days 1 to 9 after conception (44 ± 0.87 days, mean ± standard error) compared to the controls (38 ± 0.68 days). The delay was not observed after galactose exposure later in gestation.

We conclude that prenatal exposure to galactose or its metabolites substantially decreases oocyte number in the rat. The most striking effects were observed when exposure occurred during the premeiotic stages of oogenesis. This reduction in oocyte number might result from interference with germ cell migration, proliferation, or differentiation. The data suggest that the effects of galactose on the rat ovary are less pronounced after the initiation of meiosis. The reduction in the number of oocytes in prenatally treated rats is clearly not related simply to growth reduction secondary to galactose administration.

Prenatal galactose or its metabolites primarily reduce the number of small oocytes and follicles. The absence of effects on the medium and large follicles is unexplained but not without precedent for other ovotoxic agents. Mandl (*9*) reported that radiation reduced the number of small follicles 90 percent in the rat, and Krarup (*10*) noted oocyte destruction by postnatal exposure to polycylic aromatic compounds—without reduction in the number of medium or large follicles.

Prenatal toxic effects on oocytes or their precursors by galactose or its metabolites could be a cause of premature ovarian failure in human galactosemia. Restriction of galactose intake in pregnancies at risk for this disease might reduce or prevent fetal ovarian damage and subsequent premature ovarian failure, although galactose synthesized by the fetus or mother could still have toxic effects (*3*).

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Pheromone Orientation: Role of Internal Control Mechanisms

Abstract. *Male American cockroaches walk a zigzag path upwind toward a source of female sex pheromone. Although the maximum width of the pathway is regulated by the width of an odor plume, many turns are made before the edge of a wide plume is encountered. In addition to the pheromone regulation of the insect's orientation movements, an internal mechanism appears to influence the zigzag turning pattern.*

It is generally agreed that orientation of insects toward distant sex pheromone sources is not controlled by chemotaxis, that is, by the concentration gradient of the odor, but rather by an indirect anemotactic (wind-directed) mechanism (*1*). Orientation of both walking and flying insects is never observed to be straight or direct, but occurs in irregular zigzag or sinusoidal pathways that can be characterized by two components, namely, turns (*2*) and straighter connecting portions. The mechanism controlling orientation during the straight portions is believed to entail the use of the wind direction to establish the insect's course and to correct deviations. The mechanisms that control or interact to regulate turning, however, are poorly understood.

I used a time-lapse camera system (*3*) to photograph individual male cockroaches orienting to synthetic female sex pheromone in a wind tunnel. By analysis of the insects' pathways, I compared the position of turning with the boundaries of the plume and determined the effect on the pathway of changing the width of the plume. This analysis could provide direct evidence for the pheromone regulation theory, which proposes that a turn is made only when the insect detects the decrease in odor concentration at the edge of the plume (*4*). An alternative theory is that the turning pattern is influenced or generated internally within the insect's nervous system (*5*).

An individual male was placed in a wire cage centered 0.3 m from the downwind end of a 2.5-m wind tunnel (wind speed, 22 cm/sec). After a period of 12 to 15 minutes to allow the male to adjust to its new surroundings, the side door of the cage was opened, and the male was observed for a 2-minute control period during which no pheromone was presented. Males generally ceased moving in the cage several minutes after being placed in the tunnel and usually remained motionless during the control period. A dispenser containing synthetic female sex pheromone, (±)-periplanone B (*6*), was then placed in the tunnel 2 cm above the floor and centered at the upwind end. Arousal, elicited after 0.5 to 2.0 minutes, was characterized by rapid antennal movements and locomotion. The male would then leave the cage and turn upwind, indicating a positive anemotactic polarization of the odor plume (*7*). While proceeding upwind in the narrow plume, each cockroach tended to remain within the boundaries of the plume and close to the center line of the wind tunnel (Fig. 1, B to D). Pathways in the wide plume varied considerably and included wide zigzags traversing the entire width of the plume (Fig. 1F), turns at random points within the plume (Fig. 1G), and relatively direct upwind paths characterized by a long-period sine pattern (Fig. 1G).

The coordinate positions of the insect were entered into a computer by projecting the photographic negative onto a bit-pad digitizer. Coordinates were then aligned and scaled according to reference points marked on the wind tunnel floor. Computer programs with x and y coordinates designating the distance from the source and the distance from the center axis of the plume, respectively, were used to determine the anemotactic angle (upwind angle, defined by successive data points), the turning rate (the angle made by three successive data points), the position of sign-reversal turns, and the locomotion rate (Table 1). Orientation pathways were graphically displayed superimposed on the boundaries of the plume, which were calculated from digitized photographs of white titanium tetrachloride smoke released from the same dispensers as the pheromone (*8*). The narrow plumes were similar in dimension and structure to those described previously (*9*).

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Table 1. Movement characteristics of male American cockroaches in a narrow or wide sex pheromone plume. Values are means ± standard error for ten trials.

Movement parameter	Plume width	
	Narrow	Wide
1. Walking speed (cm/sec)	5.5 ± 0.6	5.1 ± 0.5
2. Turning rate (degrees/turn)	23.1 ± 1.3	19.9 ± 2.1
3. Anemotactic angle (degrees)	21.2 ± 2.8	25.5 ± 3.4
4. Number of sign-reversal turns per pathway	20.5 ± 2.3	14.2 ± 1.2*
5. Distance between sign-reversal turns (cm)	11.8 ± 1.0	17.3 ± 1.6*
6. Angle of sign-reversal turns (degrees)	33.3 ± 3.9	34.1 ± 4.7
7. Maximum pathway width (cm)	14.7 ± 2.7	26.4 ± 5.2*
8. Variance of each data point from center plume axis	20.3 ± 5.8	109.9 ± 35.3*
9. Distance of sign-reversal turns from center plume axis (cm)	2.9 ± 0.5	8.4 ± 1.9*

* Significantly different from the narrow plume value (t-test; $P = .05$).

Several parameters, such as the walking and turning rates and the mean absolute anemotactic angle, were similar for the narrow and the wide plume (Table 1, items 1 to 6), whereas the maximum width of the pathway, the variance of points from the center axis of the plume, and the location of sign-reversal turning points were significantly larger in the wide plume (Table 1, items 7 to 9). Although the movement characteristics from point to point in the two types of plumes were similar, the cockroaches in the wide plume tended to move further from the center line before initiating a sign-reversal turn. Not all zigzags entirely crossed the wide plume, and the average sign-reversal turning point was considerably within the plume boundaries (*10*).

From these results, two conclusions can be drawn. (i) The width of the pheromone plume has a direct effect on the width of the orientation pathway, and (ii) many sign-reversal turns are made before the insect encounters the edge of the plume. Although the first conclusion supports the pheromone regulation model, the second indicates that this model does not completely explain the observed orientation pathways.

The concept that an internal mechanism controls turning also explains other phenomena observed in flying moths. When pheromone release is stopped abruptly, moths continue to zigzag for 1 or 2 seconds in a pattern indistinguishable from that elicited when the pheromone was present (*11*). Moths also cast back and forth after losing contact with a pheromone plume, zigzagging with a larger anemotactic angle and progressively longer paths than those observed under pheromone-stimulated conditions (*11*). As these behaviors occur after the complete removal of pheromone from an airstream, the turning pattern must be generated by an internal mechanism or program rather than by the perception of a change in pheromone concentration.

The orientation system for the control of turning during anemotaxis must be more complex than those that have been previously suggested and should include (i) odor-regulated sign-reversal turns, (ii) stochastic, internally initiated turns, (iii) internally controlled turns patterned by a previous stimulus, and (iv) internally generated patterns of turns. A challenging aspect of the study of this orientation system is understanding how these behaviors are adapted to more variable, real environmental conditions. The evidence for internally generated patterns suggests mechanisms that may maintain the orientation course after temporary disruptions in the plume caused by turbulence or shifting winds and that may allow a more efficient path to be taken than one determined by always crossing from one side to the other of a wide pheromone plume.

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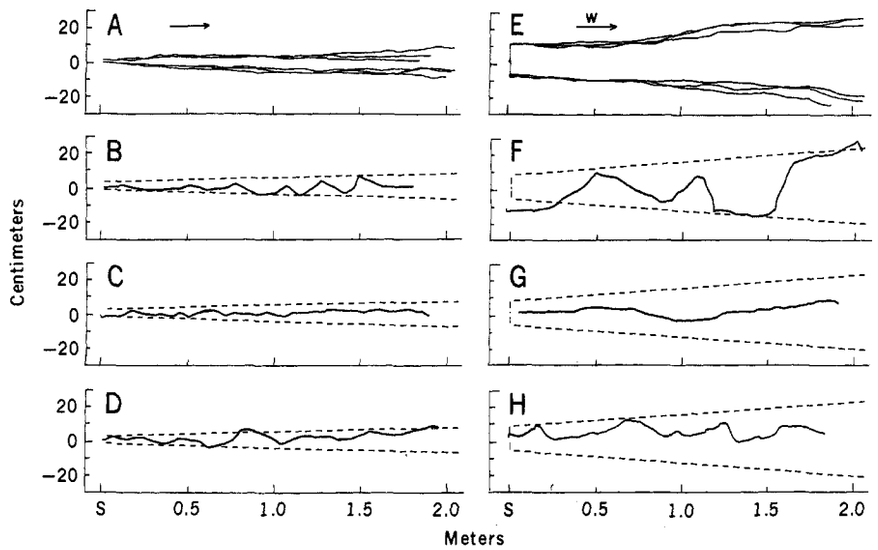

Fig. 1. Orientation pathways of male American cockroaches and smoke plume boundaries representing two different stimulus conditions. (A) Superimposed boundaries of three narrow smoke plumes. (B to D) Pathways of three different cockroaches orienting to synthetic sex pheromone in a narrow plume. (E) Superimposed boundaries of three wide plumes. (F to H) Pathways of three different cockroaches orienting in a wide plume. Computer-reconstructed drawings are rescaled from overhead photographs (35 mm). Arrow (*W*) represents the wind direction (22 cm/sec). Dashed lines indicate the average boundaries of the plumes. Outer borders are the dimensions of the wind tunnel and are scaled with reference to the pheromone source (*S*).

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2. During the straight portions of the pathway, the insect normally maintains a specific angle to the wind. Discussion of turning is restricted to turns that change the direction of the pathway to the left or right. Directly upwind is referenced as zero degrees, and the anemotactic angle may be right (+) or left (−). The insect can establish the zigzag pathway by initiating a periodic reversal of the sign of the anemotactic angle. Thus if the insect is moving left to right upwind at an angle of +30 degrees, changing the anemotactic sign would turn the insect toward −30 degrees moving right to left.
3. The camera system is described by W. J. Bell and T. R. Tobin [*J. Insect Physiol.* **27**, 501 (1981)].
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5. This theory derives from observations that silk moths and cockroaches execute frequent and spontaneous turns while walking on a servosphere apparatus (locomotion compensator) in an airstream uniformly permeated with pheromone [E. Kramer, in *Olfaction and Taste*, D. Denton and J. D. Coghlan, Eds. (Academic, New York, 1975), vol. 5, p. 329; W. J. Bell and E. Kramer, *J. Chem. Ecol.* **6**, 287 (1980)]. Pathways of flying moths also indicate that turns are made well within the estimated boundaries of the plume [(*10*); J. S. Kennedy, A. R. Ludlow,

C. J. Sanders, *Nature (London)* **288**, 475 (1980)].

6. The narrow plume dispenser contained 1.0×10^{-5} μg of synthetic (±)-periplanone B adsorbed onto 1 cm^2 of Whatman No. 1 filter paper; the wide plume dispenser contained 5.0×10^{-5} μg adsorbed onto a 15.0 by 0.5 cm filter paper strip. Males oriented in a similar manner to narrow plume sources of 10^{-6} to 10^{-3} μg of (±)-periplanone B.
7. *Periplaneta americana* males orient downwind on a servosphere in an air current of 24 cm/sec without pheromone [W. J. Bell and E. Kramer, *J. Insect Physiol.* **25**, 631 (1979)]. When sex pheromone is present in the air current, a distinct behavioral change is stimulated, and the males orient upwind.
8. Mean plume widths ± standard error at 0.5, 1.0, 1.5, and 2.0 m from the source for the narrow plume ($N = 5$) were 6.18 ± 0.5, 8.16 ± 0.9, 8.25 ± 1.0, and 13.37 ± 5.9 cm, respectively, and for the wide plume ($N = 5$) were 20.85 ± 1.0, 27.99 ± 0.5, 37.75 ± 0.8, and 44.03 ± 1.5 cm, respectively.
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10. A possible explanation of these turns is that the insect encounters nonuniformities of concentration in the plume. This may occur near the more irregular boundaries, as suggested by R. H. Wright [*Can. Entomol.* **30**, 81 (1958)], but is not expected to be significant at the central portion of the plume where many of the turns are observed. It is not known if a filament could actually be detected by a cockroach or whether it perceives only a spatially averaged response from the 5.0-cm antennae. It is equally unknown if a cockroach can temporally perceive a concentration profile across the width of the plume.
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Endogenous Opiates and Stress-Induced Eating

In discussing their results on an animal model developed in our laboratory (*1*), Morley and Levine state that the opiate antagonist naloxone attenuates stress-induced eating in rats (*2*). This model has a number of similarities to emotionally related overeating in humans (*3*), and the reported involvement of endogenous opiates suggests new treatments for this disorder.

We have been unable to repeat Morley and Levine's observations in a series of eight experiments with both Sprague-Dawley and Wistar rats given two doses of naloxone (4 and 10 mg/kg) and test-fed with Laboratory Chow and palatable chocolate chip cookies (*4*). In no instance did we observe an attenuation after naloxone in the amount eaten or the duration of food-directed oral behavior during tail-pinch stress (TP).

A possible reason for these contradictory results may be found by considering gnawing and eating as distinct behaviors. The more time that is spent in gnawing (without ingestion), the less that can be spent in biting and chewing (with swallowing). Morley and Levine found that, while only 20 percent of their animals gnawed prior to naloxone administration, this increased to 100 percent after the drug was given (*2*). Thus, their conclusion that "naloxone suppresses ingestive behavior without affecting gnawing" is misleading since they actually appear to have observed an increase in gnawing behavior at the expense of eating.

We think there is a logical reason that increased gnawing might have been observed. Animals that normally eat quietly during mild TP may be induced to shred or demolish food pellets by increasing the pressure to painful levels (*1*). We thus interpret Morley and Levine's statements that "a number of these rats demolished one or both of the pellets without ingesting" and "rats squeaked at tail-pinch pressures below those necessary to induce eating, gnawing, or licking during the control trial" as evidence for pain. Naloxone may, for example, have lowered a nociceptive threshold such that pressures that ordinarily are compatible with eating during TP may now become painful and produce gnawing or shredding of the food. Alternatively, naloxone may have potentiated the release of striatal dopamine (DA) during TP (*5*), in analogy to its enhancement of DA release by amphetamine and increased stereotypy (*6*). We have discussed the similarities between the neural effects of amphetamine and TP (*1, 7*), and in either case an excessive release of DA may be conducive to gnawing instead of eating.

In addition to facilitating the effect of the indirect DA agonist amphetamine, naloxone also potentiates the actions of the DA antagonist chlorpromazine (*8*). We found that low doses of the DA antagonist haloperidol attenuate TP-induced oral behaviors (*1*) and we examined whether naloxone would potentiate that effect. Our results support the concept that, while naloxone alone again had no effect upon TP behavior, a combination of naloxone plus haloperidol compared to haloperidol alone significantly suppressed oral behaviors (*9*). Our data suggest that any effects of naloxone on TP behaviors may be mediated indirectly through DA. There is also abundant biochemical and anatomical evidence for interactions of enkephalin and DA (*10*). In addition, the pharmacological specificity of naloxone has been questioned (*11*), and we thus believe that Morley and Levine's unequivocal conclusion that "stress-induced eating is mediated through endogenous opiates" is highly speculative.

Morley and Levine say that their hypothesis was supported by the observations that chronic TP produced "self-addiction," which was manifested by naloxone-precipitated withdrawal symptoms (*2*). We have been unable to reproduce this effect in experiments with rats given chronic TP in the presence and absence of food. This detail was not specified in Morley and Levine's report and is important because rats pinched in the absence of food show considerable agitation and escape attempts (*1*). Such attempts result in tail damage, and continued TP is clearly very painful to the animals. Rats pinched in the presence of food do not exhibit such marked pain responses after long-term TP. Our protocol was similar to that of Morley and Levine (*2, 12*). Neither TP group in our experiment exhibited marked withdrawal behaviors when tested after day 10 of TP (mean 0.53 per 15 minutes after saline and 0.68 per 15 minutes after naloxone). In contrast, the morphine-dependent rats exhibited 15.0 vigorous withdrawal behaviors in the 15-minute period after naloxone. We thus find no evidence of opiate dependence in rats given long-term TP, even when this involved pain.

In addition to these troublesome failures to confirm Morley and Levine's conclusions in our laboratory, we feel that it is necessary to comment on some other inadequacies in their presentation. The most important of these are inaccurate or misleading attributions to others (*13*), and the failure to distinguish their own data from those of others (*14*). Their acknowledgement to one of us [reference 19 in (*2*)] was without our knowledge or endorsement of the results or interpretations.

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4. Groups consisted of four to eight adult male rats that had been screened for reliable TP-induced eating. This screening procedure, typically performed on the day preceding the experiment, apparently is the only major difference between our method and that of Morley and Levine (*2*). We have also performed an experiment similar to that described by Lowy *et al.* [M. T. Lowy,

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