kittens under twelve weeks of age, only four gave total responses to catnip. The youngest of these was between six and seven weeks old.* It is not uncommon for the first response (aside from fear-avoidance) to appear as late as four months of age.

D. Stability

Even while obviously distraught or ill cats may give

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* These figures have little statistical meaning since it is impossible to distinguish at this age between genetic non-responders and those animals which fail to respond because of maturational factors.

a high intensity response, others tested on several occasions have shown considerable instability. These latter animals were all housed under sub-optimal conditions and the instability may have been due in most cases to upper respiratory infections which were endemic in this particular research colony. A few selected individuals that have been maintained for periods of one to ten years under "optimal" conditions are probably the most indicative.

A Manx female (No. 1)* which has been used as a breeder for nine years has never failed to give a high intensity response. Although the presentation of catnip to her has been for the most part on a very irregular basis, probably in excess of 100 responses have been observed. She has been maintained under a variety of conditions ranging from a private home to a small laboratory breeding colony. The same was true for a 5 year old son (No. 4) of this cat which on one occasion for a period of several weeks was tested almost daily and not infrequently more than once a day. This particular cat, although he was severely ill with chronic uremia, gave a full intensity response one hour preceding his death. Another son, three years old, also gives a response every time he is tested. An intimate knowledge of the above cats, and others which have been kept under both laboratory and domestic conditions indicates

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* These numbers refer to those in Figure 3.

that the response of an individual may be very stable or predictable. Under more adverse conditions such as those often found in animal shelters and research colonies, responses may be erratic for a number of reasons. Among these reasons emotional state appears to be important.

Castration appears to have no effect upon the response. Two out of three castrated males and two out of three spayed females* have been observed to respond. An additional male which was castrated at about four years of age continued to respond with no detectable change for more than a year postoperatively.

A female which had been characterized as a non-responder since her only reaction to catnip for two years was one of indifference, suddenly gave a high intensity response. This was first noted in the seventh week of gestation and persisted into the third week of lactation, although becoming reduced to low intensity. By the sixth week of lactation it had virtually disappeared. She again showed a low intensity response during a subsequent estrus. A second animal characterized as a non-responder for about ten months, during which time she was frequently offered catnip, also gave a sudden high intensity response. This lasted for a few days

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* In the case of females it is often difficult without autopsy to determine whether the animals have been spayed. It was impossible or undesirable to perform such autopsies in connection with the routine screening of cats for responses.

during which she was suspected of being in mild estrus. She then reverted to a refractory attitude toward catnip.

While the effect of castration seems to indicate that no hormonal influence is involved, these last two cases are contrary to this interpretation. Chapter 3 deals with attempts to resolve this conflict.

E. Experiments Differentiating Sensory and Central Components of the Response

A complete catnip response seldom lasts more than 15 minutes and usually considerably less time. Apparently the animal is satiated at the end of this time for another response cannot be evoked for at least an hour, perhaps longer. The response may apparently be extended by interrupting the reaction. For example, competing stimuli such as food, threat or sex may be used to divert the animal's attention in the midst of a response for some minutes, but approximately the same total time is spent in actual response. Such an effect may be due to an interruption of the olfactory fatigue process. No experiments have been conducted under circumstances where this possibility has been eliminated, (*viz.* in a uniform nepetalactone-containing atmosphere).

One of the first questions to be asked concerned the way in which nepetalactone induced a response. The facts that intensive sniffing often preceded the response and that respiratory infections interfered with it or abolished it, suggested that it was mediated through an olfactory input. To test this hypothesis, topical xylocain (2%) was sprayed and swabbed into the nostrils of several cats. The result in all instances was an abolition of the response. To control for the distress caused to the cats by this procedure, a few individuals were treated similarly with a physiological saline solution. In some cases an animal served as its own control on alternate days. The controls responded normally in most cases. Finally, bilateral lesion of the olfactory tracts of one cat which produced complete anosmia eliminated the response. This individual had lesions elsewhere, the olfactory tracts being unintentionally involved. This animal (I/4) is described in more detail in Chapter 4 as are similar operations not resulting in olfactory tract lesions which do not interfere with the response. The evidence seems to be strongly suggestive that the response is mediated by impulses induced in the primary olfactory neurons by nepetalactone by whatever membrane phenomena are involved in olfaction.

Among the more interesting aspects of the study of the catnip response was the demonstration of a central component and the ease with which it can be distinguished from sensory components.

An olfactometer (Figure 7) was employed for these tests. This device consists of a polyethylene bag on an aluminum frame producing a chamber into which odorants can be introduced. Two sources of purified filtered air, one of which is passed through a solution of catnip tea, can be independently controlled with respect to flow rate. This control, coupled with dilutions of the tea, allowed a wide range of concentrations to be effected. The standard air source is from the compressed air line. This is passed through an oil, moisture and dust trap, a flow meter, and an activated charcoal filter and flow equilizer. The test air source is from a tank supply and is also passed through a flow meter and activated charcoal filter and flow equilizer. This is then passed through a sintered glass filter submerged in the catnip solution in an Erlenmeyer flask. A second flask serves as a trap. A straight condensing tube is used as a primary mixing chamber and a second baffled condensing tube as a final mixing chamber. The tea is prepared by steeping catnip leaves for 15 minutes in boiled distilled water and then filtering. 20 grams of leaves in a liter of water was used as a standard solution. A good responder reacts to the atmospheric concentration produced by bubbling air through this solution at a 1 to 10 ratio with standard air. No attempt has been made to determine the absolute concentration being delivered at this rate but this has been roughly estimated at nne part nepetalactone in 10^{9}-10^{11} parts of air.

An atmosphere of nepetalactone which consistently elicits a response in a given cat was designated concentration A for that individual. If a cat was put in a restraining tube (Figure 8) and placed in the olfactometer at its concentration A for 15-20 minutes and then released in the olfactometer, no response followed. The test air flow rate was then increased and, if necessary, the standard air flow rate reduced until a concentration, B, was found at which response occurred. In some cases it was necessary to give the cat an impregnated object or leaves to reach this threshold concentration. If the subject was tested in the olfactometer at concentration A and allowed to respond and terminate its response, no concentration B could be found which would induce further reaction. This phenomenon was observed in 20 out of 26 tests, employing seven animals, all of which were high intensity responding males. One animal, used in 5 of the 20 successful tests, was especially consistent. His concentration A was reached by delivering test air at 1 liter/min. with standard air at 10 liters/min. (1:10). His concentration B was reached at approximately a 1:1 ratio of test and standard air. The other animals were less consistent and usually required a higher test air concentration to reach their concentration B. This ranged from 2:1 to pure test air at 10 liters/min., or the presence of dried leaves or an object impregnated with catnip tea.

The interpretation of these findings is that under the first set of conditions (restrained) olfactory adaptation has occurred and that this is overcome by increasing the catnip concentration. Under the second set of conditions, both olfactory adaptation and some "central specific fatigue" (in the ethological sense) leading to inhibition of the catnip response has occurred. In this case an increase in concentration is ineffective in inducing a response. The most frequent cause of unsuccessful tests appears to have been the failure to olfactorily adapt the restrained subject with the result that a response (often weak) was given upon release. A second cause of failure was the inability to elicit a response in a subject after release from restraint, presumably because no concentration could be found which would overcome olfactory adaptation. It must be borne in mind that olfactory adaptation is not equivalent to sensory fatigue (Adrian, 1953; Hainer, _et_. _al_., 1954; Moncrieff, 1956), but is a central phenomenon which occurs at some as yet unidentified higher level. The locus of the specific catnip fatigue may involve a neural system which is at a phylogenetically higher or lower anatomical level, but is certainly later in the sequence of neural events. Therefore, it would appear that the catnip response is modulated by activity of the system involved in olfactory adaptation.

Figure 7. Schematic representation of the olfactometer: ac - air cylinder; al - air line; cfe - charcoal filter and flow equalizer; ct - catnip tea; ef - exhauset funnel; fm - flow meter; fmc - final mixing chamber; if - inlet funnel; odt - oil and dust trap; ot - overflow trap; pmc - primary mixing chamber; sgf - sintered glass filter; tc - test chamber.

Figure 8. Cat in restraining tube.

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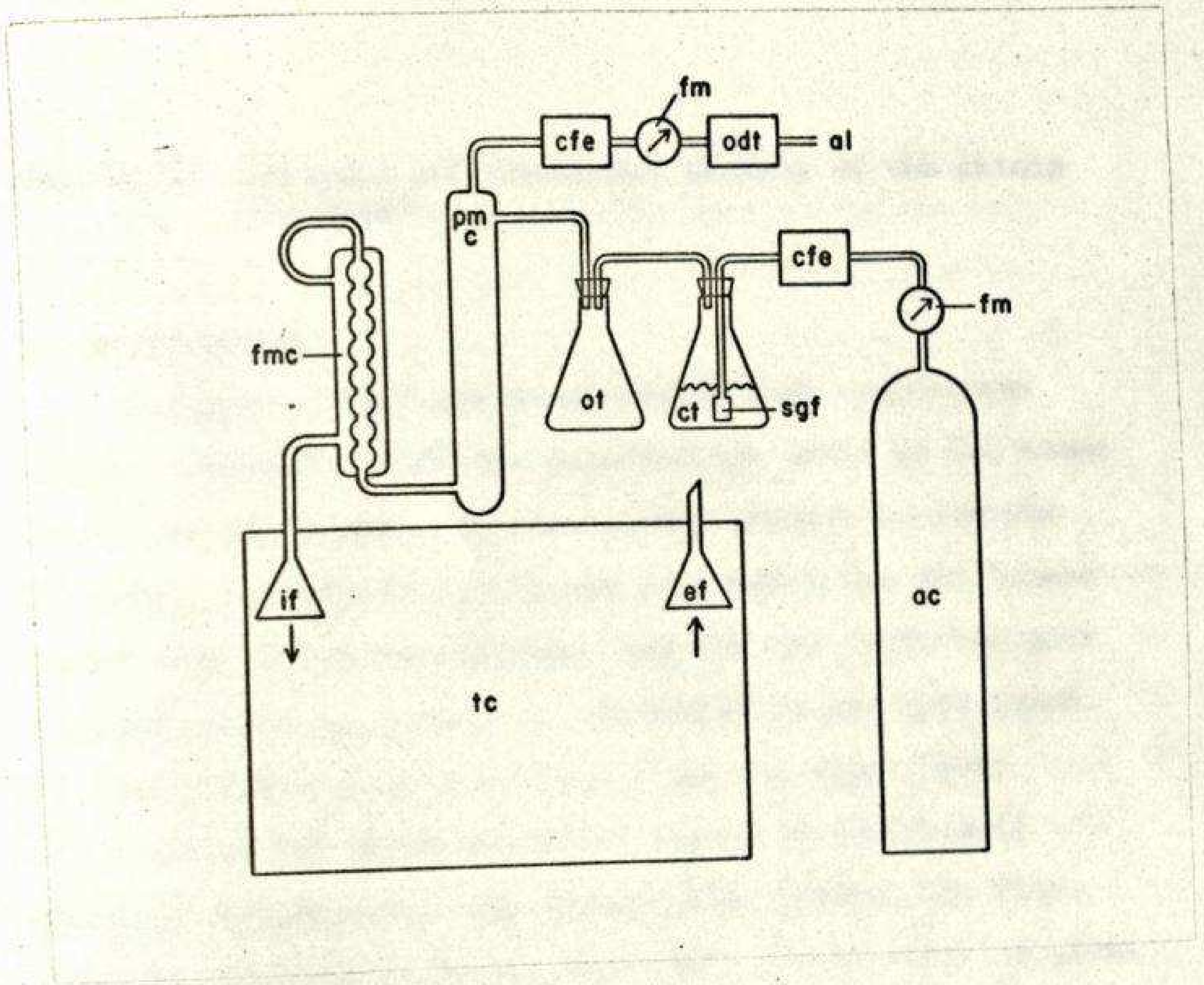

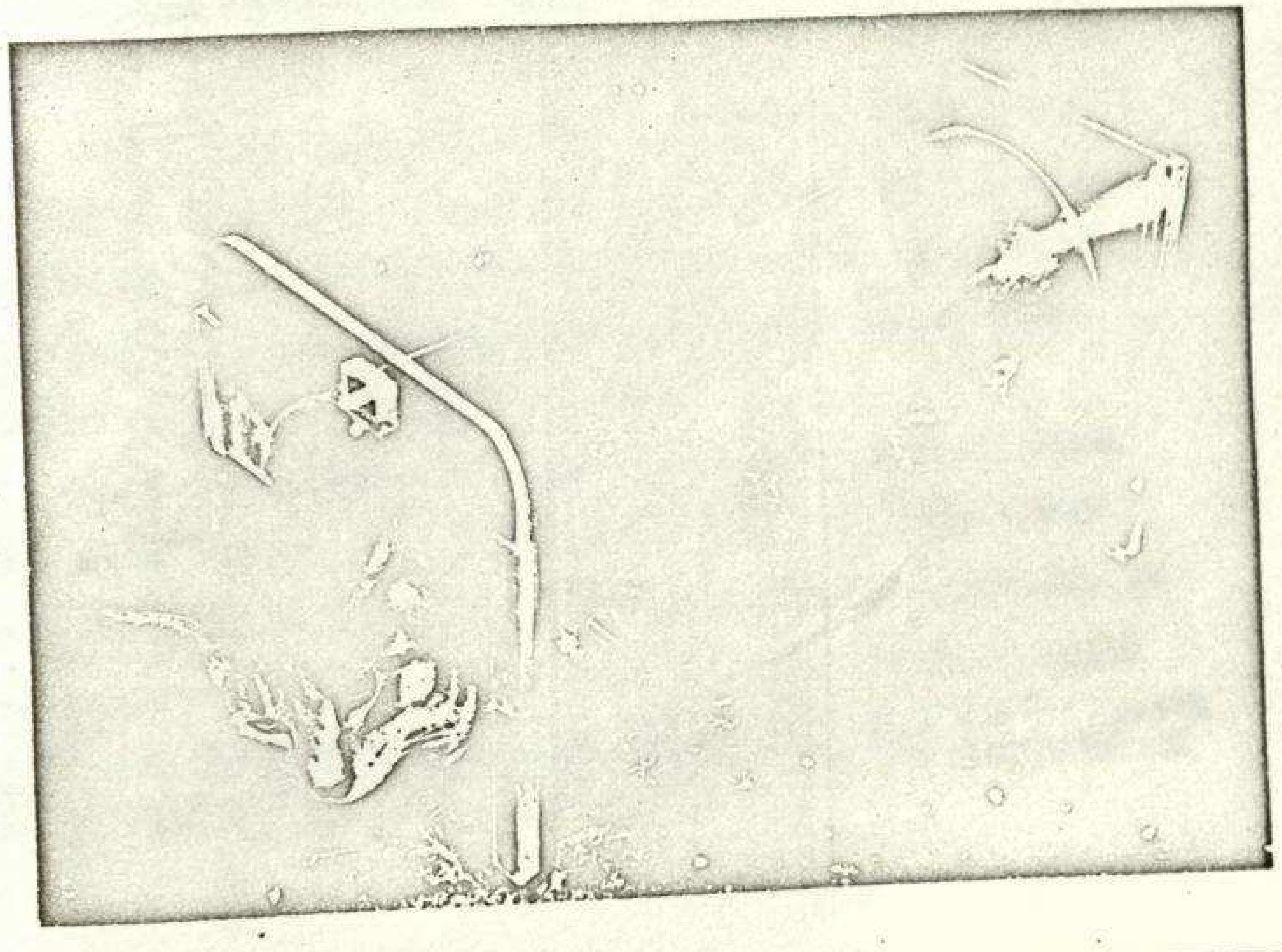

Chapter 3. Hormonal and Pheromonal Aspects of the Catnip Response*

A. Introduction

Le Magnen (1952) has demonstrated that spontaneous changes correlated with the reproductive cycle in the human female result in dramatic sensitivity changes to certain odorants. Specifically, changes were noted for the "stale urine" odor of certain steroids and for the synthetic musk exhaltolide (a C_{15} lactone). Threshold values were found to vary by as much as a million times for these odors while values for other molecules showed no significant increase or decrease. The relationship between the fluctuations and hormone levels were confirmed in cases of gonadectomy and replacement therapy. Greatest sensitivity was found to relate to high estrogen level.

The implication made from this work was that these changes represented some remnant of a primitive system of reproductive regulation which, because of the absence or repression of concomitant behavioral signs in the human female, would be difficult to study.

A hormonal influence upon the catnip response, which was suggested by preliminary observations of female cats during spontaneous estrus, indicated a possible parallel to

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* This investigation was supported in part by a Public Health Service fellowship (number MPM 18,520) from the Institute of Mental Health, Public Health Service.

the situation found in man. This initiated the present effort to reproduce under controlled conditions the phenomena which had been observed in cats during spontaneous estrus. In addition a search for catnip-like activity in some compound produced by the cat was undertaken.

B. Methods

Six female cats were housed for the duration of these experiments with a tomcat in quarters adequate for normal reproductive activities. These quarters were well lighted and air-conditioned, the temperature being held at approximately 70° F. Two females shared a cage with a floor space of eight square feet and a head room of two feet. The male occupied a similar but somewhat larger cage by himself. In addition, each animal was allowed time to exercise freely in the room, usually alone, but sometimes in pairs. The females employed for this work were either non-responders, low intensity responders or high intensity responders with respect to catnip. Each was injected with hormones (estrogens, 1-2 mg., and/or gonadotropins, 100 International Units)* and subsequent behavioral changes followed and correlated with response towards catnip.

Evaluation of sexual receptivity was based principally upon the responses described by Michael (1961) under

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* Ovocyclin® (estradiol dipropionate) and Equinex® (pregnant mares' serum).

the categories 1) early proestrus, 2) late proestrus, 3) estrus, and 1 and 2) metestrus. In early proestrus the female cat will tolerate perineal tapping with a glass rod and deviate the tail. No lordosis can be provoked at this time and vaginal probing is firmly, but not violently rejected. In late proestrus perineal tapping causes a full postural response with lordosis and treading of the hind feet. Vaginal probing is tolerated but an after reaction cannot be induced as a rule. In estrus the cat responds much as in late proestrus, but with increased intensity. Vaginal probing rapidly elicits a strong after-reaction. Metestrus first resembles estrus but is distinguishable by the difficulty or impossibility of causing an after-reaction with vaginal probing. The signs of sexual receptivity gradually disappear until a state of anestrus is reached. Finally, 4) copulation with the tomcat was occasionally used as an index to verify estrus.

Response to catnip was graded according to the four categories 1) sniffing, 2) licking and chewing with head shaking, 3) chin and cheek rubbing, and 4) head-over roll and body rubbing. In all cases catnip was presented as dried leaves. Because these criteria represent two continuous spectra of behavior it has been necessary and possible to give intermediate gradations. Also, individual differences in the animals employed have been taken into account when these have been noted.

Concurrently with the above-mentioned experiments, urine from male, anestrus female, and estrus female cats was collected. This was extracted with ether, evaporated on filter paper, and bio-assayed for catnip-like activity with animals which had been observed extensively with respect to their behavior towards catnip.

C. Results

The injection of estrogen initiated a normal pattern of courtship and mating behavior (Leyhausen, 1960; Michael, 1961) except that the dosage given was calculated to produce a somewhat longer than normal estrus. In several cases courtship display was manifested continuously for 30 days following the initial injection.

In the following figures the intensities of the responses are graded according to the two sets of criteria outlined above. The open circles denote catnip response and the solid circles represent the state of sexual receptivity.

Figures 9 and 10 show the reactions of two non-responding female cats to estrogen treatment on two separate trials. One of these (VII/2) manifested complete indifference towards catnip prior to, during, and after hormone injection although her courtship display and mating behavior were normal on both occasions. The second female (VI/4) responded in virtually the same manner. The two questionable peaks in the catnip response curve result from ambiguity in differentiating spontaneous courtship display from

Figure 9. Sexual motivation (solid circles) and catnip response (open circles) curves of a non-responding adult female (VII/2) following estrogen injection. Vertical axis, intensity (see text, p. 22 ff); horizontal axis, time in days. E = estrogen injection.

Figure 10. Sexual motivation and catnip response curves of a non-responding adult female (VI/4) following estrogen injection. See legend of Figure 9 for explanation of graph.

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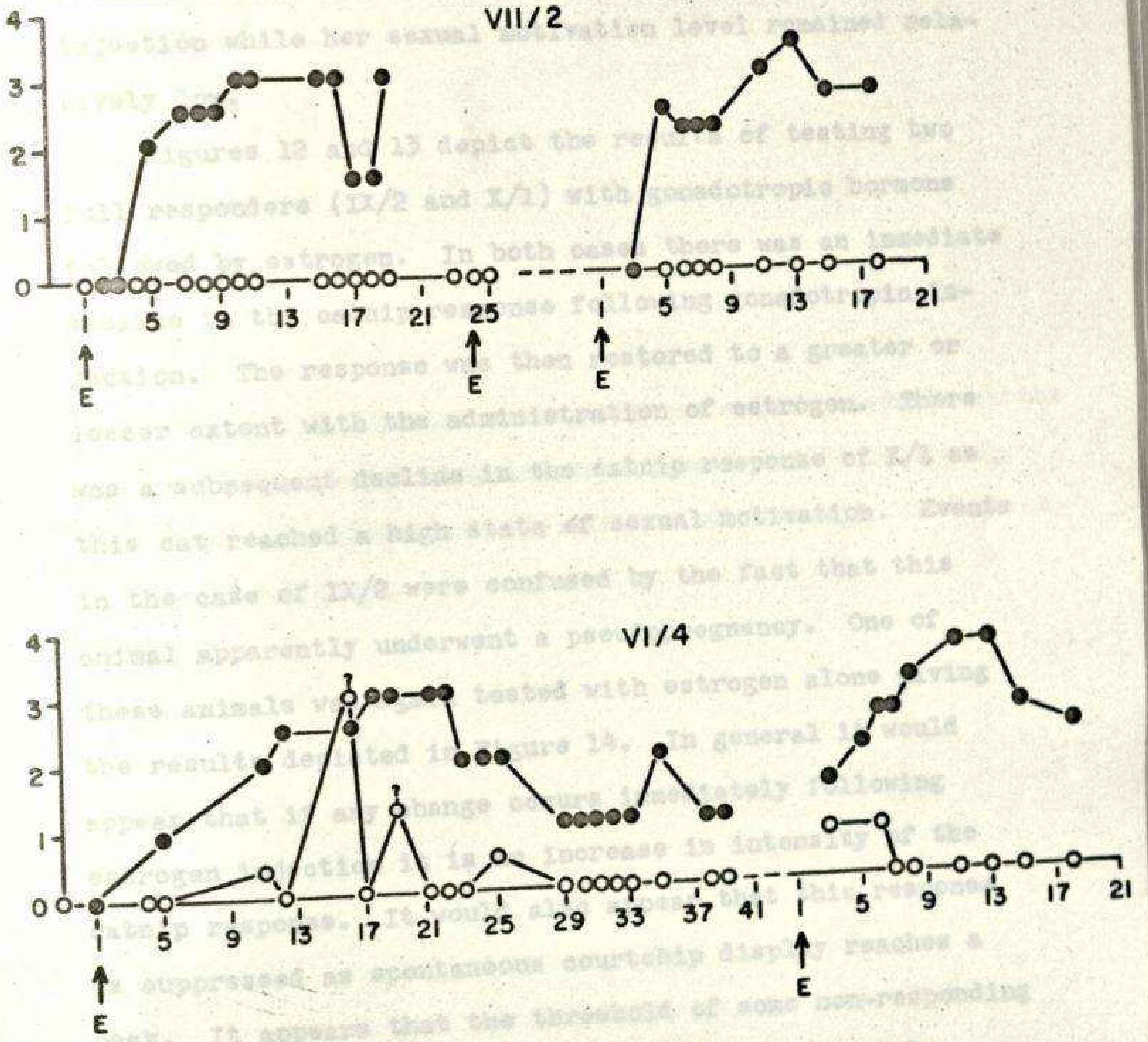
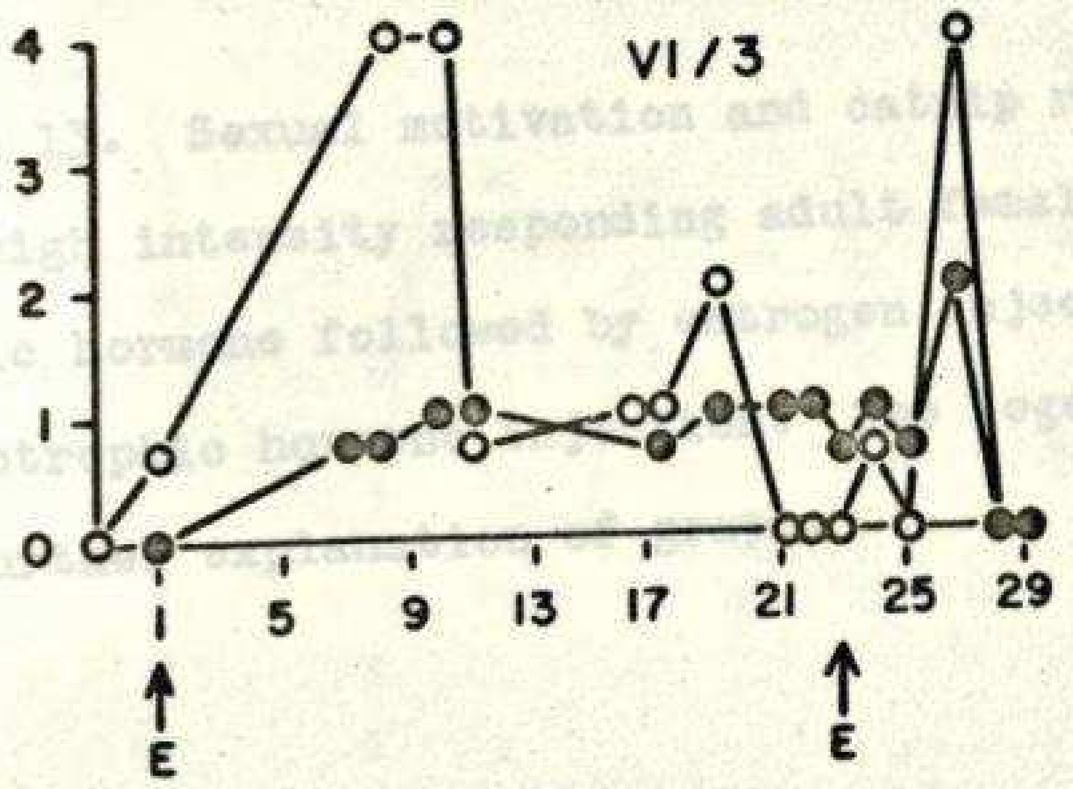


a catnip response.

Figure 11 shows the curve of a third non-responding female (VI/3) which was immature. This cat manifested dramatic changes in her catnip response following estrogen injection while her sexual motivation level remained relatively low.

Figures 12 and 13 depict the results of testing two full responders (IX/2 and X/1) with gonadotropic hormone followed by estrogen. In both cases there was an immediate decline in the catnip response following gonadotropin injection. The response was then restored to a greater or lesser extent with the administration of estrogen. There was a subsequent decline in the catnip response of X/1 as this cat reached a high state of sexual motivation. Events in the case of IX/2 were confused by the fact that this animal apparently underwent a pseudopregnancy. One of these animals was again tested with estrogen alone giving the results depicted in Figure 14. In general it would appear that if any change occurs immediately following estrogen injection it is an increase in intensity of the catnip response. It would also appear that this response is suppressed as spontaneous courtship display reaches a peak. It appears that the threshold of some non-responding females is genetically set at a level which cannot be reached by any known degree of stimulation. Furthermore, the threshold is not lowered sufficiently, if at all, by

Figure 11. Sexual motivation and catnip response curves of a non-responding immature female (VI/3) following estrogen injection. See legend of Figure 9 for explanation of graph.


VI/3
4
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25
29
E
E

Figure 12. Sexual motivation and catnip response curves of a high intensity responding adult female (IX/2) to gonadotrophic hormone followed by estrogen injection. GH =-gonadotrophic hormone injection. See legend of Figure 9 for further explanation of graph.

Figure 13. Sexual motivation and catnip response curves of a high intensity responding adult female (X/1) to gonadotrophic hormone followed by estrogen injection. GH - gonadotrophic hormone injection. See legend of Figure 9 for further explanation of graph.

Figure 14. Sexual motivation and catnip response curve of animal IX/2 on repeat test with estrogen injection alone. See legend of Figure 9 for explanation of graph.

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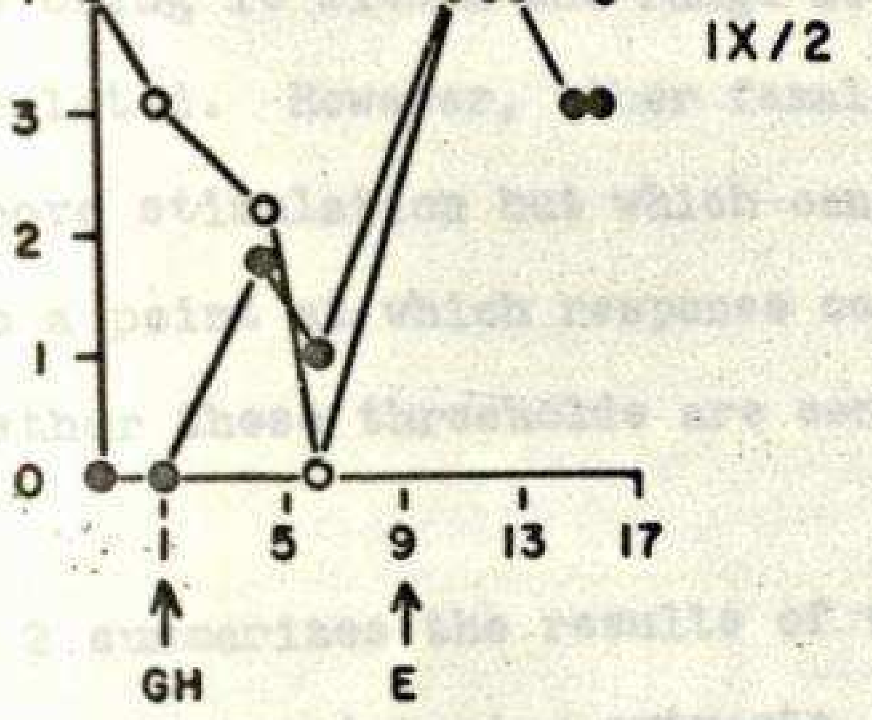

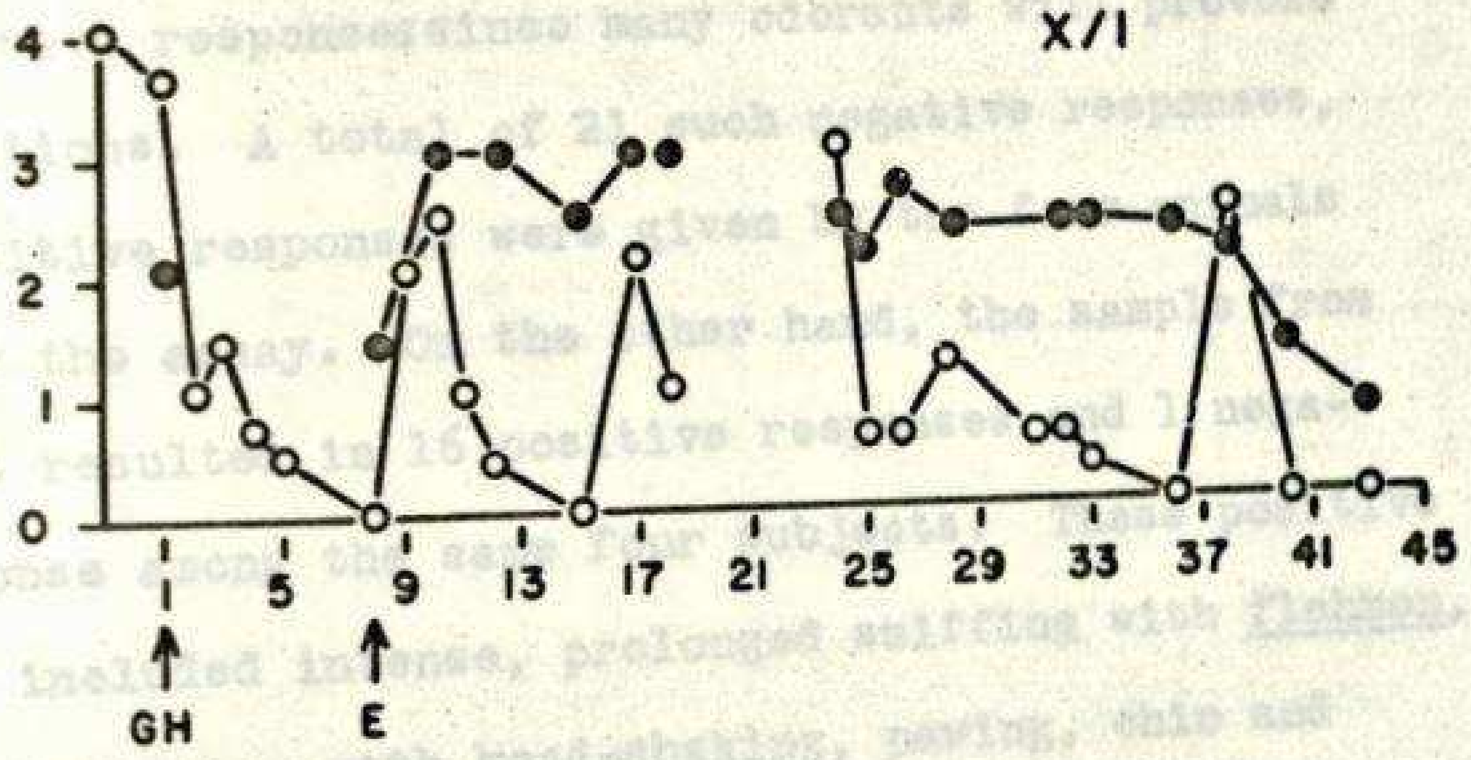

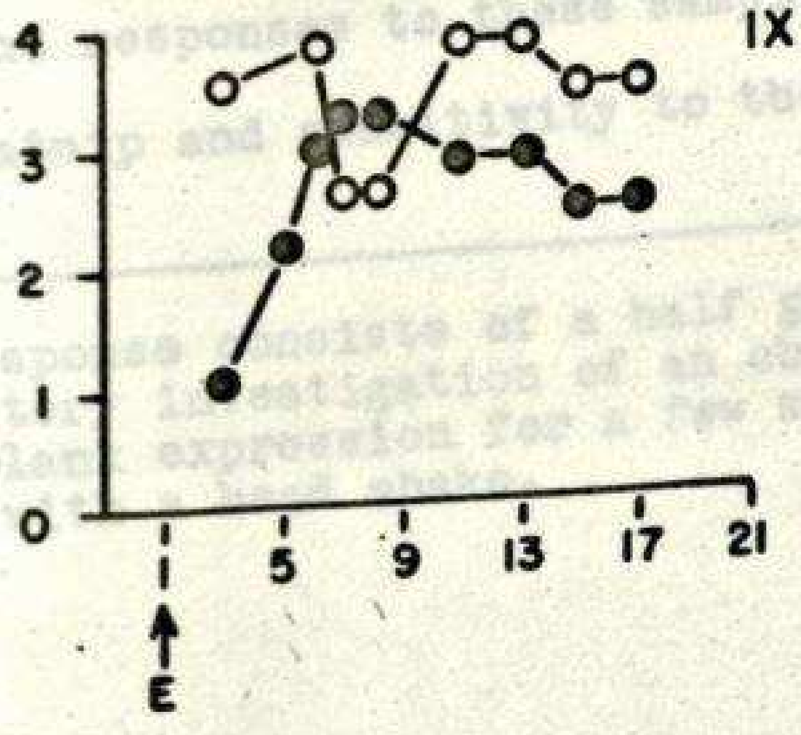

estrogen to bring it within the range at which a response can be stimulated. However, other females have thresholds normally above stimulation but which can be lowered by estrogen to a point at which response occurs. It is still unclear whether these thresholds are sensory or motivational.

Table 2 summarizes the results of various tests for catnip-like activity in urine extracts. The samples from the adult females (both anestrus and estrus) resulted only in cursory sniffing and occasional *flehmen** and were designated negative responsessince many odorants will provoke these reactions. A total of 21 such negative responses, and no positive responses were given by the four animals chosen for the assay. On the other hand, the sample from the tomcat resulted in 16 positive responses and 1 negative response among the same four subjects. These positive responses included intense, prolonged sniffing with *flehmen*, licking and chewing with head-shaking, pawing, chin and cheek rubbing, head-over roll and body rubbing, *i.e.* responses very similar to the catnip response. The intensity of the responses to these samples was seldom as strong as with catnip and sensitivity to the unknown active princi-

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* This response consists of a half gape to the jaw following the olfactory investigation of an object. The animal maintains a blank expression for a few moments and then terminates it with a head shake.

Number of positive and negative responses of four cats

Sample Source	"Harper" Adult ♂ Catnip Responder		"Fidel" Immature ♂ Catnip Responder		"Schizi" Adult (Anestrus) ♀ Catnip Non-responder		"Saigon" Immature ♀ Catnip Responder	
	+	-	+	-	+	-	+	-
"Ebu" Male Adult	0	1	7	0	1	0	8	0
Female Adult (Anestrus)	0	2	0	4	0	1	0	5
Female Adult (Estrus)	0	2	0	2	0	3	0	2

Table 2. Catnip-like responses induced by urine extracts.

ple was not found to be distributed among individuals in the same way as sensitivity to catnip. That is, some cats which responded vigorously and consistently to catnip were indifferent to the samples, and *vice versa*. Further testing of the adult male and female was interrupted by the latter coming into estrus and distracting the male which was housed in the same area. Subsequently, about two dozen other cats have given catnip-like responses to the samples from the tomcat. However, as these animals were not available for prolonged study no tabulation of their responses was made. Finally, a fear avoidance response was noted among several immature kittens upon the presentation of urine extract samples. These responses were similar to those obtained with catnip.

D. Discussion

In addition to the general objections to the loose behavioral parameters used for correlation in these studies and the inherent difficulties involved in presenting olfactory stimuli, at least three specific considerations must be taken into account in order to interpret data from these tests. These are 1) individual differences in the sexual behavior of a given cat. Such differences, which may be great, can be attributed to a variety of causes, *e.g.* instinctive differences, maturational factors, learning, etc. 2) Differences related to the genetic setting of thresholds must be considered. It is the hormonal influence upon one of these thresholds which is of interest in the present context. Special account must be taken of specific fatigue (in the ethological sense) of finally 3) the catnip response and the possibility that equivalent components (e.g. chin and cheek rubbing, head-over roll, etc.) of courtship display may result in cross fatigue. These remarks serve to indicate the complexity of variables which for various reasons it has been impossible to control satisfactorily. In general the above experiments have failed to demonstrate any simple effect of estrogen upon olfactory sensitivity. This failure seems best interpreted as resulting from the fact that the catnip response is an unreliable criterion by which to judge sensitivity to catnip in that it fails to distinguish alterations of sensitivity (olfactory) from motivational changes. This stems not only from the fact that the behavioral patterns elicited by estrogen and catnip are so similar in some aspects as to make interpretations ambiguous, but that spontaneous courtship display may be as effective in causing a "hetero-specific" fatigue to catnip as the "auto-specific" fatigue of catnip itself. This would suggest that some "neutral" response, e.g. lever-pushing, should be substituted through operant conditioning for the catnip response in order to measure sensitivity to catnip.

The results obtained from the urine extract experiments appear to provide a hypothetical explanation of the catnip response. It is postulated that catnip coincidentally mimics a pheromone of the cat which is capable of eliciting or reinforcing specific postural displays of courtship. Perhaps the pheromone will be found to share the molecular "common denominator" of the active compounds reviewed in the general introduction of this thesis. It must be emphasized that olfactory aspects of reproductive behavior in the domestic cat represent only a small and non-essential portion of the total repertoir used by this animal in its reproductive activities. That is to say that olfactory stimuli are neither necessary nor sufficient for reproduction (Sawyer, 1960). As a consequence, additional evidence of various sorts has been sought to support this hypothesis. This is presented in connection with other studies described below.

Chapter 4. Neurological Correlates of the Catnip Response

A. Introduction

Harris (1959), Sawyer (1959) and Sawyer and Kawakami (1961), among others, have produced evidence from lesions, hormone implantation and electrical stimulation that "centers" exist in the hypothalamus for the regulation of sexual behavior and the trophic control of the reproductive system. While there is some disagreement as to the precise localization of the "centers" within the hypothalamus, which are apparently neural targets for ovarian hormones, they have been clearly shown to be functionally, if not anatomically, separable. Destruction of the behavior "center" results in cessation of all courtship and reproductive behavior, which cannot be restored or induced with exogenous estrogen even though the trophic condition of the primary and accessory reproductive organs responds normally to hormone treatment. Stimulation of the behavior "center" with implanted crystalline estrogen will bring about behavioral estrus in the absence of normally concomitant changes in the reproductive system. On the other hand, ablation of the trophic control "center" abolishes the normal responses of the reproductive system to exogenous estrogen while leaving behavioral responses intact. Additionally, Michael (1962) has demonstrated with autoradiographic techniques that certain cells of the mid-hypothalamus have a preferential affinity for estrogen. These researches are leading to a clearer understanding of the neural control or influence on reproductive processes, including hormonal-neural interaction in the pituitary feedback mechanism. Figure 15 summarizes, in a much simplified fashion, some of these relationships. Furthermore, with the elucidation of a separate "center" for reproductive behavior as a target for sex hormones, the question arises as to how the "center" may be affected by the numerous exogenous stimuli which determine or modify reproductive behavior. Evidence has been presented which suggests that the response to catnip is due to the fact that the active principal (nepetalactone) mimics a pheromone which elicits courtship display. How close this mimicry is remains to be seen. It is suspected that nepetalactone is far more effective than the pheromone in provoking certain limited components of courtship for it can initiate a strong response even uder inappropriate conditions. This may relate to physical properties of nepetalactone (*e.g.* volatility) which make it a more powerful odorant than the natural product although not necessarily a good substitute for it under natural conditions. Nevertheless catnip provides a convenient means for studying the neural pathways involved in coupling the presumed pheromone to the behavior "center." The present study was conducted as an attempt to trace these pathways.

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The conclusion that the catnip response is mediated wholly by an olfactory input is based upon evidence discussed previously. Thus, one or more of the possible routes from the primary and secondary olfactory areas to the hypothalamus will be involved in the integration of olfactory stimuli and sexual behavior. At least three alternative pathways from the olfactory bulb to the pre-optic region of the hypothalamus and the septal nuclei have been described. One consists of a direct input of bulbar afferents from the medial olfactory stria to the septal nuclei (or via the olfactory tubercle). A second is comprised of an input via the stria terminalis from the amygdala. The third route, the most circuitous, is by way of the fornix from the pyriform and entorhinal cortex. Finally, the septal nuclei and indeed all rostral (pre-optic) areas of the hypothalamus contribute fibers to, and receive fibers from, the medial forebrain bundle which apparently connects to all portions of the mid and lateral hypothalamus. Figure 16 summarizes these relationships.

B. Methods

All lesions produced in this study were generated with a standard R.F. (radio frequency) lesion maker. Cats were placed in a stereotactic instrument under nembutal anesthesia and electrode placements made according to the stereotactic coordinates of Jasper and Ajmone-Marsan (1961). Small holes were drilled in the skull, the dura mater cut, and

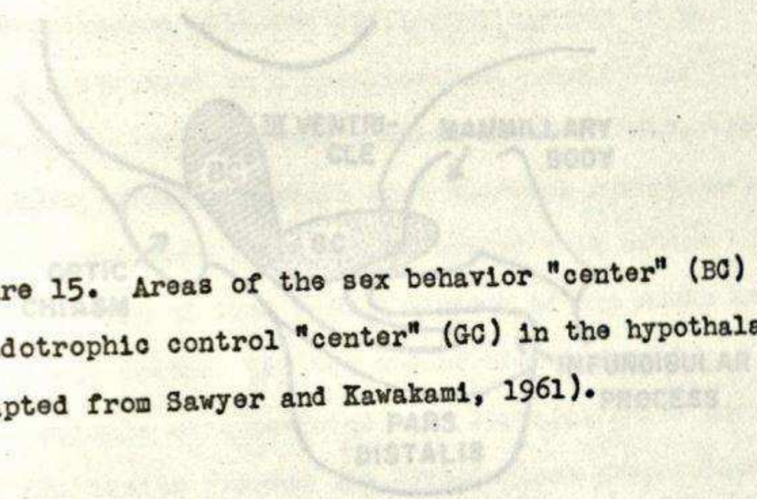


Figure 15. Areas of the sex behavior "center" (BC) and gonadotrophic control "center" (GC) in the hypothalamus (adapted from Sawyer and Kawakami, 1961).

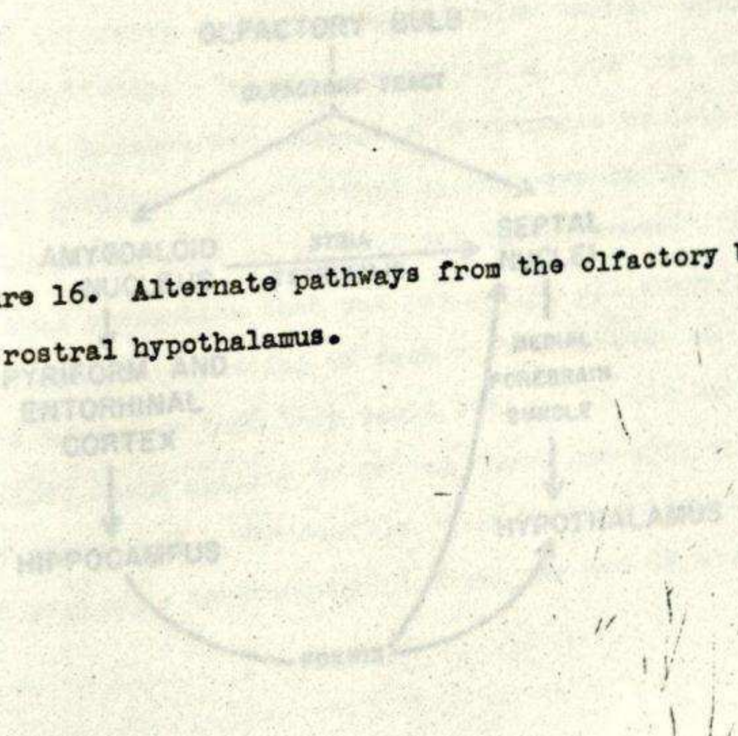
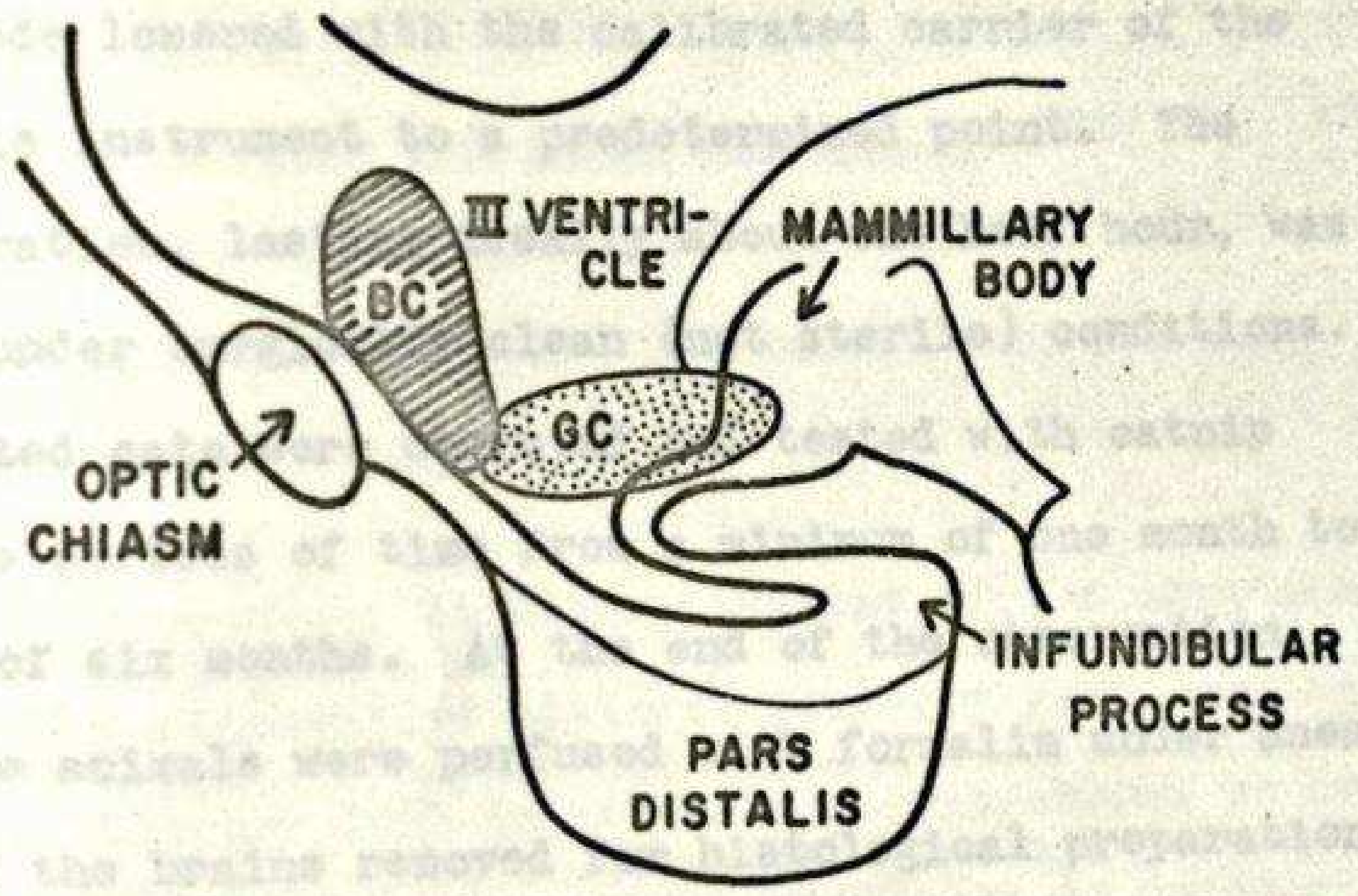


Figure 16. Alternate pathways from the olfactory bulb to the rostral hypothalamus.


III VENTRICLE
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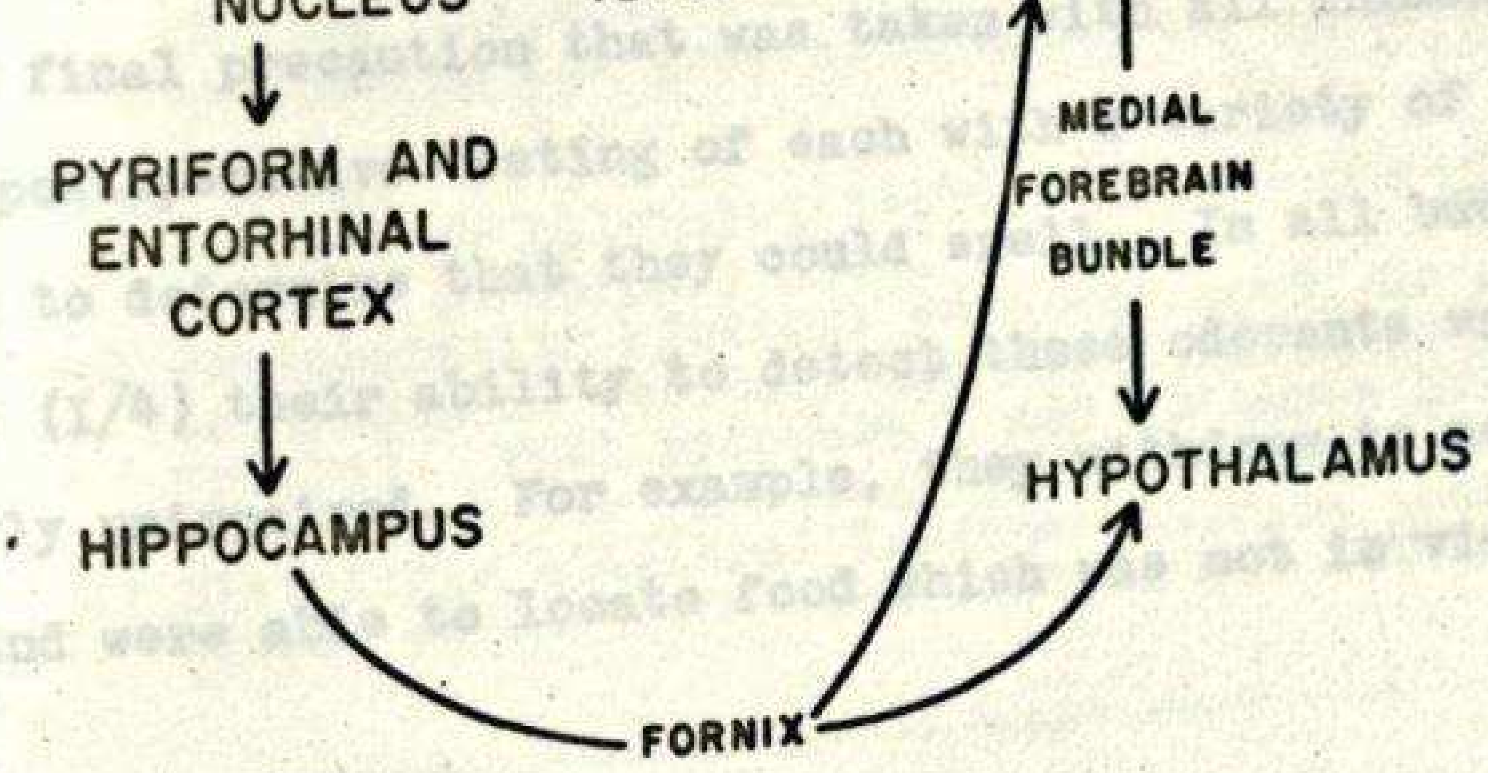
OLFACTORY BULB
OLFACTORY TRACT
AMYGDALOID NUCLEUS
STRIA TERMINALIS
SEPTAL NUCLEI
PYRIFORM AND ENTORHINAL CORTEX
MEDIAL FOREBRAIN BUNDLE
HIPPOCAMPUS
HYPOTHALAMUS
FORNIX

the electrode lowered with the calibrated carrier of the stereotactic instrument to a predetermined point. The entire operation, lasting ideally about one half hour, was performed under surgically clean (not sterile) conditions.

Operated cats were observed and tested with catnip for various periods of time from a minimum of one month to a maximum of six months. At the end of the observation period, the animals were perfused with formalin under anesthesia and the brains removed for histological preparation. 16 μ sections were prepared through an area including the lesion sites. Two out of every ten sections were stained and mounted for examination, a fiber and a cell stain being used alternately.

All animals used were adult males which gave typical high or low intensity catnip responses under various conditions preoperatively. Females were rejected from this series of experiments because the absence of a response postoperatively could possibly occur through spontaneous or induced hormonal changes as well as by surgical interference.

One final precaution that was taken with all animals was the postoperative testing of each with a variety of odorants to determine that they could smell. In all but one case (I/4) their ability to detect these odorants was apparently unimpaired. For example, they withdrew to noxious smells and were able to locate food which was not in view.

C. Results and Discussion

Lesions in the amygdala and stria terminalis: (See Fig. 17.)

Operations on six animals were performed in this series of experiments and will be discussed briefly as six case histories.

1) Animal I/4:
   - a) Operation: bilateral lesions of the amygdala, 30 August 1961.
   - b) Postoperative history: recovery good, no interest in catnip from 31 August 1961 until 17 October 1961 (six trials). Cat showed no avoidance to noxious odorants (e.g. iso-valeric acid). Sacrificed for histology 17 October 1961.
   - c) Histology: large lesions in the amygdala reaching greatest bilateral extent in the anterior amygdala. Other irregular lesions, principally unilateral in the central, medial and basal nuclei of the amygdala, the putamen and globus pallidus. The olfactory tract and possibly the stria terminalis were bilaterally involved in the lesions.

2) Animal II-III/4:
   - a) Operation: bilateral lesions of the amygdala, 13 October 1961.
   - b) Postoperative history: recovery good, no interest in catnip 16 October 1961 to 27 October 1961 (4 trials). Full intensity response 27 November 1961 to 20 December 1961 (several trials). No response or weak response 26 January 1962 to 2 March 1962 (10 trials). Sacrificed for histology 2 March 1962.
   - c) Histology: Unavailable for detailed description. Cursory inspection showed obvious bilateral lesions in the general area of the amygdala.

3) Animal IV/2:
   - a) Operation: bilateral lesions of the pre-pyriform cortex, 6 February 1962.
   - b) Postoperative history: recovery good, no response to catnip 12 February 1962 to 1 March 1962 (2 trials). Full response 5 and 12 March 1962. Sacrificed for histology 26 March 1962.
   - c) Histology: bilateral lesions reaching greatest extent at Fr. 9.0* (the central and lateral

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* Stereotactic coördinates of Jasper and Ajmone-Marsan (1961).

nuclei of the amygdala) and involving caudate nucleus in its entirety at this level.

4) Animal IV/3:
   a) Operation: bilateral lesions of the basal-medial amygdala, 13 February 1962.
   b) Postoperative history: recovery good, no interest in catnip 1 March 1962. Full response to catnip 5, 12, 26 March 1962. Sacrificed for histology 26 March 1962.
   c) Histology: large bilateral lesions in the posterior portion of the basal nucleus of the amygdala reaching greatest extent at Fr. 10.0 - 11.0. The basal portion of the medial nucleus of the amygdala partially involved in bilateral lesions at Fr. 11.0. Hippocampal formation unilaterally involved at Fr. 9.0 - 10.0.

5) Animal VIII/1:
   a) Operation: bilateral asymmetrical lesions of the stria terminalis, 27 July 1962.
   b) Postoperative history: recovery good, no interest in catnip 30 July 1962 to 9 September 1962 (10 trials). Sacrificed for histology 30 September 1962.
   c) Histology: bilateral asymmetrical lesions of the stria terminalis at Fr. 8.0 (left side) and Fr. 12.0 (right side). The lesion on the right side involved a small part of the caudate nucleus and the internal capsule, that on the left a small part of the caudate nucleus and a fragment of the fornix.

6) Animal IX/1:
   a) Operation: bilateral asymmetrical lesions of the stria terminalis, 20 August 1962.
   b) Postoperative history: physical recovery good but cat lacked alertness for remainder of testing program. Indifferent towards estrous female although successfully mated prior to surgery. Failure to groom properly. Indifferent to catnip 27 August 1962 to 1 October 1962 (10 trials). Sacrificed for histology 2 October 1962.
   c) Histology: bilateral symmetrical lesions of stria terminalis and small portions of adjacent fornix and caudate nucleus at Fr. 10.0. This was due to a "leak" in the electrode. Unilateral lesion of endopeduncular nucleus, portion of medial forebrain bundle, hippocampus and optic tract on right side.

Only limited, but notwithstanding, very interesting conclusions can be drawn from this series of experiments. The lesions of the amygdala are inadequate to ascertain whether or not any sub-nuclei of this structure are unnecessary for the maintenance of the catnip response. It is only obvious that large irregular lesions do not interfere with it. On the other hand, lesions of the stria terminalis which abolish the catnip response are best interpreted as indicating that the input of the amygdala to the rostral hypothalamus is necessary for the retention of this response. No other fiber tract in the experimental subjects has been interrupted in its entirety either uni- or bilaterally and no bilateral ablation of anything more than a very small portion of any nuclei was detected (e.g. caudate nucleus). Finally, contributions to the stria terminalis other than from the amygdala are relatively unimportant although the critical experiment which would eliminate this possibility was unsuccessful in this series of operations, bilateral symmetrical lesions having been generated by virtue of a "leaky" electrode. The question of whether or not the amygdala - stria terminalis sequence represents the pathway from the olfactory bulb is as yet unanswered. But it is evident that impulses must arrive in the rostral hypothalamus from the amygdala (and still possibly from the medial olfactory stria) in order to initiate a catnip response.

<u>Lesions in the suprachiasmatic nucleus</u>:

1) Animal IV/1:
    a) Operation: bilateral asymmetrical lesions of the medial forebrain bundle, 2 February 1962.
    b) Postoperative history: recovery good. No interest in catnip 5 February 1962 to 25 June 1962 (8 trials).
    c) Histology: large bilateral lesion suprachiasmatic nucleus. Electrode apparently deflected or cat misplaced in stereotactic apparatus.

2) Animal V/2:
    a) Operation: bilateral lesions of the suprachiasmatic nucleus, 2 May 1962.
    b) Postoperative history: cat blind. Typical catnip response 7 May 1962 to 24 May 1962 (4 trials). Sacrificed for histology 24 May 1962.
    c) Histology: incomplete lesion of SCh on left side. Optic chiasma partially destroyed to right of mid-line. SCh intact at all levels. From a previous operation (chronic implant of recording electrodes) lesions were found in hippocampus (right side) and amygdala. Similar but smaller lesions were present on the left side but included the optic tract.

3) Animal V/4:
    a) Operation: bilateral lesions of the suprachiasmatic nucleus, 24 May 1962.
    b) Postoperative history: recovery good. No response to catnip 25 May 1962 to 26 June 1962 (5 trials). Sacrificed for histology 29 June 1962.
    c) Histology: obvious lesion in area of SCh. Very little, if any, of the nucleus left intact.

4) Animal VI/1:
    a) Operation: bilateral lesions of the suprachiasmatic nucleus, 26 June 1962.
    b) Postoperative history: recovery good. No response to catnip 2 July 1962 to 24 July 1962 (15 trials). Sacrificed for histology 2 August 1962.
    c) Histology: complete destruction of the suprachiasmatic nucleus on the right side. Extensive, ? incomplete damage on the left side. Large midline lesion in the optic chiasma.

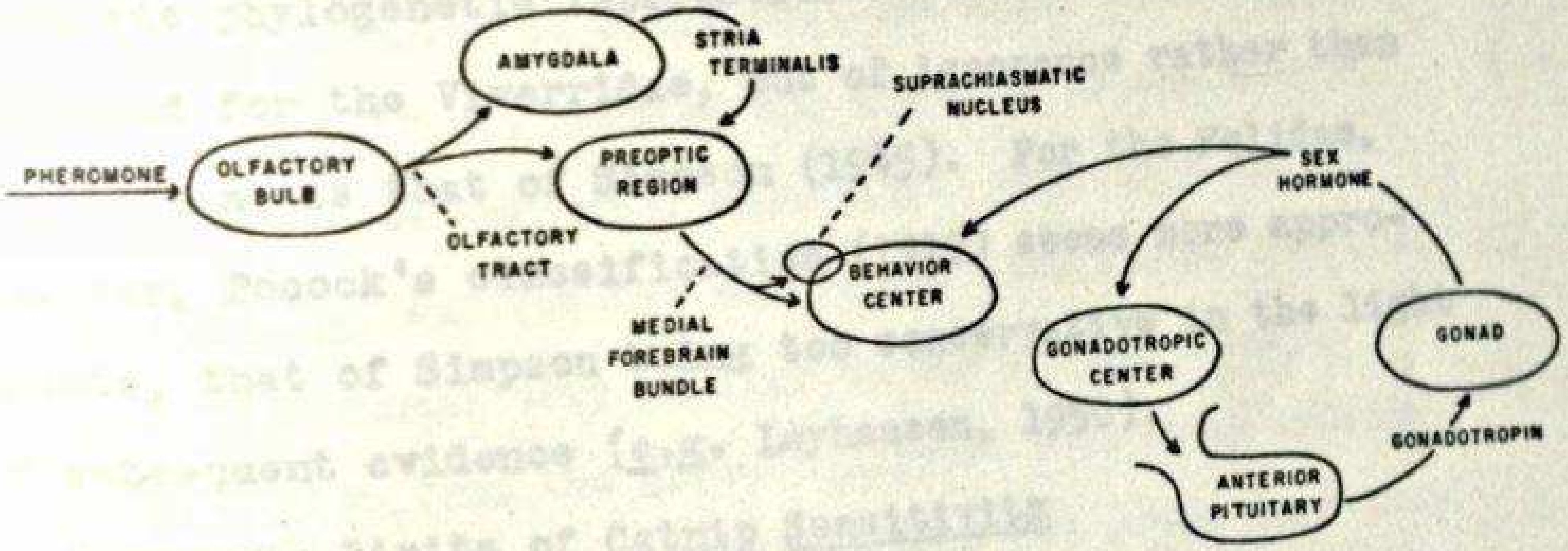
It would appear that the region of the suprachiasmatic nucleus is important for the catnip response. Unfortunately the fundamental anatomical and functional relationships of this nucleus are virtually unknown. However, it is clear that it does not correspond precisely to the "sex behavior center" of Sawyer and Kawakami (1961), although it may be within this area. It also seems improbable that it acts as a simple relay station in the sequence. More probably its reception of extrinsic stimuli (in this case catnip) results in efferent impulses which "activate" the "sex behavior center." Hence the simplest possible system, taking into account the available evidence, is that depicted in Figure 17.

A number of problems yet remain to be discussed. These revolve around what may appear to be inconsistencies, but which can fairly well be rationalized.

It will have been noted that only evidence from males was admitted in the above experiments, because females are unreliable for the various reasons mentioned above. Yet the neural models proposed by various other workers and which have been integrated with the present data to produce a unified hypothesis are based upon work on females. This action seems justified on a number of considerations and inferences. First, it is assumed that the sexes have much the same hypothalamic "apparatus." This assumption rests on the fact that the male or female may be made to behave as the opposite sex by manipulating hormone balances.

Secondly, in the case of cats at least, many of the courtship behavior patterns in both sexes are identical, although their intensity may differ. As a consequence of these considerations, the model depicted in Figure 17 may represent either sex. Verification must await appropriate experiments.

Figure 17. Presumed pathways involved in the integration of hormonal and pheromonal determinants of sexual behavior.


PHEROMONE
OLFACTORY BULB
AMYGDALA
STRIA TERMINALIS
PREOPTIC REGION
SUPRACHIASMATIC NUCLEUS
OLFACTORY TRACT
MEDIAL FOREBRAIN BUNDLE
BEHAVIOR CENTER
SEX HORMONE
GONADOTROPIC CENTER
GONAD
GONADOTROPIN
ANTERIOR PITUITARY

Chapter 5. Taxonomic and Phylogenetic Considerations of the Catnip Response*

A. Introduction

Evidence has been presented which was interpreted as indicating that catnip and related active compounds mimicked a pheromone of the domestic cat. The purpose of the present paper is to reveal investigations made to determine the taxonomic scope of the catnip response and to speculate upon its phylogenetic implications. The taxonomy here followed for the Viverridae, out of ignorance rather than conviction, is that of Simpson (1945). For the Felidae, however, Pocock's classification (1917) seems more appropriate, that of Simpson being too conservative in the light of subsequent evidence (e.g. Leyhausen, 1950).

B. Taxonomic Limits of Catnip Sensitivity

The first endeavors made were to define the taxonomic limits of the catnip response. To this end the available non-Felid Feloidea (Viverridae and Hyenidae) were surveyed.

Results of testing Viverridae: 22 animals in 10 genera, representing four of the extant six sub-families of Viverrids, were tested with dried catnip leaves in the same manner as cats are customarily tested. The results of these

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[*] This investigation was supported principally by the Graduate Committee for the Study of Evolutionary Biology, Harvard University.

tests are summarized in Table 3. The data are too scant to draw any conclusions beyond the general one that Viverrids show little or no interest in catnip. The single positive response of a binturong (*Arctictis binturong*) is based upon the fact that this animal sniffed, pawed and licked the sample with head-shaking. The other binturong sniffed the sample intensely and showed prolonged interest. One could not escape the impression that this animal was trying hard to identify a smell that it could not quite place but recognized as familiar. One water civit (*Atilax paludinosus*) sniffed, sneezed and ate some of the sample. The others showed only mild curiosity. One civit (*Civittictus civetta*) sniffed the sample and then thrust its head forward in a manner very similar to the motion of chin rubbing. Aside from the above-mentioned responses nothing beyond sniffing was noted although this was often more than cursory.

Catnip tests of Hyenidae: An unconfirmed report that a male hyena "used to roll for catnip" could not be verified. The particular animal had lived several years since the observation and upon testing was found to be completely indifferent towards the sample. A second hyena (female) was also indifferent. A third animal was tested in a slightly irregular fashion. It was necessary to coax him from his lair with bits of food (meat). He devoured these eagerly until one was thrown to him after having been rolled in catnip.

Sub-families	Genera	+	?+	?-	-	I
Viverrinae:	*Genetta* (3)	0	0	0	2	1
	Viverra (1)	0	0	1	0	0
	Civettictis (2)	0	0	0	1	1
Paradoxurinae:	*Nandinia* (5)	0	0	3	2	0
	Paguma (2)	0	0	1	0	1
	Arctictis (3)	1	1	0	0	1
Herpestinae:	*Herpestes* (1)	0	0	0	1	0
	Atilax (3)	0	1	1	1	0
	Ichneumia (1)	0	0	0	0	1
Cryptoproctinae:	*Cryptoprocta* (1)	0	0	1	0	0

Table 3. Results of testing Viverrids with catnip. Figure in parentheses indicates number of individuals tested. + = positive, ?+ = possibly positive, ?- = probably negative, - = negative, I = indeterminate, animal would not or did not investigate leaves.

This he avoided. The procedure was repeated several times, and without fail he ate the plain meat and rejected that with catnip. No further testing of Hyenids was attempted.

C. Distribution of Catnip Sensitivity among the Felidae

The living Felidae comprise three subfamilies, viz. Pantherinae (the so-called greater cats), Acynonychinae (the cheetas), and the Felinae (the so-called lesser cats).

Catnip responses among the Pantherinae: To the subfamily Pantherinae belong the lion (*Panthera leo*), tiger (*P. tigris*), leopard (*P. pardus*), jaguar (*P. onca*) and snow leopard (*Uncia uncia*).

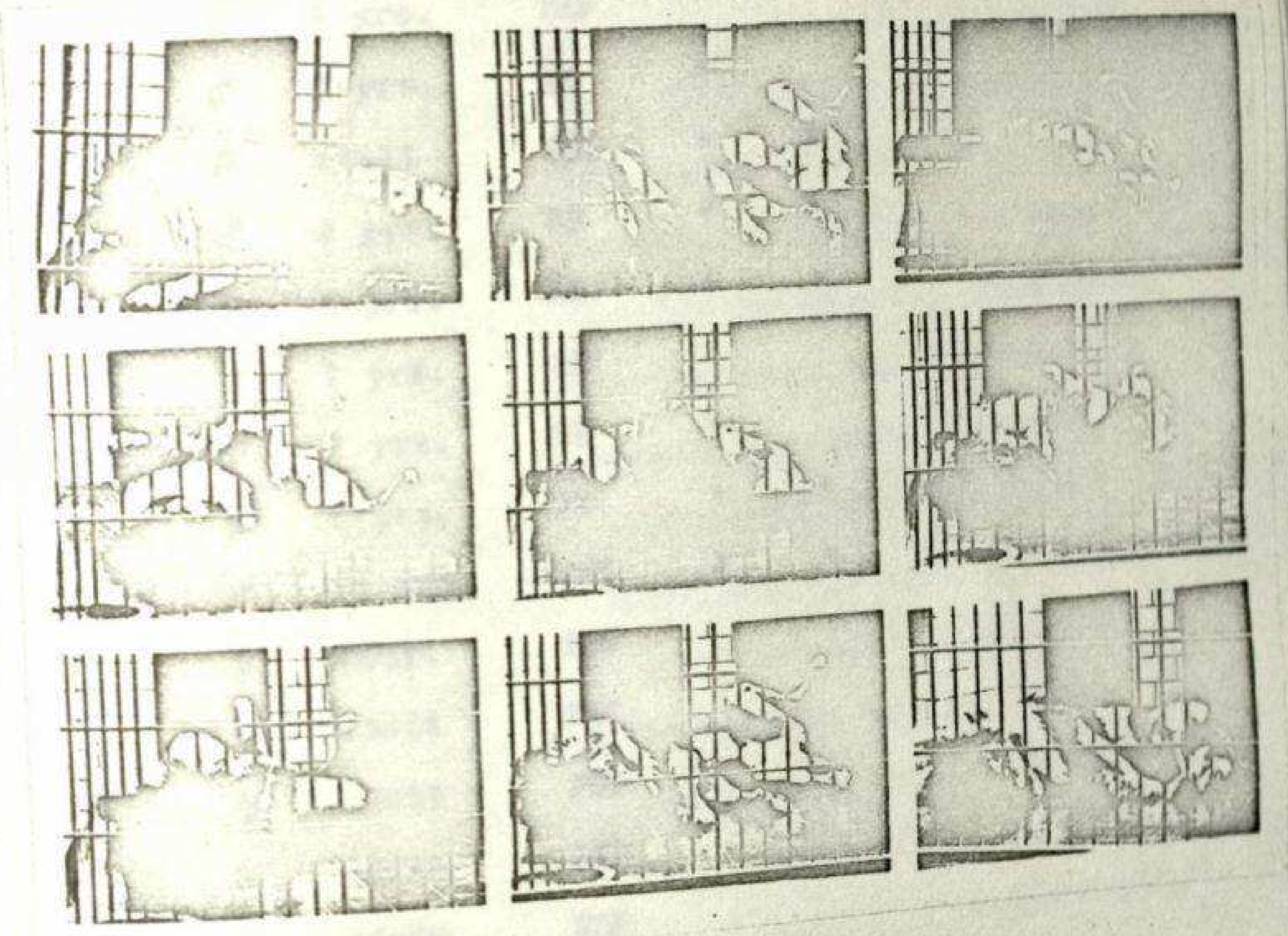
Table 4 shows the results of testing 16 lions, 5 of which were retested after a 4-month interval. 14 of these individuals gave spectacular responses which were closely similar to that of domestic cats (Figure 18). The two individuals that did not respond were the oldest and youngest animals tested (20 years and 9 weeks). The inescapable conclusion from this evidence is that catnip is extremely effective in provoking a catnip response among lions.

Table 5 depicts the responses of 23 tigers to catnip. Two of these were inconclusive, 13 negative with respect to the typical components of a catnip response and 8 which gave various incomplete responses. At a glance it is obvious that catnip is either ineffective or only partially effective in eliciting a catnip response from this species.

	Sex	Approx. Age	Source	S	L & C c̄ HS	C & CR	HOR & BR
1	♂	11 yrs.	PZG	+	+	+	+
1'				+	+	+	+
2	♂	11 yrs.	PZG	+	+ ⟷	+	
2'				+	+	+	+
3	♂	11 yrs.	PZG	+	+	+	++
3'				+	+ ⟷	+++	+
4	♂	11 yrs.	PZG	+	+	++	
4'				+	+	+	
5	♂	10 yrs.	NZP	+ ⟶		+	+++
6	♂	7 yrs.	NZP	+ ⟶		+	+++
7	♂	9 wks.	NZP				
8	♂	adult	BZ	+	+	+	+
9	♂	20 yrs.	RB				
10	♂	adult	FPZ	+	+	+	+
11	♀	11 yrs.	PZG	+	+		
11'				+	+	+	+
12	♀	1 yr.	PZG	+	+	+	+
13	♀	10 yrs.	NZP	+ ⟶		+	+++
14	♀	18 yrs.	SIZ	+ ⟶		+++	+++
15	♀	18 yrs.	SIZ	+ ⟶		+	+++
16	♀	18 yrs.	BZ	+	+	+	+

Table 4. Catnip responses of lions. S = sniffing, L & C c̄ HS = licking and chewing with head shaking, C & CR = chin and cheek rubbing, HOR & BR = "head-over" roll and body rubbing. Subjective intensity of response component: + = strong, ++ = very strong, +++ = extremely strong. ⟷ = sequence of components reversed. ⟶ = components omitted. ' = repeat test. Sources: Bronx Zoo (BZ), Franklin Park Zoo (FPZ), National Zoological Park (NZP), Philadelphia Zoological Garden (PZG), Ringling Brothers Circus (RB) and Staten Island Zoo (SIZ).

Figure 18. Catnip response of a male lion.



	Sex	Approx. Age	Source	S	L & C $\bar{c}$ HS	C & CR	HOR & BR
1	♂	8 mos.	PZG				
1'		1 yr.					
2	♂	1 yr.	PZG				
3	♂	1 yr.	PZG				
4	♂	adult	PZG				
5	♂	4 yrs.	NZP				
6	♂	7 yrs.	BZ	+			
7	♂	adult	SIZ	+	+		
8	♂	9 yrs.	RB	+	+		
9	♂	9 yrs.	RB	+	+		
10	♂	9 yrs.	RB				
11	♂	2 yrs.	RB	+			
12	♂	2 yrs.	RB	+	+	+	
13	♂	1½ yrs.	FPZ	+	+		
14	♀	adult	PZG				
15	♀	adult	PZG				
16	♀	adult	PZG				
17	♀	adult	NZP				
18	♀	adult	NZP				
19	♀	adult	NZP				
20	♀	adult	BZ				
21	♀	adult	BZ	+	+	+	
22	♀	11 yrs.	RB				
23	♀	3 yrs.	FPZ				

Table 5. Catnip responses of tigers. See Table 4 for explanation of symbols.

Perhaps the most fantastic of all responses noted among all species tested are the startle responses of some of the younger tigers.* In two cases these were violent. Tiger number 2, a zoo born, tame animal, trotted over to the dried catnip leaves when these were placed on the floor of his cage. One sniff caused him to leap several feet into the air, urinating in the process, fall flat on his back, scramble to his feet and dash head-long into the wall of his cage. Tigers number 1 and 3 gave similar, but less violent responses, not losing bladder control. When animal number 1 was retested four months later, he withdrew from catnip with a startle response to an adjacent cage and would not re-enter the original testing area even with coaxing for over an hour. Since there is nothing physically noxious about catnip, these responses (similar to but more intense than those of domestic cats and other species) must be considered to have some special biological meaning.

Table 6 gives the results of testing 18 leopards with catnip. Three animals failed to respond although in two of these cases extenuating circumstances may reasonably be thought to have inhibited normal reaction. A fourth animal failed to respond on a repeat test, for which no explanation is proferred. On the whole, catnip appears to be highly effective in eliciting typical responses from leopards (Figure 19).

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* These animals were sexually immature. The lion and tiger are generally four years old before they become reproductively active.

	Sex	Approx. Age	Source	S	L & C c̄ HS	C & CR	HOR & BR
1	♂	adult	PZG	+	+	+	+
1'				+	+	+	+
2	♂	adult	PZG	+	+	+	+++
2'							
3	♂	10 yrs.	NZP	+	+	+	+
4	♂	2½ yrs.	NZP	+ ⟶	⟶	⟶ +	+
5	♂	adult	NZP				
6	♂	adult	BZ	+	+ ⟷	⟷ + ⟷	⟷ +
7	?	adult	SIZ				
8	?	adult	SIZ				
9	♂	adult	FPZ	+ ⟶	⟶	⟶	⟶ +
10	♂	adult	FPZ	+	?+	?+	+
11	♂	1 yr.	FPZ	+	+	+	+++
12	♀	18 mos.	PZG	+	+	+	+
12'				+	+	+	
13	♀	9 yrs.	PZG	+	+	+	+
14	♀	adult	NZP	+ ⟶	⟶	⟶ +	+
15	♀	adult	NZP	+ ⟶	⟶	⟶ +	+
16	♀	adult	BZ	+	+	+	+
17	♀	adult	FPZ	+ ⟶	⟶	⟶ +	+
18	♀	adult	FPZ				

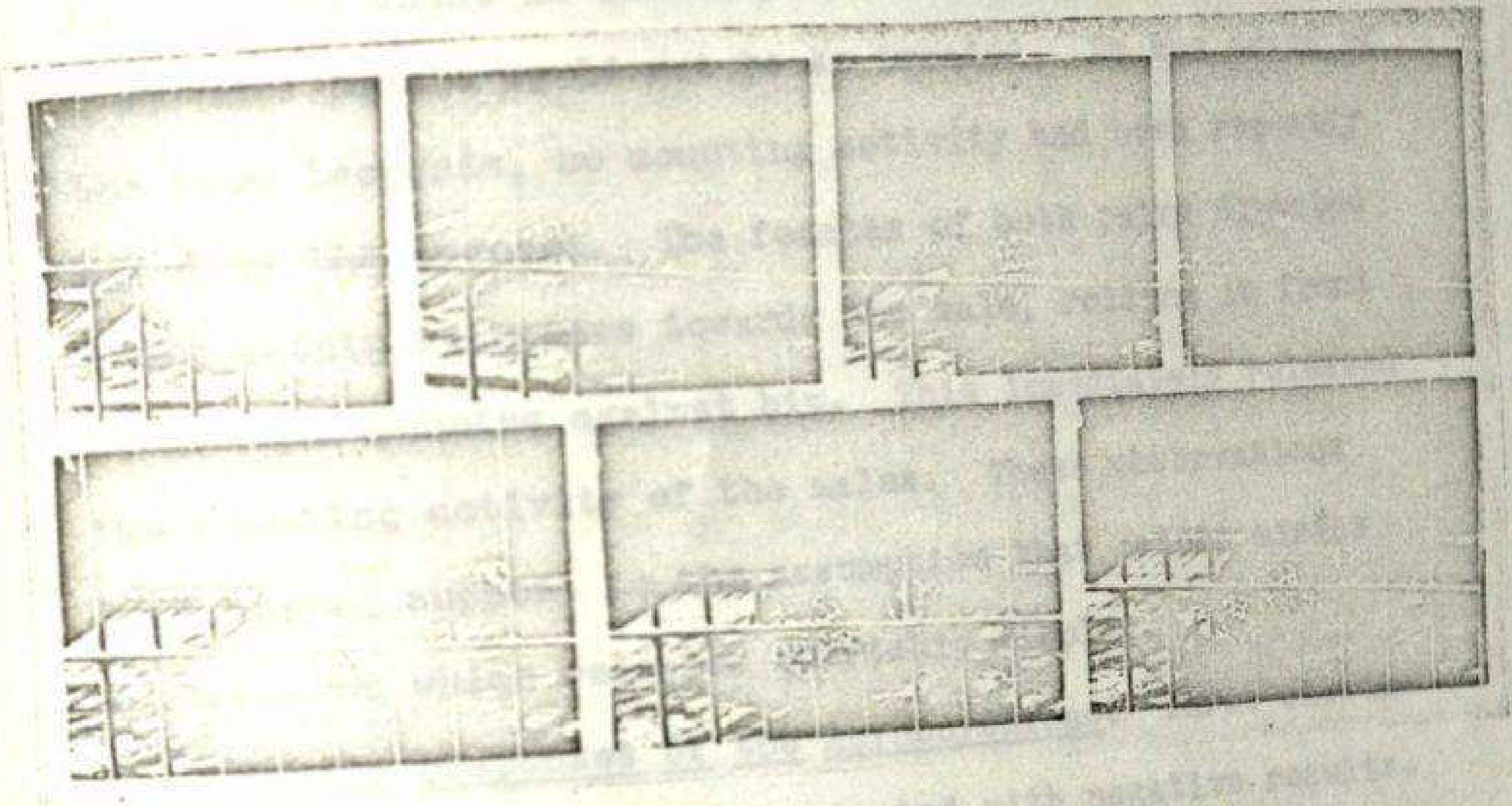
Table 6. Catnip responses of leopards. See table 4 for explanation of symbols.

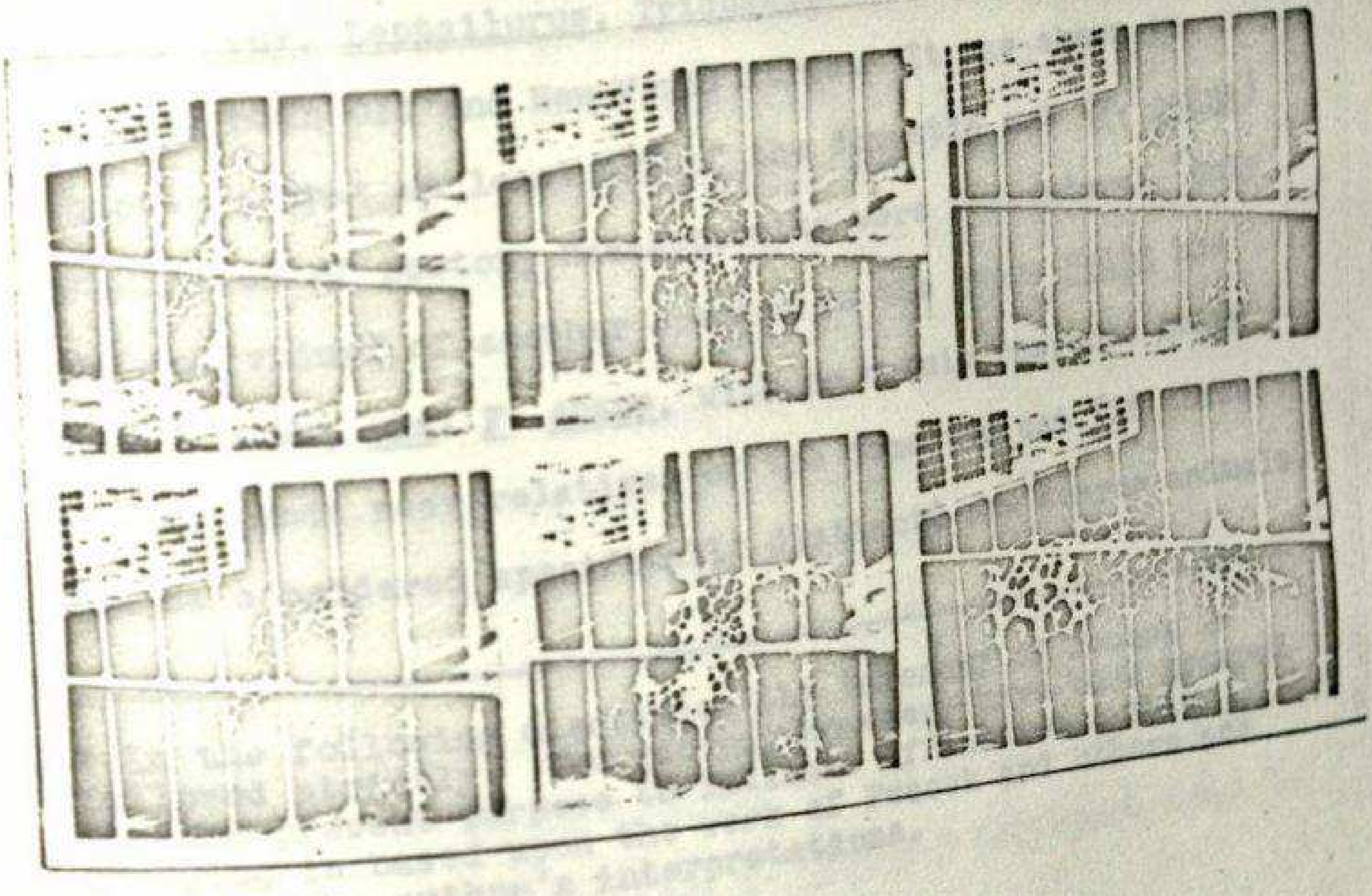
Only eight jaguars have been tested, but the results indicate that this species is characteristically sensitive to catnip. Seven animals (4 males and 3 females) gave strong responses while one male showed only mild interest. One conspicuous difference between the response of jaguars and all other Felids is the propensity for this species to tuck the head into the chest with the top of the head on the ground. Other species accomplish this head-over roll position by turning the head laterally, which is also done by jaguars. It would be interesting and informative to know if this particular motion is characteristic of the courtship display of jaguars. Unfortunately the individual selected for photographic documentation (Figure 20) employed the more typical lateral roll.

Only four snow leopards have been tested, all of which gave full responses. These animals consisted of two pairs, each pair having been housed together for a considerable period of time. In both instances the females responded prior to the males and the males subsequently made attempts to mount the females although neither was in estrus. In domestic cats it is not uncommon to find a male which has been housed with a familiar female attempting to mount during the latter's diestrus. Such mounting is usually grudgingly tolerated by the female and the male does not persist. The mounting is usually provoked by some accidental or coincidental assumption of a receptive posture on

Figure 19. Catnip response of a male leopard.

Figure 20. Catnip response of a female jaguar.





the part of the female and the immediate willingness of the male to mount is due only to his familiarity with her. A strange female would not be so treated. In the cases of the snow leopards, no mounting activity had been recently noted by the keepers. The females of both pairs directed their catnip responses towards the male, rolling in front of him and rubbing against him. This immediately released the mounting activity of the males. These observations lend strong support to the assumption that catnip mimics a pheromone which releases courtship display.

Catnip responses of the Acynonychinae: Three cheetas (*Aconynyx jubatus*) have been tested with negative results.

*Catnip responses of the Felinae**: The first group of felines to be considered will be *Felis* and the related genera *Lynx*, *Leptailurus*, *Trichaelurus*, and *Puma* representing both Old and New World forms. It was shown in Chapter 1 that at least 69% of the domestic cat (*F. catus*) population of Boston, Massachusetts were responders. Only one individual of another species in the genus *Felis* has been tested, *viz*. *F. chaus*, with no catnip response being given. Most near relatives of the domestic cat (if these can be considered specifically distinct) are scarce animals,

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* In the following discussion the taxonomy of Pocock is followed strictly. The genera, however, have been grouped for the present purpose to indicate affinities. This grouping is based upon the work of Pocock and others and includes the author's interpretations.

having been displaced by feral domestics or by hybridization with domestics (*e.g.* *F.* *sylvestris*). They also are rather unspectacular animals from the show point of view and little effort is made to obtain them for display in zoological gardens. As a consequence, no comparison of the species in this genus is possible and probably none will ever be practicable. Two bobcats (*L.* *rufus*) and one European lynx (*L.* *lynx*) have been offered catnip. *L.* *lynx* and one of the two *L.* *rufus* gave a full intensity response. Once again, no great attempt is made to procure lynxes for zoos, usually a maximum of one being displayed. However, the fact that catnip has been used so successfully for trapping bobcat and lynx that it is available commercially expressly for this purpose suggests that responding among these species is commonplace. Two servals (*Leptailurus* *serval*) were tested with negative results. One specimen of Pallas' cat (*T.* *manul*) was offered catnip with negative results. Five pumas (*P.* *concolor*) were tested for catnip response. Two males gave full intensity responses while one was indifferent. One female gave a weak response and one was inconclusive.

A group of closely related Old World lesser cats includes the genera *Prionailurus*, *Protofelis*, *Zibethailurus*. An 18 year old leopard cat (*Prionailurus* *bengalensis*) showed no interest in catnip. Of two golden cats (*Protofelis*) offered catnip, one, *P.* *temmniki* (African), gave a full response while *P. aurata* (Asiatic) gave no response. Two fishing cats (*Zibethailurus viverrensis*) tested gave inconclusive but probably negative results. One was extremely nervous while the other was very defensive.

Other New World lesser cats include *Leopardus*. Personal testing of five ocelots (*L. pardalis*) proved four to be responders and one to be a non-responder. Data gathered by questionnaire gave four responders and 13 non-responders.* Six margay cats (*L. weidii*) personally observed, yielded four responders and two non-responders. Three additional non-responders were reported through the above-mentioned questionnaire.

Herpailurus and *Dendrailurus* are two New World forms of uncertain affinities. Four jaguarundis (*H. jaguarundi*) were tested with negative results as was a single pampas cat (*D. pajeros*). This latter animal, however, was of such an intractable nature that the test must be considered inconclusive.

The clouded leopard (*Neofelis nebulosa*) is a somewhat aberrant Asiatic feline. A single individual gave a probable positive response. This animal was so timid and nervous that it would not go into a response while being observed, although it approached the catnip leaves with

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* The author has reservations about the validity of the data gathered by this method.

obvious curiosity. Subsequently the leaves were found strewn about the cage apparently having been rolled in.

Discussion: In the absence of contrary evidence, it would appear to be safely concluded that a typical high intensity catnip response is given only by Felids. The fact that both Pantherines and Felines are represented by several species which characteristically give high intensity catnip responses indicates that this character is a primitive one shared by a common ancestor of such diverse forms as house-cats and lions, or lynxes and snow leopards, etc. On the other hand, the present paucity of data allows no certain conclusion to be drawn as to the inclusion or exclusion from this group, of Acynonychinae (cheetas), although preliminary results with three individuals were negative. Such data would be of great interest from the taxonomic point of view.

Within the Pantherinae, the lion (P. leo) and tiger (P. tigris) are almost universally recognized as being the most closely related species. The anatomical and other evidence (Pocock, 1929; Merriam & Stock, 1930; Leyhausen, 1950) draw attention to this fact. It is therefore of some interest to note that with respect to catnip the tiger differs greatly from the lion, the latter being more typical of the sub-family. These two species, which until very recently were broadly sympatric, were never known to hybridize in nature although they do so with great facility in captivity. In this connection a single "ligeress" (female hybrid of a lion X tigress) has been reported to be indifferent towards catnip.[*] The responses of her parents, unfortunately, are unknown. No serious explanation of the reproductive barrier in the wild has ever been offered. One immediately suggests itself from the present work.

It has been previously hypothesized that catnip and certain other molecules mimic a pheromone of the domestic cat which releases courtship display. This same argument is now extended to include all species which give such a response. This would appear to be a reasonable assumption inasmuch as the catnip response of these species also resembles components of their courtship display where the latter has been observed (Cooper, 1942; Leyhausen, 1950).

Nothing can as yet be said about the species specificity of the postulated pheromones beyond the fact that nepetalactone shares a strong common functional capacity with those of all species of Pantherines (with the exception of the tiger) and with many species of Felines. Nepetalactone, matatabilactone (Sakan, *et. al.*, 1959; 1960) and actinidine (Sakan, *et. al.*, 1959; 1960) have all been systematically investigated to some extent[†] and no obvious

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[*] Personal communication from Gerald de Bary, Director, Hogle Zoological Garden, Salt Lake City, Utah.

[†] It was the author's privilege to view a short color moving picture at the invitation of Dr. Akiru Fujino of the responses of lion, leopard and jaguar to matatabilactone and actinidine.

differences in response to these molecules have been noted from species to species. It would appear likely that most species produced a similar pheromone to elicit courtship and utilize other parameters for conspecific recognition. Only when such other parameters become ambiguous would this primitive and presumably conservative mechanism be altered to insure reproductive isolation. Hence, among the Pantherinae, the two most closely related species (lion and tiger) show significant differences in their response to nepetalactone while the most divergent species (snow leopard and lion) are similar in this response.

Finally, it seems necessary to dispose of one possible explanation for the catnip response and in so doing add support to the contention that nepetalactone is mimicking a pheromone. Plants of the genus Nepeta are indiginous to the Old World (it is at present unknown if all or even many of the species produce volatile substances which are active in eliciting a courtship-like response from cats). Yet various New World cats show a sensitivity to catnip which is no less intense than their Old World relatives (e.g. jaguar, puma, bobcat, lynx, ocelot, margay cat, etc.) This appears to rule out the possibility that the plant plays an essential role in the reproductive affairs of Felids. It has been noted, however, that at least one other plant, matatabi (Actinidia polygama), from Japan, produces molecules which elicit catnip-like responses as reported by Sakan, et. al. (1959; 1960). This, however, does not seriously weaken the argument that the presence or absence of "active" plants does not relate to the retention or loss of sensitivity to nepetalactone and related compounds. This is especially clear where sympatric species show a difference in sensitivity (e.g. lion and tiger were broadly sympatric until a century ago).

General Conclusion:

The main hypothesis advanced in this thesis is that catnip and certain other materials coincidentally mimic a pheromone of the cat which is capable of eliciting or reinforcing specific courtship displays. The evidence supporting this contention is derived from many unrelated sources.

1) The catnip response and courtship display are very similar.

2) Field observations indicate that catnip-like displays occur at sites known to have been marked by the urine of tomcats.

3) Catnip-like activity has been found in ether extracts of tomcat urine.

4) Cross fatigue of the catnip response and courtship display appears to occur.

5) The "central neural substrate" of the catnip response and courtship behavior appear to be intimately related.

6) Mounting activity of two male snow leopards was provoked by catnip responses of two females.

7) There is no correlation between the distribution of plants having catnip-like activity and that of cats which are sensitive to them.

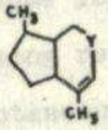
8) There is a striking difference in response to catnip between lions and tigers which may be due to the unknown

mechanism which reproductively isolated these two species in nature (but not in captivity).

No explanation other than the one here advanced has been found to be consistent with all of the evidence. Perhaps the most important aspect of this study is the promise it holds that many fundamental problems of speciation among the Felids can be solved. It would also be profitable to look for, or look more closely at, similar phenomena in other mammalian groups.

Summary:

1) The gross motor aspects of the catnip response in the domestic cat are described in detail. Four typical stages of response have been identified, 1) sniffing, 2) licking and chewing with head shaking, 3) chin and cheek rubbing and 4) "head-over" roll and body rubbing. These represent an increasing intensity scale. Additional patterns seen occasionally are digging or pawing, scratching, salivating, washing or grooming.

2) The compounds thus far identified as eliciting a catnip response are reviewed and their molecular "common denominator" pointed out. 

3) The analysis of an extensive pedigree indicates that the catnip response (nepetalactone sensitivity) is inherited as an autosomal dominant.

4) A survey of a random breeding cat population (Boston, Massachusetts) showed 69% of the population to be responders and 31% to be non-responders. From these data a frequency of .45 responding ($+^{\underline{n}}$) and .55 non-responding (n̲) alleles was calculated.

5) The components of chin and cheek rubbing and "head-over" roll and body rubbing of the catnip response and courtship display of the cat are noted to be virtually identical.

6) A fully developed catnip response usually begins to appear at six to seven weeks of age in cats that are genetically destined to be responders. Prior to this kittens often show fear and avoidance responses to catnip.

7) The catnip response is mediated by an olfactory input, and it has been possible to distinguish a fatigue of the catnip response from olfactory adaptation.

8) The effect of estrogen injection upon the catnip response in six female cats varied from nil (in animals characterized as genetically insensitive to catnip) to a dramatic increase of intensity in responders. Observations indicate that estrogen causes some immediate increase in intensity of catnip response among responding animals but that the response wanes as spontaneous courtship display reaches a peak. This suggests that a "hetero-specific" fatigue between courtship display and the catnip response may occur.

9) Catnip-like activity has been found in urine extracts from a tomcat. This finding has led to the hypothesis that catnip mimics a pheromone of the cat produced to reinforce or release courtship display. It is speculated that the unknown substance from tomcat urine will share the configuration of the common denominator of the various compounds capable of eliciting a catnip-like response.

10) Catnip sensitivity was abolished by the bilateral lesions of the stria terminalis and the suprachiasmatic

nucleus. This evidence is interpreted as meaning that an afferent supply from the amygdala, while not necessarily in the direct pathway from the olfactory region to the "sex behavior center," is indispensible for the maintenance of this sensitivity. It is also supposed that the supra-chiasmatic nucleus, while not coincident with the "sex behavior center," is closely related structurally and functionally to it and probably serves as an integrating center for this particular extrinsic stimulus.

11) The results of testing 22 animals in the family Viverridae (10 genera in 6 sub-families) indicate that the typical catnip response is absent from this family. Three individuals in the family Hyaehadae tested with catnip showed no interest. It is concluded from these data and observations that the catnip response is restricted to the Felidae.

12) Among the Felidae in the sub-family Pantherinae, all species except the tiger characteristically give high intensity, typical catnip responses. Only three cheetas (sub-family Acynonychinae) have been tested. All were indifferent. Numerous species of the sub-family Felinae, representing a diversity of forms, have given responses. From this evidence it is concluded that sensitivity to catnip is a primitive characteristic in the Felidae. The interpretation of the absence of responses from cheetas must await confirmation as to their inclusion or exclusion

from the responding category.

13) The striking difference between the responses to catnip of the closely related lion and tiger is explained by suggesting that this difference may be related to a reproductive isolating mechanism.

14) The hypothesis that the catnip plant (or other "active" plants) contributes to the reproductive habits of cats is rejected because no relationship could be found between the distribution of the plant and animals which are sensitive to it.

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