

Fig. 3. Transmission of feline leukemia scheme showing the latent period in weeks (T) and histological analyses (H).

litter of five 4-day-old kittens received  $1.15 \times 10^9$  whole leukemic cells; and the second litter of four 1-day-old kittens received 2.3 g equivalents of cell-free suspension prepared by techniques of differential centrifugation (Fig. 3) (4). Lymphosarcoma was histologically proven in three of the four kittens inoculated with cell-free suspension within 8 weeks of inoculation. Three of five kittens that were definitely leukemic, and one kitten that was questionably so—all inoculated with whole-cell suspension—also were proved to be histologically leukemic within 11 weeks after inoculation.

The "C"-type particles isolated from the plasma of cats with both spontaneous and experimentally induced leukemia showed morphological and physical characteristics that are very similar to murine leukemic viruses, particularly the virus described by Rauscher (8). Since the morphology and maturation of these two different animal leukemic viruses are very similar, it is not surprising that their densities are similar.

This is the first description of the maturation stages of the "C"-type viral particles in plasma of cats with leukemia. Our study suggests that feline leukemia viral particles undergo maturation stages similar to those found in mice, and, like the murine leukemia virus, mature forms are predominant in the plasma (9). The size of the particles in plasma was slightly larger than those reported by Jarrett *et al.* and by Rickard *et al.*; however, the size of budding particles observed in tissue was in the range described by Rickard *et al.*

Although transmission of feline leukemia was reported by Jarrett *et al.*, they observed a prolonged period of latency of 9 months (10). The present transmission study which utilized both

cellular and cell-free inoculum demonstrates that feline leukemia can be induced as soon as 5 weeks after inoculation. This short period of latency in the recipients may be a reflection of the viremic state of the donor and perhaps of the large amount of virus inoculated.

Density-gradient analyses of plasma in conjunction with electron microscopic examination can be an effective means to detect the viremic state in the cat, and, in turn, it may be useful for selecting the best leukemic donors among populations of other animals, including man. This method appears to be a promising approach for the detection of the ideal donor where the natu-

ral period of latency may exceed 5 years or more, as it does in several animal species.

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11. Supported by NIH grant CA05562-06A1, USDA grant 529-15-1, and PHS contract PH 43-65-609 within the special virus-leukemia program of the National Cancer Society.

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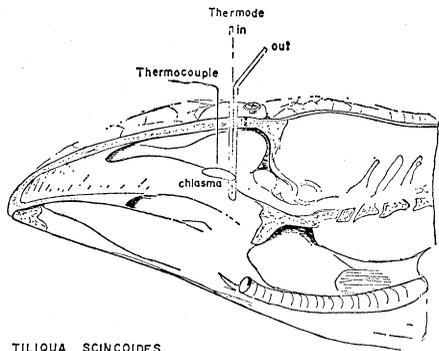
### Tiliqua scincoides: Temperature-Sensitive Units in Lizard Brain

**Abstract.** *Extracellular action potentials were recorded from units in the pre-optic area of the brain of the Australian blue-tongued skink (Tiliqua scincoides) during periods of local heating and cooling of the brain (20° to 36°C) with water-perfused thermodes. In this temperature range most spontaneously firing neurons were temperature-insensitive, but eight showed sensitivity to the thermal stimulus. Five warm neurons increased their activity when the brain temperature was raised, and three cold neurons showed increased activity with fall in temperature.*

The existence of sensitivity to temperature in a reptilian brain was first described by Rodbard *et al.* in 1950 (1), who changed the brain temperature in turtles and observed cardiovascular responses. Only recently was this sensitivity related to thermoregulation by Hammel *et al.* (2), who showed that local heating or cooling of the anterior brain could affect thermoregulatory behavior of the Australian lizard *Tiliqua scincoides*. Since the presence has been shown (3) of temperature-sensitive neurons in the hypothalamus of warm-blooded species such as the cat, it was of interest to seek, in the reptilian brain, neurons re-

sponding to temperature even though Hammel *et al.* could find no physiological thermoregulatory response in these lizards.

Again we used the Australian blue-tongued skink. All surgery was performed under ether anesthesia or cold lethargy; the animals were then allowed to recover, and the experiments proceeded without further anesthesia. With the head immobilized in a specially built holder, a U-shaped, water-perfused thermode was implanted in the brain, aimed more or less at the preoptic region (Fig. 1)—that is, perpendicularly to the skull surface, 2 to 4 mm rostral from the pineal eye, on



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Fig. 1. Diagrammatic representation of the preparation: thermocouple and microelectrodes were positioned symmetrically with respect to the thermodes.

the right side of the head, 1 mm from the midline. The thermode permitted a 10°C displacement of the brain temperature at 2 mm distance, and the temperatures explored ranged roughly from 20° to 36°C. Two millimeters rostral from the thermode a thermocouple was implanted, and the local temperature was recorded.

At the same distance from the thermode, but on the contralateral side of the brain, a stainless-steel microelectrode, insulated to the tip, was positioned stereotaxically. The brain was assumed to be isotropic to heat; therefore the temperature at the tip of the electrode was believed to be the same as that of the thermocouple, since they were equidistant from the thermode. The extracellular action potentials were displayed on an oscilloscope and by loud speaker, and were counted auto-

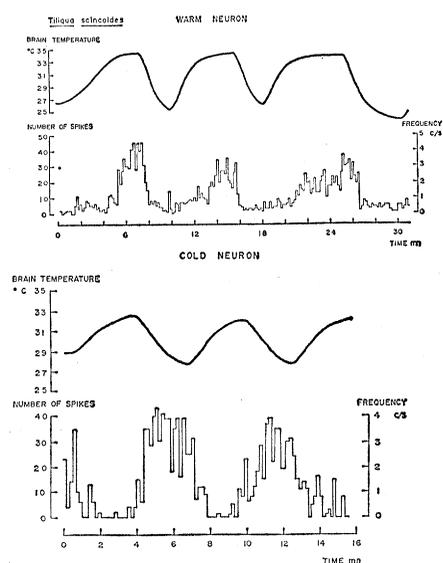


Fig. 2. Responses of a warm and a cold neuron, showing thermocouple temperature (top) and number of impulses for a 10-second period (bottom).

matically; the count for each 10-second period was printed-out on a digital printer.

Most of the neurons, or groups of neurons, studied had spontaneous activities that did not change with alterations of local brain temperature. Some of the units fired at more or less fixed intervals for extended periods, but others had quite variable discharge rates. By analogy with those described in mammals, these neurons were designated temperature-insensitive. Eight other neurons all located rostral to the optic chiasma were found, with a clear correlation between brain temperature and neuronal activity.

Five neurons increased their spontaneous activity with increase in brain temperature (Fig. 2, top). By use of the same analogy with similar neurons found in the mammalian brainstem, this kind of neuron was designated warmth-sensitive or warm neuron. Three neurons showed an opposite behavior: their activity increased when the brain was cooled (Fig. 2, bottom); they were consequently designated cold-sensitive or cold neurons. The cold neurons differed from the warm neurons in that they fired in bursts synchronous with the respiratory rhythm, whereas the warm neurons fired more or less continually.

An idea of the temperature-sensitivity of the units can be obtained by plotting the activity against temperature; each point (Fig. 3, top) represents the number of spikes during a 10-second period, at the indicated brain temperature, for one warm and one cold neuron. Figure 3 (bottom) summarizes the data from all temperature-sensitive neurons studied: the temperature-sensitivities of the warm units and cold units varied between +0.09 and +1.0 and between -0.26 and -0.7 impulses per second per 1°C, respectively. For comparison, the warmth-sensitive neurons and cold units of the dog (4), cat (3), and rabbit (5) ranged between +1.2 and +21 and between -0.4 and -0.82 impulses per second per 1°C, respectively. Thus it appears that the sensitivity of the warm units of *Tiliqua* is about 10 percent of that of corresponding units of the warm-blooded animals for which studies are available, but that the cold units of all species seem to be comparable in sensitivity. It is remarkable that the activity curves of warm and cold neurons do not overlap in the range of body temperatures preferred by *Tiliqua* (30° to 37°C) (1).

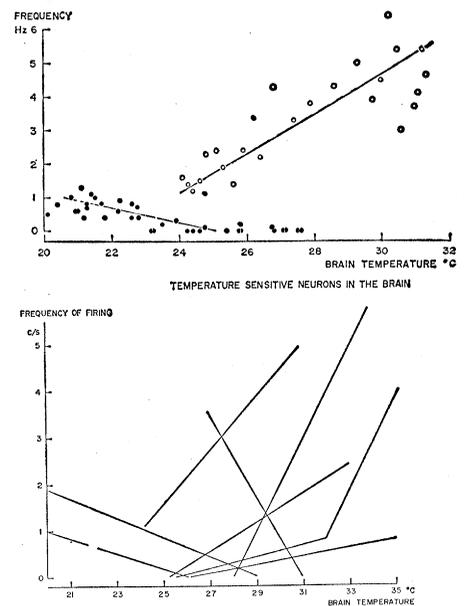


Fig. 3. (Top) Temperature sensitivities of a warm and a cold neuron. (Bottom) Summary of results obtained on eight temperature-sensitive neurons.

Similarities are thus apparent between mammalian and reptilian brains as regards sensitivity to temperature and the presence of temperature-sensitive neurons. For example, the local heating or cooling of the preoptic region and anterior hypothalamus evokes thermoregulatory behavior in both the endotherm and ectotherm; moreover, in these regions of the brainstem are found concentrations of spontaneously active units that are temperature-sensitive and have both positive and negative temperature coefficients. However, the gap between these neurons and behavior is much too large to allow firm conclusions regarding the existence of a link between these neurons and thermoregulation. On the other hand, perhaps one may imagine that in *Tiliqua* we have the roots of the later-evolved physiological hypothalamic thermostat.

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