alternately with 100 μg of *Z* isomer and with 92.5 μg of *Z* plus 7.5 μg of *E* isomer on rubber septa. The test was conducted over 12 consecutive nights.
6. The *E* isomer was prepared by sodium metal reduction of the tetrahydropyranyl ether of 11-tetradecynol in anhydrous liquid ammonia followed by acetylation with a mixture of acetic acid and acetic anhydride (10 : 1.5, by volume). Slow spinning band distillation of the product then gave, according to capillary GLC analysis (*4*), pure compound.
7. J. A. Klun and J. F. Robinson, *Ann. Entomol. Soc. Amer.* **64**, 1083 (1971).
8. The redbanded leafroller is also inhibited by the *E* isomer as noted by W. L. Roelofs and A. Comeau, *J. Insect Physiol.* **17**, 435 (1971).
9. J. A. Klun and J. F. Robinson, *Ann. Entomol. Soc. Amer.* **65**, 1337 (1972).
10. A small proportion of the opposite geometric isomer increases the potency of the oriental fruit moth synthetic pheromone (M. Beroza, C. R. Gentry, G. M. Muschik, in preparation).
11. R. L. Augustine, Ed., *Catalytic Hydrogenation* (Dekker, New York, 1965), p. 71; *Reduction* (Dekker, New York, 1968), p. 116.
12. W. L. Roelofs and A. Comeau, in *Chemical Releasers in Insects, Proceedings of the 2nd International Congress on Pesticide Chemistry, IUPAC, Tel Aviv, Israel, 1971*, A. S. Tahori, Ed. (Gordon & Breach, New York, 1971), vol. 3, pp. 91–114.
13. W. L. Roelofs, R. T. Cardé, R. J. Bartell, P. G. Tierney, *Environ. Entomol.* **1**, 606 (1972).
14. Formulation was 12/20-mesh cork plus (*E*)-11-tetradecenyl acetate (7 percent by weight) plus paraffin (8 percent). A chloroform solution of paraffin and *E* isomer was added to the cork granules, and the solvent was evaporated. A "Cyclone" Seed Sower was used to distribute 40 g of granules (2.8 g of *E* isomer) on a row (97.5 m) of corn growing along the perimeter of each of four fields. The exact granule distribution pattern is not known. Ten insect traps baited alternately with a mixture of 100 μg of *Z* isomer plus 4 μg of (*E*)-11-tetradecenyl acetate on a rubber septum and with four unmated European corn borer females were positioned 9 m apart in each of the rows treated with *E* isomer, and ten similar traps were positioned in untreated areas 27.4 m distant, but within the same row treated with *E* isomer.
15. We thank Dr. D. K. Hotchkiss, Department of Statistics, Iowa State University, for statistical analysis of the data; D. B. Willey for technical assistance; and the European Corn Borer Laboratory staff, Ankeny, Iowa, for supplying moths used in this study. Journal Paper No. J-7483 of the Iowa Agriculture and Home Economics Experiment Station. Supported in part by Iowa Agriculture and Home Economics Experiment Station Project 1890.

13 February 1973; revised 28 March 1973 ■

Brain Calcium: Role in Temperature Regulation

Abstract. *Perfusion of the preoptic-anterior hypothalamus with excess calcium ion in ground squirrels produces a drop in core temperature. The magnitude of the drop is directly dependent on ambient temperature. Respiration, heart rate, and oxygen consumption are also reduced during perfusion of calcium ion. It is concluded that the depression of body temperature during calcium ion perfusion is due to generalized depression of the neurons of the preoptic-anterior hypothalamus.*

Recently it has been reported that alterations of the electrolyte balance of the cerebrospinal fluid can cause marked changes in deep body temperature. Perfusion of the cerebral ventricles of cats, primates, and rabbits with excess Ca^{2+} causes a drop in rectal temperature, whereas excess Na^{+} results in a rise in rectal temperature (*1*). Direct perfusion of these ions into the posterior hypothalamus causes similar changes in body temperature of primates and cats (*2*).

Myers and Veale (*3*) proposed an ionic mechanism for the internal temperature set point in which the ratio of Ca^{2+} to Na^{+} in the posterior hypothalamus determines the core temperature. We now report that perfusion of excess Ca^{2+} in the preoptic-anterior hypothalamus (POAH) of ground squirrels also causes a marked drop in rectal temperature. The level of the decrease of the body temperature is directly related to the ambient temperature (T_a) and is probably due to generalized depression of autonomic function.

In each of six ground squirrels (*Citellus beecheyi*) a guide tube was implanted stereotaxically and fixed to the skull with dental cement. The tip of the guide tube was located just dorsal to the POAH. The ionic balance of the POAH was selectively altered with a modified push-pull cannula lowered through the guide tube (*4*). A reciprocal infusion pump (Harvard Apparatus) was used to drive and collect the perfusion solutions. The precise location of the area perfused was determined by histological section (Fig. 1).

The animals were restrained in a sealed chamber, and oxygen consumption was monitored continuously with a Beckman G-2 paramagnetic oxygen analyzer. Rectal temperature and air temperature in the chamber were recorded continuously with thermistors. In several of the experiments, heat rate, respiratory rate, and pinna temperature were also recorded. The data were collected on a Vidar digital data acquisition system and stored on magnetic tape for computer analysis and plotting.

Each animal was allowed to equilibrate in the chamber for a minimum of 1 hour prior to perfusion. The perfusion flow was maintained at a constant rate of 20 μl/min; it consisted of normal Ringer solution (NaCl, 154 m*M*; KCl, 5.4 m*M*; and $CaCl_2$, 2.3 m*M*) or Ringer solution that contained either 6.9 or 20.7 m*M* excess concentration of $CaCl_2$. In these solutions the osmolarity was maintained constant by adjusting the concentration of NaCl appropriately.

Table 1. Effect of Ca^{2+} on core temperature and metabolism. Abbreviation: *N*, the number of animals.

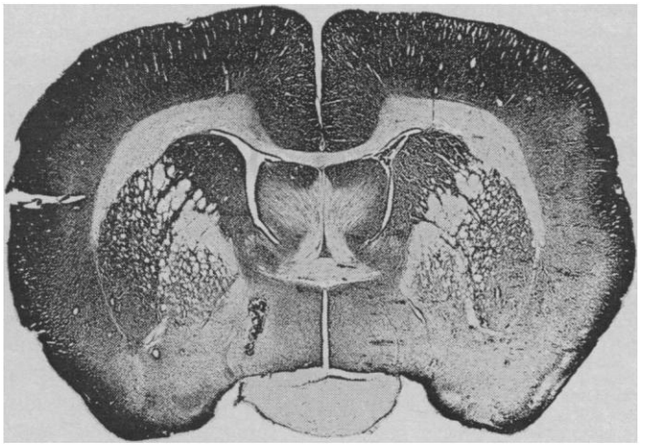
N	Concentration of Ca^{2+}	$\Delta\bar{T}_r$* (°C)	T_a† (°C)	O_2 uptake (cm^3 g^{-1} hr^{-1})
2	Normal	− 0.17	25	1.10
1	Normal	− 0.10	12	1.90
6	6.9 m*M* excess	− 1.58	25	0.68
6	6.9 m*M* excess	− 4.51	12	0.81
2	20.7 m*M* excess	− 2.25	25	0.25

* Mean change in rectal temperature. † Ambient temperature.

The effects of 1-hour perfusions are listed in Table 1. Perfusion of normal Ringer solution in the POAH had no effect on rectal temperature or metabolism at a T_a of either 12° or 25°C. When Ringer solution containing an excess of Ca^{2+} (6.9 m*M*) was perfused in the same region, the initial response was a marked drop in the consumption of oxygen followed by a fall in rectal temperature. The decrease in rectal temperature after 1 hour of perfusion was dependent upon the T_a. Animals perfused at a T_a of 12°C showed significantly ($P < .01$) greater drops in rectal temperature than those perfused at a T_a of 25°C. There was no significant difference in oxygen consumption at these two ambient temperatures.

When 20.7 m*M* excess Ca^{2+} was perfused at an air temperature of 25°C, the metabolic rates of two squirrels dropped to less than 0.25 cm^3 of O_2 per gram per hour and rectal temperature dropped only 1.2° and 3.3°C, respectively. At the end of the perfusion period respiration was extremely weak and irregular. The animals were immediately removed from the chamber, artificially respirated, and kept warm with a heat lamp for approximately 2 hours but could not be revived.

Figure 2 shows the effects of changing air temperature during perfusion of the POAH with 6.9 m*M* excess Ca^{2+}. At time zero, the T_a begins to fall and the oxygen consumption increases so as to maintain a stable rectal temperature. At the beginning of perfusion (*On*) the initial response is



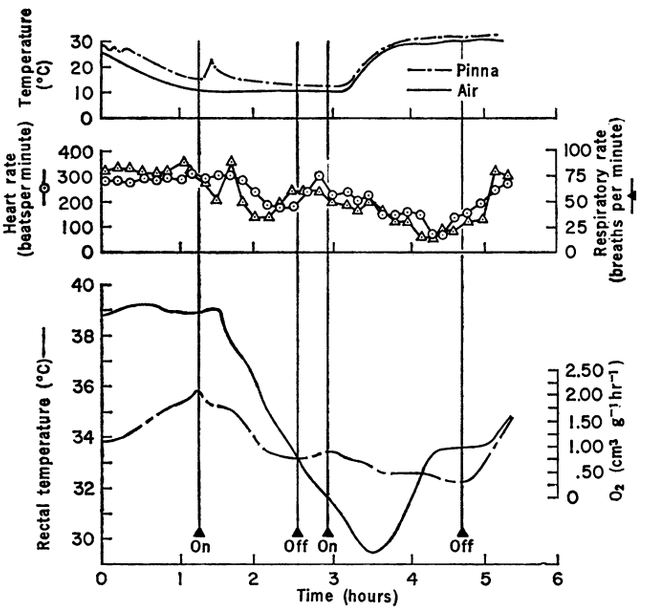


Fig. 1 (left). Histological section of the brain of the animal represented by the data in Fig. 2. The section was cut at 50 μm and stained with cresyl violet. The area perfused is shown by the stained region produced by injection of methylene blue below the anterior commissure on the left side of the photograph. Fig. 2 (right). Record of oxygen consumption, rectal temperature, heart rate, respiratory rate, and vasomotor responses (indicated by pinna temperature) to perfusion of Ringer solution containing 6.9 m*M* excess Ca^{2+} in the preoptic-anterior hypothalamus. Perfusion duration is indicated by *On-Off*. Air temperature is altered during this experiment to demonstrate the dependence of body temperature on ambient temperature.

a reversal in the metabolic trend accompanied by vasodilation, as indicated by pinna temperature. After a short time lag the rectal temperature begins to fall. The respiratory rate and heart rate also decrease markedly. Perfusion is stopped midway through the record and the heart rate, respiratory rate, and metabolism begin to recover, while rectal temperature continues to fall. The Ca^{2+} perfusion is again initiated, which causes another fall in respiration, heart rate, and metabolism. During this second period of perfusion, ambient temperature is elevated to 30°C. Following the increased air temperature the fall in body temperature is reversed and reaches a new equilibrium at 33.8°C. It is during this equilbirated period that the respiratory rate, heart rate, and total body metabolism are at their lowest levels. Perfusion is then stopped, vital functions increase, and rectal temperature recovers to normothermic levels.

If the Ca^{2+}/Na^{+} ratio in the posterior hypothalamus determines the set point for core temperature, then perfusion of excess Ca^{2+} at a given concentration should cause a consistent change in rectal temperature independent of T_a. Myers and Buckman (*5*) have shown in normothermic hamsters that the deep hypothermia produced by perfusion of excess Ca^{2+} in the cerebral ventricles is directly related to the T_a. The lower the T_a (to −10°C) the greater the drop in core temperature. Additionally, the hypothermic response is dependent upon the concentration of Ca^{2+}, with a maximum depression of core temperature seen when 100 m*M* excess Ca^{2+} was used. In an earlier paper Myers and Yaksh (*2*) demonstrated that perfusion of excess Ca^{2+} in the posterior hypothalamus of monkeys caused not only a depression of core temperature but also cardiac arrhythmia and a decline in respiratory rate. We report similar results when the POAH was perfused with 6.9 m*M* excess Ca^{2+}. The hypothermia produced by perfusion of Ca^{2+} was directly related to T_a, while O_2 consumption, heart rate, and respiratory rate were equally suppressed regardless of T_a.

The marked depression of these vital functions suggests that perfusion of Ca^{2+} may alter the excitability of the neurons in the POAH. It is known that Ca^{2+} has a stabilizing effect on neuronal membranes and that the excitability of myelinated nerve fibers decreases when the external (Ca^{2+}) is elevated and increases when it is lowered (*6*). In addition, excess Ca^{2+} in the cerebrospinal fluid has been shown to decrease both rate and depth of breathing in anesthetized animals and has a narcotic effect on conscious cats (*7*). These effects of Ca^{2+} in the cerebrospinal fluid or hypothalamus could directly suppress heat production and subsequently depress body temperature without directly altering the hypothalamic set point for temperature regulation.

Therefore, in ground squirrels, excess Ca^{2+} perfusion of the POAH appears to exert a narcotic effect by reducing the excitability of the hypothalamic neurons. The lowered excitability may cause a decrease in activity of both heat production and heat loss pathways. The resultant core temperature is then determined passively by the ΔT between the body temperature and ambient temperature.

JAMES L. HANEGAN
BILL A. WILLIAMS
National Aeronautics and Space Administration, Ames Research Center, Moffett Field, California 94035

References and Notes

1. W. Feldberg, R. Myers, W. Veale, *J. Physiol.* **207**, 403 (1970); R. Myers, W. Veale, T. Yaksh, *ibid.* **217**, 381 (1971); W. Feldberg and P. Saxena, *ibid.* **211**, 245 (1970).
2. R. Myers and T. Yaksh, *ibid.* **218**, 609 (1971); R. Myers and W. Veale, *ibid.* **212**, 411 (1971).
3. R. Myers and W. Veale, *Science* **170**, 95 (1970).
4. R. Myers, *Physiol. Behav.* **5**, 243 (1970).
5. ——— and J. Buckman, *Amer J. Physiol.* **223**, 1313 (1972).
6. B. Frankenhaeuser and A. Hodgkin, *J. Physiol.* **137**, 218 (1957); B. Frankenhaeuser and H. Meves, *ibid.* **142**, 360 (1958).
7. I. Leusen, *Physiol. Rev.* **52**, 1 (1972).
8. J.L.H. is supported on a National Academy of Sciences postdoctoral fellowship at the Ames Research Center, Moffett Field, California.

26 April 1973