The effects of electrolytic and neurotoxic lesions of the suprachiasmatic nucleus (SCN) and preoptic area (POA) of the anterior hypothalamus were studied by temperature telemetry in the golden hamster (Mesocricetus auratus) examined under two ambient temperature conditions: 24°C and 6°C. Although attempted lesions with microinjections of ibotenic acid proved unsuccessful, electrolytic lesions of the SCN eliminated the circadian rhythm of body temperature (CRT), indicating an active role of this nucleus in the establishment of the CRT. Electrolytic lesions of the POA, but not of the SCN, resulted in an increased amplitude of the CRT at both 24°C and 6°C, with the lower ambient temperature enhancing this amplitude change to a greater extent. These results suggest that the POA and the SCN are independently responsible for the homeostatic and circadian regulation of body temperature, respectively. The increased amplitude of the CRT after POA lesions raises the possibility that the thermoregulatory system may oppose rather than defend the circadian control of body temperature in normal animals, which is consistent with several recent behavioral findings.

Key words: Body temperature; Circadian rhythm; Suprachiasmatic nucleus; Preoptic area

Introduction

The body temperature of rodents and other mammals is homeostatically controlled by autonomic and behavioral effector mechanisms. Body temperature is also under circadian control and oscillates daily in the absence of variations in the thermal environment. Although the precise neuroanatomical identity of the control sites has yet to be determined, there is considerable evidence that the homeostatic control of body temperature is exerted by hypothalamic structures at or around the preoptic area and that the circadian control is exerted by structures at or around the suprachiasmatic nucleus. The extent to which these two regions of the brain interact in the control of body temperature has received very little attention, and consequently the homeostatic and circadian controls of body temperature have been traditionally examined separately.

The fact that homeostatic and circadian control have been studied separately does not imply that the two processes are independent of each other. It has been widely assumed that the circadian system imposes a daily variation on the thermoregulatory set point, and that this variation is responsible for the circadian rhythm of body temperature. On the other hand, the recent finding that suprachiasmatic lesions eliminate body temperature rhythmicity but do not affect its homeostatic regulation seems to suggest that the homeostatic control of body temperature is independent from the circadian control. Therefore, it is important to assess the roles of the preoptic area (POA) and suprachiasmatic nucleus (SCN) in the control and expression of the body temperature rhythm. In the present study in golden hamsters, we investigated the roles of the SCN and POA in the control of body temperature through selective brain lesions utilizing both electrolytic and excitotoxic techniques.

Materials and Methods

Animals: Forty-eight male golden hamsters (M. auratus) aged 2-4 months were housed in individual plastic cages (21 x 30 x 20 cm) lined with wood shavings and were fed Prolab rodent pellets and water ad lib. Radio transmitters for the monitoring of body temperature and locomotor activity (Model VM-FH, Mini-Mitter Co., Sunriver, OR) were implanted i.p. under sodium pentobarbital anesthesia (80 mg kg\(^{-1}\), i.p.). After implantation, the animals were placed in cages placed on top of radio receivers (Model RA-1010, Mini-Mitter Co.) located in a temperature controlled chamber. The radio receivers were attached to a computer data acquisition system (Dataquest III, Data Services, St. Paul, MN), so that temperature could be recorded in 6 min bins for extended periods. The animals were monitored in this fashion for a minimum of 10 days to establish their
baseline temperature and activity data prior to the lesions. Because even in unoperated hamsters circadian rhythmicity tends to become less robust after long exposure to constant darkness, whereas exposure to constant light can cause arrhythmicity in rats and ‘splitting’ in hamsters, the animals were maintained under a 14 h light, 10 h dark cycle (500 lux) throughout the experiment.

Brain lesions: Brain lesions were performed stereotaxically under sodium pentobarbital anesthesia (80 mg kg$^{-1}$). In 16 animals, electrolytic lesions (anodal, 4 mA, 10–15 s) were aimed at the SCN, along the midline between the base of the third ventricle and the optic chiasm (AP +0.6, V −8.3, L 0.0 mm from bregma). In another group of 16 animals, electrolytic lesions (anodal, 2 mA, 10–15 s) were aimed at the medial POA with bilateral electrode penetrations rostral to the crossing of the anterior commissure (AP +1.3, V −8.0, L ±0.7 and −0.7 mm from bregma). Because electrolytic lesions destroy both local cell bodies and fibers of passage, they ordinarily do not allow determination of whether the observed effects are due to the destruction of the area aimed at or due to the severing of the fibers of passage through this area. Therefore, we attempted to produce neurotoxic lesions of the POA and SCN with ibotenic acid (α-amino-3-hydroxy-5-isoxazoleacetic acid), which has been previously shown to produce localized brain lesions that spare fibers of passage. The dose found to be effective in other parts of the brain (6 μg) produced seizures and respiratory distress followed by death when injected into the SCN of four animals and POA of five animals. Therefore, we used a smaller dose of 3 μg (0.3 μl of a 10 μg μl$^{-1}$ solution), microinjected into the SCN (eight animals) and POA (eight animals) under the anesthetic and stereotaxic conditions described above. All animals were returned to their cages and maintained at an ambient temperature of 24°C for a minimum of 10 days, after which time the ambient temperature was lowered to 6°C and maintained for 10 or more days.

At the end of the experiment (total 34–46 days), the brains of all animals that received lesions were removed after lethal injection of sodium pentobarbital (180 mg kg$^{-1}$) and preserved in 10% formalin. Serial brain sections were cut at 60 μm with a cryostat, mounted onto gelatin-coated slides and stained with cresyl violet. Although cresyl violet is not as useful as other stains in the fine morphological analysis of the SCN, it is appropriate for gross inspection of location and extent of lesions conducted in this study.

Data analysis: Analysis of the body temperature data consisted of calculations of the mean level, range, and robustness of the daily rhythm over blocks of 10 days. The mean level of a rhythm was calculated as the arithmetic mean of all readings during the 10-day period (2400 data points). The range was calculated as the difference between the maximum and minimum values, the maximum value being defined as the highest reading recorded at least 10 times during the 10 days, and the minimum value being defined as the lowest reading recorded at least 10 times. To prevent occasional outliers (particularly after POA lesions) from skewing the group means, range values were truncated at 10°C (which is approximately five times the average range of unoperated hamsters). The robustness of a rhythm was calculated as the value of the Qn statistic (for P = 24 h) in the Sokolove-Bushell periodogram procedure.17

Results

Histological analysis of the brain slices indicated that nine animals had large electrolytic lesions of the SCN, as shown in Figure 1 (left). These lesions were medially located at the base of the third ventricle, caudal to the crossing of the anterior commissure.
They extended dorsally past the boundaries of the SCN. Nine other animals had electrolytic lesions of the medial POA, as shown in Figure 1 (right). In five of these animals, the lesions extended caudally into the SCN. Electrolytic lesions that completely spared both the SCN and POA were produced in nine animals (not shown). Micro-injections of ibotenic acid (3 µg) into either the SCN or POA of nine animals produced no lesions. (As explained in the Materials and Methods, higher doses produced convulsions followed by respiratory distress and death.) Histological or temperature records from the remaining 12 animals were incomplete and were not used in the data analysis.

The brain lesions affected the three variables differently. As exemplified by the records of four representative animals in Figure 2, electrolytic lesions of the SCN (SCNX) eliminated circadian rhythmicity without considerably affecting the range and mean level of oscillation of body temperature. Electrolytic lesions of the POA (POAX) transiently affected rhythmicity and mean level and had a long-lasting effect on the range of oscillation (which was considerably increased). Electrolytic lesions that

![Graphs showing body temperature changes over time for SCNX, POAX, CTLX, and NONE](image_url)

**FIG. 2.** Segments of the records of body temperature of four animals before and after brain lesions. All animals showed a clear daily rhythm of body temperature before the lesion (performed on day 8). The post-lesion records varied according to the type of lesion. Mean group results are shown in Figure 4. (SCNX: bilateral lesion of the suprachiasmatic nucleus; POAX: bilateral lesion of the medial preoptic area; CTLX: lesion sparing both SCN and POA; NONE: no detectable lesion)
spared both the SCN and POA (CTLX) had only a minimal disruptive effect on all three variables. Microinjections of ibotenic acid, which produced no lesion (NONE), also had negligible effects on the body temperature rhythm.

In order to facilitate the analysis of the effects of the brain lesions, the baseline (pre-lesion) data of all 36 animals, plus those of 24 other animals studied under the same conditions, were used to compute frequency distributions of rhythmicity, range, and mean level of body temperature. As shown in Figure 3, the three variables are approximately symmetrically distributed. From these distributions, the 95% confidence interval for rhythmicity of body temperature can be inferred to range from a $Q_p$ of 60 to 200. Similarly, the 95% confidence intervals for the range

![Graph showing frequency distributions of rhythmicity, range, and mean level of body temperature.](image)

FIG. 3. Frequency distributions of the rhythmicity, range, and mean level of the rhythm of body temperature of 80 unoperated golden hamsters.

of oscillation and for the mean level of body temperature are from 1.8 to 3.2°C and from 36.1 to 37.9°C.

The group means for the post-lesion recordings are shown in Figure 4. At 24°C, the mean rhythmicity of the animals without brain lesions (NOX) was not different from the baseline mean, whereas that of animals with control lesions (CTLX) was slightly reduced. The mean rhythmicity of animals with SCN lesions (SCNX) and preoptic lesions extending into the SCN (BOTH) was not only below the baseline mean but also below the significance line of the $\chi^2$ periodogram. The mean rhythmicity of animals with lesions restricted to the POA (POAX) was not significantly reduced. In all five groups, mean rhythmicity was slightly lower at 6°C than at 24°C.
Analysis of variance (ANOVA) confirmed a significant effect of type of lesion ($F(4, 31) = 16.07, p < 0.01$) and ambient temperature ($F(1, 31) = 4.56, p < 0.04$) and revealed no interaction between the two variables ($F(4, 31) = 0.59, p < 0.10$).

The range of oscillation of body temperature at an ambient temperature of $24^\circ$C was increased in POAX and BOTH animals and decreased in SCNX animals (essentially because of the loss of circadian rhythmicity) but was not significantly altered in the other two groups. Exposure to $6^\circ$C slightly increased the range in all groups. ANOVA confirmed a significant effect of type of lesion ($F(4, 31) = 9.61, p < 0.01$) and ambient temperature ($F(1, 31) = 13.79, p < 0.01$) and revealed no interaction between the two variables ($F(4, 31) = 2.57, p < 0.05$). The mean body temperature was reduced in all groups at $6^\circ$C, but especially in the BOTH group. Accordingly, ANOVA revealed significant effects of type of lesion ($F(4, 31) = 5.07, p < 0.01$), ambient temperature ($F(1, 31) = 12.66, p < 0.01$), and their interaction ($F(4, 31) = 4.67, p < 0.01$).

In all four animals with lesions restricted to the POA, the range of oscillation of body temperature was dramatically increased, as shown for one of the animals in Figure 5(A). In this animal, the range of oscillation of locomotor activity was also increased by the lesion. However, the change in the activity rhythm does not seem to account for the change in the temperature rhythm. Thus, another POAX animal showed increased temperature range without increased activity range (Fig. 5B) and an animal with a control electrolyte lesion displayed an increase in the range of activity without an increase in the range of body temperature (Fig. 5C).

**Discussion**

In animals that received SCN lesions, the body temperature rhythm was abolished but the mean level of body temperature was not significantly affected. In POA-lesioned animals (without concomitant SCN lesions), the temperature rhythm was maintained but exhibited a marked increase in its range of oscillation. These findings are consistent with previous observations of disrupted rhythmicity but persistent homeo-
static control of body temperature in SCN-lesioned hamsters as well as with observations of persistent rhythmicity by disrupted homeostatic control in POA-lesioned rats. Together these results suggest that the circadian and homeostatic control of body temperature are exerted independently by separate brain regions: the SCN and the POA, respectively. However, the fact that mean body temperature was reduced in the BOTH group to a larger extent than in the POA group suggests that the SCN may play a role in the homeostatic control of body temperature when the POA is destroyed. This functional arrangement is compatible with the results of anatomical studies showing that cells in the SCN project not only to the POA but to many other hypothalamic and extrahypothalamic structures.

The integration of the circadian and homeostatic control of body temperature has traditionally been conceived as the result of a circadian variation in the thermoregulatory set point. The observation that the range of oscillation of the body temperature rhythm is enhanced in POA-lesioned animals suggests that the thermoregulatory system actually opposes the oscillation in body temperature imposed by the circadian system. Thus, in intact animals the POA would be responsible for the homeostatic adjustments that reduce the amplitude of the oscillations prescribed by the SCN. POA lesions would free the SCN from inhibition, thus leading to increased amplitude of the temperature rhythm. This concept of an opposition between the circadian system and the thermoregulatory system is consistent with previous findings that the daily rhythm of ambient-temperature selection in rats and hamsters opposes the autonomously-generated daily rhythm of body temperature. Naturally, an opposition (rather than integration) of the thermoregulatory and circadian systems would not seem to be evolutionarily adaptive. In this respect, it has been suggested that the circadian rhythm of body temperature in contemporary homeotherms serves no actual purpose and is only a remnant from the (evolutionarily adaptive) rhythm of early ectotherms.

**Conclusion**

The homeostatic and circadian controls of body temperature in the golden hamster are exerted by distinct areas of the hypothalamus: the preoptic area and the suprachiasmatic nucleus, respectively.

**References**


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