TWENTY-ONE HOUR LIGHT-DARK CYCLE ACCELERATES VAGINAL OPENING IN THE RAT

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The estrus cycle of rats and hamsters is regulated by the daily light-dark cycle. The suprachiasmatic nucleus of the hypothalamus appears to generate a rhythm with a frequency of approximately one cycle in 24 hours. This rhythm is exactly synchronized with the external light-dark cycle by impulses received from the eyes through a retinohypothalamic projection. Lesions that destroy the suprachiasmatic nucleus at two days of age produce constant vaginal estrus in rats and alter the time of vaginal opening in blinded neonatal rats.[1,2]

This paper reports a pilot study demonstrating that a 21-hour light-dark cycle accelerates vaginal opening in rats, a finding which suggests that the early menarche in blind girls[3] and the accelerated vaginal opening of rats reared in darkness[4] are most probably caused by acceleration of normal 24-hour circadian rhythms.

MATERIALS AND METHODS

Sprague Dawley outbred albino rats (ARS Sprague Dawley, Madison, Wis.) from a colony at this institution were used in this study. Each nursing rat and her litter were housed in individual plastic cages. Animals were exposed to illumination provided by a 7½ watt incandescent bulb 40 cm. above the cage. The bulb was connected to a Flexopulse HG110A6 Timer (Eagle Signal Company, Davenport, Iowa). Animals were exposed either to a 21-hour light-dark cycle or a 24-hour light-dark cycle from birth and were inspected for vaginal opening during the lights-on phase of the cycle.

RESULTS

Fifteen animals reared in a 4-hour light, 20-hour dark cycle had vaginal opening at 38.4 ± 2.77 days. This figure may be compared to the 39.9 ±

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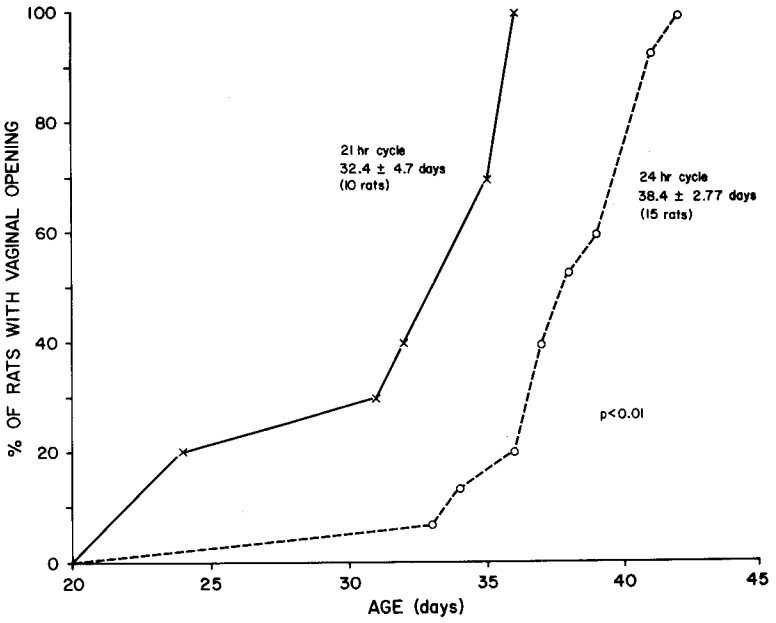

Percentage of rats with vaginal opening exposed to a 21-hour light-dark cycle or a 24-hour light-dark cycle. Each point on the graph represents cumulative numbers of rats with vaginal opening. The ten rats on a 21-hour light-dark cycle had vaginal opening significantly earlier than the fifteen rats on a 24-hour light-dark cycle.

0.4 day vaginal opening reported by Relkin[4] for an 8-hour light, 16-hour dark cycle, and the 40.4 ± 0.3 day vaginal opening reported by Mosko[1] for a 12-hour light, 12-hour dark cycle. (The smaller variations in these opening times, compared to those in the present study, probably result from inbreeding; for example, Relkin used the inbred albino Holtzman strain in his experiments.) Within these limits, increasing the ratio of light to dark appears to cause little or no delay in the time of vaginal opening in the rat. Ten animals reared in a 10½-hour light, 10½-hour dark cycle had vaginal opening at 32.4 ± 4.7 days. The difference between the mean vaginal opening times of the animals on the 21 and 24 hour cycles is significant ($t = 3.85$ $p < 0.01$, two tailed) (see figure).

DISCUSSION

In a blind animal the suprachiasmatic nucleus rhythm is "free running," that is, somewhat greater or less in frequency than one cycle in 24 hours.[5] This rhythm is synchronized with and probably drives other physiologic

rhythms, including plasma corticosterone levels and pineal N-acetyltransferase levels in rats. In blinded animals, these rhythms are also free running, though synchronized with each other.[6]

Blind adult human beings are known to have a free running frequency of about one cycle in 25 hours,[7] but the free-running frequency of children is unknown. One may, therefore, suggest that the free-running frequency in a child is greater than one cycle in 24 hours — perhaps one cycle in 23 hours— and slows with age. Such slowing with age has recently been demonstrated in hamsters.[8] The higher frequency would explain both the early menarche in blind girls and the early vaginal opening of rats reared in constant darkness.[9]

The explanation seems to lie in the rhythmic daily surges of gonadotrophin releasing hormone, probably dependent on the suprachiasmatic nucleus.[1] These surges appear to increase in intensity as the animal approaches puberty.[10] A physical condition, forced oscillation, may account for the increase.

I suggest that gonadotrophin releasing hormone-secreting cells have their own free-running frequency but are held in synchrony with the suprachiasmatic nucleus. However, as the animal approaches puberty, the free-running gonadotrophin releasing hormone secreting cell frequency slows, approaching the suprachiasmatic frequency, and resonance occurs. (Resonance is already well documented in animals.[11]) Hormonal surges increase in intensity at this time because in any physical system undergoing forced oscillation the amplitude of the oscillations surges to a maximum at resonance. This phenomenon may be likened to the surge in amplitude of the sound coming out of a radio speaker as the radio is tuned to a particular station. In an animal entrained to a 21-hour light-dark cycle, hormonal surges necessary to trigger puberty occur earlier, because the system resonates earlier in time.

Further, the phenomenon of resonance may explain the elevated human plasma gonadotrophin levels at birth, followed by a fall between the ages of four and 11 years. This elevation and fall is especially striking in agonadal children.[10]. At birth, the free-running gonadotrophic releasing hormone secreting cell frequency may be much higher than at puberty, specifically one cycle in 12 hours. Because this frequency is harmonic of one cycle in 24 hours, the system resonates, producing the elevated gonadotrophins. Because of the subsequent slowing of the frequency between the ages of four and 11 years, resonance is lost. But at puberty, when the frequency has slowed to one cycle in 24 hours, resonance again occurs, resulting in the

gonadotrophin surge necessary for secondary sexual development. The surge at puberty is greater than the neonatal surge because of the growth and maturation of the brain that have taken place during the interval.

SUMMARY

Rats reared in a 21-hour light-dark cycle had a significantly ($p < 0.01$) earlier vaginal opening than rats reared in a 24-hour light-dark cycle. This finding implies that the early menarche in blind girls and the accelerated vaginal opening of rats reared in constant darkness may be caused by free-running circadian rhythms that are greater than one cycle in 24 hours.

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