the cochlea. If such a period occurs during human auditory development, then its onset would probably occur prenatally (*17*). Sound levels in incubators used for premature babies have been described in detail (*18*), but the consequences of these noise exposures on subsequent auditory development have not been described. The question of possible damaging consequences of high-level amplification from hearing aids in young children is also of concern to audiologists (*18*). It will be important to verify the existence of a critical period for acoustic trauma in other species and to determine whether the human auditory system passes through such a developmental stage.

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References and Notes

1. J. D. Miller, *J. Acoust. Soc. Am.* **56**, 729 (1974); H. Spoendlin, in (*2*), pp. 69–86.
2. D. Henderson, R. P. Hamernik, D. S. Dosanjh, J. H. Mills, Eds., *Effects of Noise on Hearing* (Raven, New York, 1976).
3. G. R. Gates and C. S. Chen, *Exp. Neurol.* **41**, 457 (1973); C. S. Chen, G. R. Gates, G. R. Bock, *ibid.* **39**, 277 (1973).
4. J. C. Saunders and K. A. Hirsch, *J. Comp. Physiol. Psychol.* **90**, 212 (1976).
5. S. A. Falk, R. V. Cook, J. D. Haseman, G. M. Sanders, *Laryngoscope* **84**, 444 (1974).
6. Outbred hamsters of the LVG:LAK strain were obtained from the Lakeview Hamster Colony, Newfield, N.J.
7. The largest threshold losses occur at frequencies below the frequency range of the traumatic noise. When threshold losses are measured behaviorally, maximum threshold loss usually occurs at a frequency slightly above that of the traumatic noise. However, when threshold losses are measured by recording cochlear microphonics from the round window, maximum threshold loss is usually observed in lower frequencies [J. D. Durrant, in (*2*), pp. 179–196].
8. We are currently examining the anatomical correlates of acoustic trauma in young hamsters (L. R. Rowe, J. C. Saunders, G. R. Bock, in preparation). We have not used noise-test intervals of longer than 5 days, but several considerations lead us to believe that the threshold shifts observed in this study are permanent and not temporary. The noise exposure was very brief (2.5 minutes), and we know of no suggestion in the literature on temporary threshold shift in humans or animals that such brief exposures might lead to long-lasting temporary threshold shifts. Furthermore, even when such shifts are induced by exposure durations of several days, most of the temporary component of the threshold shift recovers within 5 days [W. D. Ward, A. Glorig, D. L. Sklar, *J. Speech Hearing Res.* **15**, 603 (1972); W. Melnick and M. Maves, *Ann. Otol. Rhinol. Laryngol.* **83**,820 (1974)].
9. C. B. Stephens, *Acta Oto-Laryngol.* Suppl. 296 (1972).
10. J. Wersäll, *ibid.*, Suppl. 139 (1958).
11. This analysis uses a 2 × 2 × 7 factorial design, the factors being noise, anesthetic presence, and test frequency. Subjects were repeated on the frequency factor [B. J. Winer, *Statistical Principles in Experimental Design* (McGraw-Hill, New York, 1962), pp. 337–345].
12. Developing thresholds and increasing acoustic trauma correspond during the first 30 days (Fig. 2). As threshold sensitivity increases toward its mature value, mean threshold loss rises toward its maximum value. This reciprocal relationship can be considered to reflect the fact that the effectiveness of a sound in producing acoustic trauma is closely related to its sensation level (its magnitude in relation to hearing threshold) rather than to its absolute intensity level. Developmental changes in middle-ear transfer characteristics could play a significant role during this phase of threshold development.
13. H. Spöendlin, *Acta Oto-Laryngol.* **71**, 166 (1971).
14. C. W. Stockwell, H. W. Ades, H. Engström, *Ann. Otol. Rhinol. Laryngol.* **78**, 1144 (1969).
15. B. A. Bohne, in (*2*), pp. 41–67.
16. J. E. Hawkins, *Ann. Otol. Rhinol. Laryngol.* **80**, 903 (1971).
17. J. C. Sanders and G. R. Bock, in *Studies on the Development of Behavior and the Nervous System*, vol. 4, *Early Influences*, G. Gottlieb, Ed. (Academic Press, New York, in press).
18. J. H. Mills, *J. Acoust. Soc. Amer.* **58**, 767 (1975); W. F. Rintlemann and F. H. Bess, in *Childhood Deafness* (Grune & Stratton, New York, in press).
19. Supported by an otolaryngology training grant (National Institute of Neurological and Communicative Diseases and Stroke 1T01NS-15769) to J. B. Snow, Jr., and by a grant from the Deafness Research Foundation. We thank R. Stanek and E. Seifter for their assistance. This research was conducted in the Auditory Research Laboratory, Philadelphia General Hospital.

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Suprachiasmatic Nuclear Lesions Do Not Abolish Food-Shifted Circadian Adrenal and Temperature Rhythmicity

Abstract. *Daytime restriction of food and water availability in nocturnal animals phase shifts the circadian periodicity of plasma corticosteroid concentrations and body temperature. These shifted rhythms persist in animals with lesions of the suprachiasmatic nuclei who are arrhythmic under normal conditions. These findings suggest the existence of an additional "clock" that may be involved in the generation of the rhythm.*

It has been suggested (*1*) that the suprachiasmatic region of the rat brain is a central pacemaker (or biological clock) responsible for the generation of several biological rhythms. Destruction of this region is associated with a loss of rhythmicity of drinking behavior, locomotor activity, sleep and wakefulness, and adrenal cortical activity, as well as with a loss of estrus cyclicity. We reported previously (*2*) that there is a 12-hour phase shift in the circadian periodicity of plasma corticosteroid concentrations and body temperature in rats maintained under normal lighting conditions, but in which access to food and water is restricted to a 2-hour period (0930 to 1130). The present studies were designed to determine whether such phase shifting

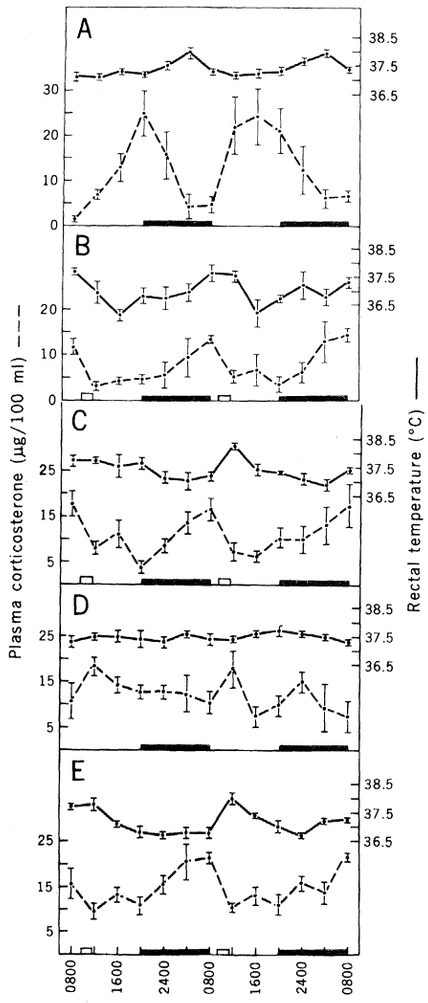

Fig. 1. Circadian periodicity (over a 48-hour period) of body temperature and plasma corticosteroid concentrations in adult female Sprague-Dawley rats. (A) Rats (N = 4) given unrestricted access to food and water and sham lesions; periodicity studied 2 weeks after the lesions were made. (B) Rats (N = 4) on restricted feeding schedule studied 2 weeks after sham lesions were made. (C) Rats (N = 7) on restricted feeding schedule studied 2 weeks after SCN lesions were made. (D) Rats (N = 5) on unrestricted feeding schedule studied 2 weeks after SCN lesions were made. (E) The same rats as in (D) studied 2 weeks later when they had been changed to the restricted feeding schedule. Vertical bars indicate ± standard error. Solid horizontal black bars indicate darkness. Open horizontal bars indicate time of daily access to food and water in animals on restricted feeding schedule. (B) and (C) show that SCN lesions do not change the shifts in the circadian patterns of body temperature and plasma corticosteroid concentrations induced by the restricted feeding schedule. The arrhythmic pattern in animals on the unrestricted schedule and with SCN lesions (D) is shifted by restricted feeding to a pattern (E) almost identical to that in the animals shown in (B) and (C). Patterns of body temperature and plasma corticosterone concentrations obtained from individual animals in (A), (B), (C), and (E) were similar to those depicted for the group.

could still occur in animals in which the suprachiasmatic nuclei (SCN) were destroyed. We found that once phase shifting of adrenal plasma corticosteroid levels and body temperature had been produced by changing the time of food presentation, such shifted circadian rhythms persisted in animals with SCN lesions. In addition, in animals rendered arrhythmic by SCN lesions, limiting the time of food presentation to 0930 to 1130 resulted in circadian patterns of plasma corticosteroid levels and body temperature that were almost identical to those in animals with sham lesions maintained on a restricted feeding schedule.

Adult, female Sprague-Dawley rats (200 g) were housed in individual cages, in a temperature and light controlled room with a photoperiod of 12 hours light and 12 hours darkness (light period beginning at 0800). Food and water were freely available. Studies were begun a minimum of 2 weeks after the rats arrived in the animal quarters. The circadian periodicity of plasma corticosteroid concentrations, body temperature, and running activity were determined as described (*2*). Vaginal smears were taken daily throughout the study. The rats were divided into two groups. In group 1, access to food and water was restricted to 2 hours (0930 to 1130) daily for 2 weeks, at which time a phase shift of plasma corticosteroid concentrations and body temperature was confirmed. Sham ($N = 4$) or SCN ($N = 12$) lesions were then placed (*3*), and circadian periodicity was determined after another 2 weeks of food and water restriction. In group 2, sham ($N = 4$) or SCN ($N = 12$) lesions were placed, and the animals were given unrestricted access to food and water for 2 weeks, at which time periodicity studies were performed. These rats were then placed on the restricted access regime and again studied for periodicity after 2 weeks. At the conclusion of the study the animals were killed and their brains perfused with 10 percent formalin. Serial coronal sections (10 μm thick) were made through the preoptic area and hypothalamus of each animal, and the sections were used to reconstruct the extent of the lesion. Data were used only from those animals in which the SCN was totally destroyed (*4*) and who displayed persistent vaginal estrus.

The circadian patterns of plasma corticosteroid concentrations and body temperature in the rats with sham lesions on unrestricted (Fig. 1A) or restricted (Fig. 1B) feeding schedules were similar to those reported for intact animals (*2*). In rats with SCN lesions, phase-shifted rhythms persisted in those animals maintained on the restricted feeding schedule (Fig. 1C). Rats with SCN lesions that were given unrestricted access to food and water showed an absence of rhythmicity in plasma corticosteroid levels and body temperature (Fig. 1D), but rhythmicity was restored in these animals when they were subsequently placed on the restricted feeding schedule (Fig. 1E).

Body weights of the rats with sham and SCN lesions maintained on the unrestricted schedule were similar (mean ± standard error, 358.0 ± 12.8 g and 355.0 ± 23.0 g, respectively), as were food (23.0 ± 3.6 g and 23.0 ± 3.1 g, respectively) and water intake (31.8 ± 1.0 ml and 29.8 ± 3.4 ml, respectively). Restricted access to food in all instances was associated with a 20 to 24 percent weight loss, a 35 to 42 percent decrease in food consumption, and a 43 to 50 percent decrease in water consumption over the time period studied, similar to our previous findings (*2*). The normal pattern of locomotor activity (90 percent occurring nocturnally) observed in control animals and animals with sham lesions (*2*) was absent in the animals on the restricted schedule: approximately 48 percent of their locomotor activity occurred diurnally (*2*). Restricted access to food was not associated with any significant changes in total running time. Locomotor periodicity was also absent in rats with SCN lesions on the unrestricted schedule, 43 percent of their locomotor activity occurring diurnally. In the rats with sham or SCN lesions, the total running time was not significantly different when comparisons were made between the animals on restricted or unrestricted feeding schedules.

The rhythms we have studied are generally believed to be generated within the central nervous system, environmental light serving as the *Zeitgeber* for determining their phase. The SCN, which is the terminus of a direct retinal hypothalamic projection (*5*), has been suggested as being the major locus responsible for the light entrainment of these rhythms (*1*). How this is accomplished is still unknown. It has been suggested (*6*) that the SCN may serve as a primary master clock, a coupler of rhythms generated in other central nervous system areas, or a component of a multioscillator system. Our previous observations (*2*) and those of others (*7*) have indicated that the rhythms under study, but not some other rhythms [for example, of pineal serotonin *N*-acetyl transferase activity (*8*) or estrogen induced luteinizing hormone and prolactin release (*9*)] may be entrained to a periodic environmental influence other than the light-dark cycle, such as a shift in the time of food and water availability. The present data indicate that not only is the SCN area not necessary for such entrainment, but that the anatomical locus responsive to the secondary (non-light) synchronizer can generate a new circadian rhythmicity in a previously arrhythmic animal with a lesion of the SCN. Moore and Traynor (*8*) reported that the phase shift in hippocampal norepinephrine associated with water deprivation is maintained in blinded animals (unfortunately, these authors gave no data for animals in which hypothalamic deafferentation was performed caudal to the optic chiasm). Further studies are required to define the central neural mechanisms responsible for the synchronization and maintenance of the phase shifted rhythms that occur in animals given restricted access to food and water.

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References and Notes

1. C. Pittendrigh, in *The Neurosciences: Third Study Program*, F. O. Schmitt and F. C. Worden, Eds. (MIT Press, Cambridge, Mass., 1974), p. 437; N. Ibuka and H. Kawamua, *Brain Res.* **96**, 76 (1975); F. K. Stephan and I. Zucker, *Proc. Natl. Acad. Sci. U.S.A.* **69**, 1583 (1972); R. Y. Moore, in *The Neurosciences: Third Study Program*, F. O. Schmitt and F. C. Worden, Eds. (MIT Press, Cambridge, Mass., 1974), p. 537.
2. D. T. Krieger, *Endocrinology* **95**, 1195 (1974). Blood samples and measurements of body temperature were obtained on individual animals at each time point studied. Plasma corticosterone determinations were performed on each of these individual samples.
3. Lesions were made with a monopolar Grass lesion maker (Model 11), and the current (100 khz, 50 volts, 20 ma) was applied for 15 seconds; coordinates for the lesions were obtained from J. DeGroot, *J. Comp. Neurol.* **113**, 389 (1959). A mortality rate of 20 percent was encountered. For sham lesions the electrodes were placed in the cortex but current was not applied.
4. In some of these animals with total SCN lesions portions of the preoptic or anterior hypothalamic areas, or both, were also destroyed, but results were identical in all of these animals despite this difference in lesion size.
5. A. E. Henderickson, N. Wagoner, W. M. Cowan, Z. *Zellforsch. Mikrosk. Anat.* **135**, 1 (1972); R. Y. Moore, *Brain Res.* **49**, 403 (1973).
6. B. Rusak and I. Zucker, *Annu. Rev. Psychol.* **26**, 137 (1965); M. H. Stetson and M. Watson-Whitmyre, *Science* **191**, 197 (1976).
7. J. T. Johnson and F. Levine, *Neuroendocrinology* **11**, 268 (1973); L. L. Bellinger, G. P. Moberg, V. E. Mendel, *Horm. Metab. Res.* **7**, 43 (1975); W. Nelson, S. Scheving, F. Halberg, *J. Nutr.* **105**, 171 (1975).
8. R. Y. Moore and M. E. Traynor, *Neuroendocrinology* **20**, 250 (1976).
9. E. R. Smith, R. Dominquez, S. Levine, *ibid.* **12**, 41 (1973); D. M. Baldwin, J. A. Colombo, C. H. Sawyer, *Proc. Soc. Exp. Biol. Med.* **151**, 471 (1976); L. C. Krey, H. Hauser, D. T. Krieger, unpublished observations.
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