Physiology & Behavior, Vol. 50, pp. 95–99. © Pergamon Press plc, 1991. Printed in the U.S.A. 0031-9384/91 $3.00 + .00

Prostaglandin E_2 Accelerates Sexual Behavior in Male Rats

MARK S. BLUMBERG

Department of Psychology, Indiana University, Bloomington, IN 47405

Received 28 August 1990

BLUMBERG, M. S. *Prostaglandin E_2 accelerates sexual behavior in male rats*. PHYSIOL BEHAV **50**(1) 95–99, 1991.—Sexual behavior in male rats is accompanied by an increase in body temperature of 1°C. It has been suggested that this increase may be, at least in part, a febrile response mediated by the endogenous central release of prostaglandins of the E series (PGE). This putative release of PGE could also affect the expression of sexual behavior, a possibility that was tested in the present experiment. PGE_2 was infused into the cerebral aqueduct and sexual behavior and hypothalamic temperature were monitored. PGE_2 infusion raised hypothalamic temperature and decreased the postejaculatory interval and ejaculation latency. The exact cause of this acceleration of sexual behavior cannot as yet be determined.

Male sexual behavior Prostaglandins Fever Brain temperature Hypothalamus

COPULATION in the male rat is accompanied by an increase in body temperature and hypothalamic temperature of approximately 1°C (10). Following ejaculation, the hypothalamus cools more rapidly than the body, a phenomenon known as "selective brain cooling" (13). This selective cooling of the hypothalamus is likely due to alterations in vasomotor tone within the nasal mucosa (12). Specifically, during copulation and as body temperature and hypothalamic temperature are increasing, the rat's mucosal blood vessels constrict. After ejaculation, these mucosal vessels dilate, resulting in the convective cooling of blood draining the nose; this blood, once it has flowed to the cavernous sinus at the base of the brain, can cool nearby brain tissue through conductive heat exchange (13).

Although this nasal vasomotor mechanism can account for small (±0.3°C) fluctuations in brain temperature, it cannot account for the 1°C rise in body temperature that occurs during copulation. An explanation of this increase can take at least two forms. First, it is possible that the act of mounting and intromitting during copulation increases body temperature. In other words, the copulation-induced increase in body temperature may be an exercise effect. Alternatively, it is possible that the autonomic arousal that accompanies sex results in the activation of heat-gain mechanisms and perhaps also a raising of thermoregulatory set-point. In other words, copulation may induce a fever (7,26).

The fact that nasal-mucosal vasoconstriction persists as body temperature increases during copulation indicates that the rat is not attempting to lose heat, contrary to what one would expect of an exercising animal (35). This cannot, however, be taken as strong evidence for an increase in thermoregulatory set-point. For example, guinea pigs constrict nasal-mucosal blood vessels at the onset of forced exercise; only after hypothalamic temperature rises to approximately 40.5°C do the mucosal vessels dilate (14). In sheep, mucosal vasoconstriction can be elicited by a variety of arousing stimuli (5). It seems likely, therefore, that mucosal vasoconstriction in copulating rats is a consequence of sympathetic arousal and not a reflection of thermal state.

Nonetheless, there are reasons for suspecting that the temperature increase that accompanies copulation is not merely the result of increased activity. For example, Andrews (3) has shown that exposure of Montane voles (*Microtus montanus*) to a novel environment results in a 1°C increase in body temperature and that an agonistic encounter within that novel arena results in a 2°C increase. Furthermore, these increases in temperature appear to be caused by adrenergic activation resulting in both heat conservation and metabolic heat production (2). Rats exposed to a large, open arena (open field stress) also show a greater than 1°C increase in body temperature that can be partially (approximately 50%) blocked by antipyretics (22,34). Thus it is possible that at least part of the copulation-induced increase in body temperature is the result of metabolic heat production, not simply exercise.

An accumulation of evidence now indicates that prostaglandins of the E series (i.e., PGE_1 and PGE_2) are neural mediators of the febrile response (36). Support for the role of PGE in fever is strong: PGE levels in third ventricular cerebrospinal fluid rise significantly during fever (6) and intracerebroventricular infusions of PGE raise body temperature (39). In addition, drugs that inhibit prostaglandin synthesis are also antipyretics; that is, prostaglandin synthesis inhibitors are capable of preventing fever as well as lowering fever once it has occurred (17,38). PGEs appear also to raise thermoregulatory set-point (32).

If copulation induces a fever, then perhaps copulation results in the central release of PGE (7). Moreover, this putative release of PGE could affect sexual behavior in a number of ways. For example, the preoptic/anterior hypothalamus (PO/AH) is important for the expression of the fever response [e.g., (39)] as well as sexual behavior [e.g., (21)]. Furthermore, there are neurons within the PO/AH that may have dual functions in thermoregulation and sexual behavior (33). Thus one might expect exogenous infusion of PGE to affect sexual behavior. This possibility is tested in the present experiment.

METHOD

Nine sexually experienced male Wistar rats, 125–165 days of age at the time of surgery, were used. These males were housed individually in standard laboratory cages under a 12L:12D lighting schedule.

Prior to the beginning of the experiment, each male was anesthetized with ketamine hydrochloride (87 mg/kg) and xylazine hydrochloride (13 mg/kg) and equipped with a battery operated telemetric thermosensor (Mini-Mitter, Inc., Sunriver, OR). This thermosensor was implanted stereotaxically in the anterior hypothalamus using the atlas of Paxinos and Watson (30). The coordinates were 0.6 mm posterior to bregma, 0.5 mm lateral to the midsagittal suture and 8–9 mm below the surface of the horizontal skull. A guide cannula was also implanted stereotaxically in the cerebral aqueduct. It was implanted on the midline, 8.6–8.8 mm posterior to bregma and 5.2–5.4 mm below the surface of the skull at bregma. The cannula was fitted with a screw top and with a stylet to keep it unobstructed between infusions. Both the thermosensor and cannula were attached to the skull using dental cement and two skull screws. The experiment began at least six days following surgery, by which time all the animals were within 3% of their presurgery body weight.

It should be noted that the cerebral aqueduct was chosen for cannula placement because access to the 3rd ventricle or the lateral ventricles was restricted by the presence of the temperature sensor in the anterior hypothalamus. The cerebral aqueduct was an acceptable choice because PGE infusion resulted in the raising of hypothalamic temperature. With this bioassay, it could be concluded that PGE was delivered to the hypothalamus because the only brain sites that produce a rise in temperature in response to direct PGE injection are the PO/AH region and the ventromedial hypothalamus (27, 39, 41).

Each thermosensor was calibrated prior to surgery and then again at the end of the experiment. Signals from the thermosensor were received by an AM radio, processed to remove noise, and then fed into a frequency counter. Temperature changes in intervals of 0.03 to 0.06°C were detectable with this system.

The drug solution was prepared by diluting 1 mg of PGE_2 (Sigma) in 1 ml of pyrogen-free saline alone or in a mixture of 0.1 ml 95% ETOH and 0.9 ml sterile saline. The control solution was vehicle alone. Both the drug and control solutions were aliquotted and stored in a freezer until used.

Each male was tested twice, once following the infusion of 8–12 μg PGE_2 and once following the infusion of vehicle. The experimental and control tests were counterbalanced across animals and were conducted at least 6 days apart.

Prior to the introduction of a receptive female, an experimental male was placed in a semicircular arena for a minimum of fifteen minutes. After the animal's hypothalamic temperature had stabilized for at least five consecutive minutes, the animal was taken from the arena, the top of its cannula was removed, and an injection cannula, connected by silastic tubing to a microliter syringe, was inserted into the guide cannula. Solution (8–12 μg of PGE_2 or 8–12 μl of vehicle) was infused at the rate of 12 μl/min. Following infusion the animal was returned to the arena.

Approximately twenty minutes after PGE_2 infusion, hypothalamic temperature peaked. At this time, a sexually receptive female was placed in the arena with the male. In the PGE_2 condition, the female was introduced only if the male's hypothalamic temperature exceeded 40°C. In one case, this criterion was not met, the test was aborted, and the animal was retested successfully 2 days later.

Copulation was followed through the first intromission of the fourth ejaculatory series. The following measures were derived from the raw data: mount latency (the time from introduction of the female to the first mount or intromission); intromission latency (the time from introduction of the female to the first intromission); mount frequency (the number of mounts without intromission); intromission frequency (the number of intromissions prior to ejaculation); ejaculation latency (the time from the first intromission to ejaculation); postejaculatory interval (the time from ejaculation to the first intromission of the next copulatory series); and postejaculatory interval-mount (the time from ejaculation to the first mount or intromission of the next copulatory series). Hypothalamic temperature was monitored throughout the test. All observations were carried out under red light illumination during the dark phase of the 12L:12D lighting schedule. The ambient temperature was 21–23°C and the relative humidity 30–50%.

TABLE 1

HYPOTHALAMIC TEMPERATURE (°C) BEFORE AND AFTER THE ICV INFUSION OF PROSTAGLANDIN E_2 OR VEHICLE

Phase of Experiment	Vehicle	PGE_2
Before Infusion (n=9)	38.3 ± 0.1	38.2 ± 0.1
Introduction of Female (n=9)	38.6 ± 0.1	40.9 ± 0.1*
First Ejaculation (n=9)	39.2 ± 0.1	40.7 ± 0.1*
Second Ejaculation (n=9)	39.2 ± 0.1	40.5 ± 0.1*
Third Ejaculation (n=8)	39.2 ± 0.1	40.2 ± 0.1*

*$p<0.0001$ in relation to vehicle.
All comparisons are by the paired t-test (two-tailed). Mean ± SEM.

At the conclusion of the experiment, histology was performed on three of the males to check for placement of the thermosensor. Two of these males were also checked for placement of the cannula. Proper placement within the anterior hypothalamus and cerebral aqueduct was confirmed in these cases.

In the measurement of copulatory behavior, both interval data (e.g., ejaculation latency) and frequency data (e.g., intromission frequency) are collected. Since the intervals separating behavioral events are not distributed normally, nonparametric statistics are appropriate (18,24). The Wilcoxon matched-pairs signed-ranks test was used to test the interval data. Frequency data were also analyzed using the Wilcoxon matched-pairs signed-ranks test while temperature data were analyzed using the paired t-test. In addition, log-survivor plots (18) were constructed to further analyze the sexual behavior data. Statistical analysis of the distributions represented by the log-survivor plots was performed using the Generalized Savage (25).

RESULTS

Table 1 shows that PGE_2 raised hypothalamic temperature above control levels prior to the introduction of the female, and this raised temperature was maintained throughout the copulatory test. Specifically, hypothalamic temperature was at least 1°C higher in the PGE_2 condition than in the control condition across all three ejaculatory series. These differences are statistically significant.

Table 2 shows the means and statistical analyses of the copulatory measures for both groups. It can be seen that the most pronounced effect of PGE_2 was a reduction of the postejaculatory interval (PEI) and the postejaculatory interval-mount in all three series. In addition, ejaculation latencies (EL) and intromission frequencies (IF) were reduced following PGE_2 infusion, al-

TABLE 2

MEASURES OF COPULATORY BEHAVIOR FOLLOWING THE ICV INFUSION OF PROSTAGLANDIN E_2 OR VEHICLE

Measure of Copulatory Behavior	Vehicle	PGE_2
Mount Latency (s) (n=9)	75 ± 15	81 ± 24
Intromission Latency (s) (n=9)	119 ± 27	107 ± 32
Mount Frequency		
Series 1 (n=8)	5.0 ± 2.0	6.2 ± 3.2
Series 2 (n=8)	3.2 ± 1.1	2.9 ± 1.3
Series 3 (n=8)	8.8 ± 4.2	3.5 ± 1.6
Intromission Frequency		
Series 1 (n=9)	12.2 ± 2.9	9.3 ± 0.8
Series 2 (n=8)	6.6 ± 0.9	5.2 ± 0.4
Series 3 (n=8)	9.6 ± 2.8	5.9 ± 0.5
Ejaculation Latency (s)		
Series 1 (n=9)	610 ± 110	413 ± 88
Series 2 (n=9)	282 ± 55	213 ± 49
Series 3 (n=8)	441 ± 183	204 ± 52
Postejaculatory Interval (s)		
Series 1 (n=9)	445 ± 57	312 ± 34*
Series 2 (n=8)	453 ± 20	350 ± 29*
Series 3 (n=7)	534 ± 34	404 ± 32*
Postejaculatory Interval-Mount (s)		
Series 1 (n=9)	410 ± 56	311 ± 34*
Series 2 (n=8)	435 ± 20	346 ± 26*
Series 3 (n=7)	533 ± 34	401 ± 31*

*$p<0.05$ in relation to vehicle.
All comparisons are by the Wilcoxon matched-pairs signed-ranks test (two-tailed).

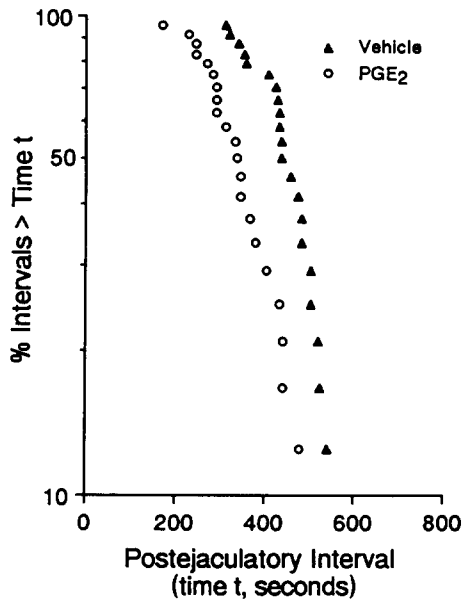

FIG. 1. Log-survivor plots of postejaculatory interval following the ICV infusion of prostaglandin E_2 or vehicle. Postejaculatory intervals through 3 ejaculatory series have been combined. See text for discussion.

though these reductions were not significant under this analysis. Mount latency and intromission latency were not affected.

Figure 1 shows the log-survivor plots for the PEIs across the two conditions; the data from all three ejaculatory series have been combined. First, we see that the plots are linear, indicating that the PEI is distributed exponentially. Second, statistical analysis of the distributions confirms that males were more likely to resume copulation earlier following PGE_2 infusion than following control infusion ($p<0.001$, N=24, Generalized Savage, Mantel-Cox). Third, a comparison of median values shows that PGE_2 reduced the PEI by 23% (Control: median PEI=438 s; PGE_2: median PEI=337 s). Finally, the slopes of the two lines are nearly identical, but the line representing the PGE_2 condition is displaced to the left of the line representing the vehicle condition. This indicates that PGE_2 infusion reduced the PEI by the same amount (approximately 100 s) regardless of the absolute length of the PEI.

Figure 2 shows the log-survivor plots of the ejaculation latencies in the two experimental conditions. Again, the data from all three ejaculatory series have been combined. First, the linearity of the plots indicates that the ELs are distributed exponentially, as expected. Second, statistical analysis of the distributions now shows that males were more likely to have shorter ejaculation latencies following PGE_2 infusion than following control infusion ($p=0.05$, N=32, Generalized Savage, Mantel-Cox). Third, a comparison of the median values shows that PGE_2 reduced the EL by 33% (Control: median EL=286 s; PGE_2: median EL=192 s). Finally, these log-survivor plots contrast sharply with those in Fig. 1. Because the two lines be-

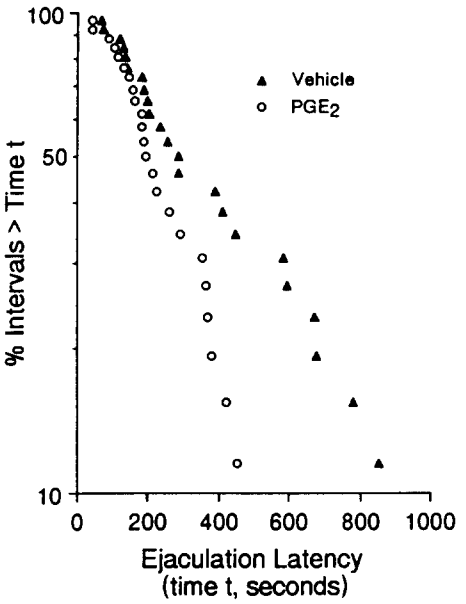

FIG. 2. Log-survivor plots of ejaculation latency following the ICV infusion of prostaglandin E_2 or vehicle. Ejaculation latencies through 3 ejaculatory series have been combined. See text for discussion.

gin diverging for values of t greater than 190 s, these plots indicate that PGE_2 was effective in reducing only those ELs that were longer than approximately 190 s.

A reduction in EL can be caused by reductions in intromission frequency, interintromission interval (III), or both. As stated above, IF was reduced by PGE_2 in all three series, although these differences were not significant. Log-survivor analyses of III were also performed individually on 5 of the animals. The effect of PGE_2 on III was not consistent; the III's were just as likely to be increased by PGE_2 as decreased. Thus the reduction in EL as shown in Fig. 2 might not have a unitary cause.

DISCUSSION

Among the behavioral effects caused by the ICV infusion of PGE_2, one sees sedation and sometimes even catatonia (16). In rats, 4.0 μg of PGE_2 infused into the cerebral ventricles significantly reduces activity for at least thirty minutes (31). I also observed sedation while the animals were heating following PGE_2 administration. During this heating, the animals assumed a prone, hunched position, and often simultaneously emitted the 22 kHz vocalization (9,11). When peak hypothalamic temperature was reached, the animals often began to walk about the cage. Regardless of their previous behavior, however, the introduction of the female served to arouse the males similarly to control animals (i.e., mount and intromission latencies did not differ between groups; see Table 2); no signs of sedation were seen thereafter.

There are a number of plausible explanations for the acceleration of sexual behavior by PGE_2. For example, PGE_2 infusion stimulates the release of luteinizing hormone-releasing hormone (LHRH) (29). Subcutaneous administration of LHRH to gonadally intact rats has been reported either to reduce ejaculation latency (28) or to have no effect (4). LHRH has no effect, however, on the postejaculatory interval (28). Thus, while the shortening of EL by PGE_2 may be due in part to its prior release of LHRH, the reduction of PEI seen here cannot be explained in this way.

Perhaps the acceleration of sexual behavior by PGE_2 is the secondary effect of increased brain temperature. We do know, however, that increasing brain temperature by means other than PGE_2 infusion does not facilitate sex. Specifically, male rats were made hyperthermic by exposure to high ambient temperature (Blumberg and Moltz, unpublished data). When transferred to a mating arena which was at room temperature, these rats copulated very slowly, often stopping to sprawl for many minutes at a time. These animals were clearly heat stressed. In contrast, males infused with PGE_2 showed no signs of heat stress even though their hypothalamic temperatures were over 40.0°C. These results suggest that if an increase in brain temperature does facilitate sexual behavior, it must be accompanied by an increase in thermoregulatory set-point so that competing heat-loss behaviors do not disrupt the expression of sexual behavior. Under these conditions, it is possible that a hot brain can result in the acceleration of sexual and other behaviors. This acceleration could result from the many ways in which brain temperature affects neuronal activity: specifically, raised neuronal temperatures result in increased neuronal metabolism (20), increased conduction velocity (37), decreased refractory period (1), and perhaps increased firing rate (8,40). The effect of brain temperature on the temporal expression of behavior has yet to be investigated adequately.

It is also possible that PGE_2 facilitated sexual behavior by directly stimulating neurons involved in the expression of sexual behavior, independent of its effect on brain temperature. In this regard, it is interesting that while the number of temperature-sensitive cells within the PO/AH is thought to be approximately 45% (33), PGE infusion may alter the firing rate of as many as 95% of PO/AH neurons (19). This suggests that PGE stimulates many temperature-insensitive neurons; these neurons may be involved in the expression of sexual behavior. If so, then it may be possible to dissociate the effects of PGE on sexual behavior and temperature.

An example of the dissociability of behavioral and thermal effects of drugs is provided by experiments on the sleep-promoting effects of endogenous pyrogen (EP) (23). EP infused into the lateral cerebral ventricles of rabbits increased slow wave sleep. This increase was dose dependent and was concomitant with increased body temperature. However, when an antipyretic (anisomycin) was infused simultaneously with EP, the EP-associated increase in body temperature was blocked without affecting the EP-induced increase in slow wave sleep.

To my knowledge, there has been only one other report on the role of PGE_2 in male rat sexual behavior. Clemens and Gladue (15) observed sexual behavior in long-term castrated, and thus sexually inactive, male rats following treatment with subthreshold doses of testosterone alone (that is, doses of testosterone that alone are not sufficient to activate copulation), PGE_2 alone, or subthreshold doses of testosterone and PGE_2 in combination. They found that only the combination of PGE_2 and subthreshold doses of testosterone restored mounting, intromitting, and ejaculatory behavior. Their results "suggest that PGE_2 interacts with testosterone to elicit masculine sexual behavior in long-term castrated rats."

The results presented here show that PGE_2 accelerates sexual behavior in intact male rats. Although PGE_2 was selected for itsfever-causing effects, it has many other effects as well. Therefore, at this time there is no basis for concluding that PGE_2 accelerated sexual behavior by first increasing brain temperature. Unfortunately, there is very little known about the relationship between brain temperature and the temporal organization of behavior. Thus it remains an open question whether PGE_2, and perhaps other neuropharmacological compounds, influence behavior via effects on brain temperature.

ACKNOWLEDGEMENTS

This research formed a portion of a doctoral dissertation submitted to the faculty of The University of Chicago. It was supported by NSF Grant DCB-8700679 and by Biomedical Research Grant PHS507RR007029 to Howard Moltz. I thank Howard Moltz and Martha McClintock for their guidance in the conception, execution, and analysis of this work. I also thank Jeff Alberts for helpful comments on an earlier draft of this manuscript.

REFERENCES

1. Amberson, W. T. The effect of temperature upon the absolute refractory period in nerve. J. Physiol. 69:60–66; 1930.
2. Andrews, R. W. Pharmacological evidence for adrenergic activation of hyperthermic responses associated with psychosocial stimulation. Comp. Biochem. Physiol. 71C:111–114; 1982.
3. Andrews, R. V. Hyperthermic reactions of voles to novel and repetitive psychogenic stimuli. Comp. Biochem. Physiol. 75A:589–592; 1983.
4. Bain, P. A.; Shrenker, P.; Bartke, A. The effect of luteinizing hormone releasing hormone on the copulatory behavior of hyperprolactinemic rats. Horm. Behav. 21:430–439; 1987.
5. Baker, M. A.; Hayward, J. N. The influence of the nasal mucosa and the carotid rete upon hypothalamic temperature in sheep. J. Physiol. 198:561–579; 1968.
6. Bernheim, H. A.; Gilbert, T. M.; Stitt, J. T. Prostaglandin E levels in third ventricular cerebrospinal fluid of rabbit during fever and changes in body temperature. J. Physiol. 301:69–78; 1980.
7. Blumberg, M. S. The interactions between sexual behavior and thermoregulation in the male rat. Unpublished doctoral dissertation. Chicago, IL: The University of Chicago; 1988.
8. Blumberg, M. S. An allometric analysis of hippocampal theta: The significance of brain metabolic rate. Brain Behav. Evol. 34:351–356; 1990.
9. Blumberg, M. S.; Alberts, J. R. On the significance of similarities between ultrasonic vocalizations of infant and adult rats. Neurosci. Biobehav. Rev. 15:383–390; 1991.
10. Blumberg, M. S.; Mennella, J. A.; Moltz, H. Hypothalamic temperature and deep body temperature during copulation in the male rat. Physiol. Behav. 39:367–370; 1987.
11. Blumberg, M. S.; Moltz, H. Hypothalamic temperature and the 22 kHz vocalization of the male rat. Physiol. Behav. 40:637–640; 1987.
12. Blumberg, M. S.; Moltz, H. How the nose cools the brain during copulation in the male rat. Physiol. Behav. 43:173–176; 1988.
13. Caputa, M. Selective brain cooling: An important component of thermal physiology. In: Szelenyi, Z.; Szekely, M., eds. Satellite symposium of the 28th international congress of physiological sciences. New York: Pergamon Press; 1980:183–192.
14. Caputa, M.; Kadziela, W.; Narebski, J. Cerebral temperature regulation in resting and running guinea-pigs (*Cavia porcellus*). J. Therm. Biol. 8:265–272; 1983.
15. Clemens, L. G.; Gladue, B. A. Effect of prostaglandin E_2 on masculine sexual behavior in the rat. J. Endocrinol. 75:383–389; 1977.
16. Coceani, F. Prostaglandins and the central nervous system. Arch. Int. Med. 133:119–129; 1974.
17. Cranston, W. I.; Luff, R. H.; Rawlins, M. D.; Rosendorff, C. The effects of salicylate on temperature regulation in the rabbit. J. Physiol. 208:251–259; 1970.
18. Fagen, R. M.; Young, D. Y. Temporal patterns of behavior: Durations, intervals, latencies, and sequences. In: Colgan, P. N., ed. Quantitative ethology. New York: Wiley; 1978:79–114.
19. Gordon, C. J.; Heath, J. E. Effects of prostaglandin E_2 on the activity of thermosensitive and insensitive single units in the preoptic/anterior hypothalamus of unanesthetized rabbits. Brain Res. 183: 113–121; 1980.
20. Hagerdal, M.; Harp, J.; Nilsson, L.; Siesjo, B. K. The effect of induced hypothermia upon oxygen consumption in the rat brain. J. Neurochem. 24:311–316; 1975.
21. Hansen, S.; Kohler, Ch.; Goldstein, M.; Steinbusch, H. V. M. Effects of ibotenic acid-induced neuronal degeneration in the medial preoptic area and the lateral hypothalamic area on sexual behavior in the male rat. Brain Res. 239:213–232; 1982.
22. Kluger, M. J.; O'Reilly, B.; Shope, T. R.; Vander, A. J. Further evidence that stress hypothermia is a fever. Physiol. Behav. 39:763–766; 1987.
23. Krueger, J. M.; Walter, J.; Dinarello, C. A.; Wolff, S. M.; Chedid, L. Sleep promoting effects of endogenous pyrogen (interleukin-1). Am. J. Physiol. 246:R994–R999; 1984.
24. McClintock, M. K.; Toner, J. P.; Adler, N. T.; Anisko, J. J. Postejaculatory quiescence in female and male rats: Consequences for sperm transport during group mating. J. Comp. Physiol. Psychol. 96:268–277; 1982.
25. Mantel, N. Evaluation of survival data and two new rank order statistics arising from its consideration. Cancer Chemother. Rep. 40: 163–170; 1966.
26. Moltz, H. E-series prostaglandins and arginine vasopressin in the modulation of male sexual behavior. Neurosci. Biobehav. Rev. 14: 109–115; 1990.
27. Morimoto, A.; Murakami, N.; Nakamori, T.; Watanabi, T. Ventromedial hypothalamus is highly sensitive to prostaglandin E_2 for producing fever in rabbits. J. Physiol. 397:259–268; 1988.
28. Myers, B. M.; Baum, M. J. Facilitation of copulatory performance in male rats by naloxone: Effects of hypophysectomy, 17 alpha-estradiol, and luteinizing hormone releasing hormone. Pharmacol. Biochem. Behav. 12:365–370; 1980.
29. Ojeda, S. R.; Wheaton, J. E.; McCann, S. M. Prostaglandin E_2-induced release of luteinizing hormone-releasing factor (LRF). Neuroendocrinology 17:283–287; 1975.
30. Paxinos, G.; Watson, C. The rat brain in stereotaxic coordinates. New York: Academic Press; 1982.
31. Poddubiuk, Z. M.; Kleinrok, Z. A comparison of the central actions of prostaglandins A1, E1, E2, F1a, and F2a in the rat. I. Behavioral, antinociceptive and anticonvulsant actions of intraventricular prostaglandins in the rat. Psychopharmacology (Berlin) 50:95–102; 1976.
32. Satinoff, E. Drugs and thermoregulatory behavior. In: Lomax, P.; Schonbaum, E., eds. Body temperature, drug effects and therapeutic implications. New York: Marcel Dekker, Inc.; 1979:151–181.
33. Silva, N. L.; Boulant, J. A. Effects of testosterone, estradiol, and temperature on neurons in preoptic tissue slices. Am. J. Physiol. 250:R625–R632; 1986.
34. Singer, R.; Harker, C. T.; Vander, A. J.; Kluger, M. J. Hyperthermia induced by open-field stress is blocked by salicylate. Physiol. Behav. 36:1179–1182; 1986.
35. Stitt, J. T. Fever versus hyperthermia. Fed. Proc. 38:39–43; 1979.
36. Stitt, J. T. Prostaglandin E as the neural mediator of the febrile response. Yale J. Biol. Med. 59:137–149; 1986.
37. Swadlow, H. A.; Waxman, S. G.; Weyand, T. G. Effects of variations in temperature on impulse conduction along nonmyelinated axons in the mammalian brain. Exp. Neurol. 71:383–389; 1981.
38. Vaughn, L. K.; Veale, W. L.; Cooper, K. E. Sensitivity of hypothalamic sites to salicylate and prostaglandin. Can. J. Physiol. Pharmacol. 57:118–123; 1979.
39. Veale, W. L.; Cooper, K. E.; Pittman, Q. J. Role of prostaglandins in fever and temperature regulation. In: Ramwell, P. W., ed. The prostaglandins, vol. 3. New York: Plenum Press; 1977:145–167.
40. Whishaw, I. Q.; Vanderwolf, C. H. Hippocampal EEG and behavior: Effects of variation in body temperature and relation of EEG to vibrissae movement, swimming and shivering. Physiol. Behav. 6:391–397; 1971.
41. Williams, J. W.; Rudy, T. A.; Yaksh, T. L.; Viswanathan, C. T. An extensive exploration of the rat brain for sites mediating prostaglandin-induced hyperthermia. Brain Res. 120:251–262; 1977.