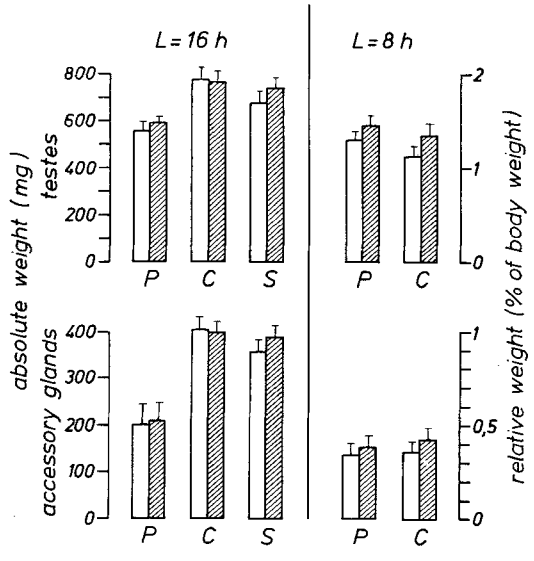
operated (S), i.e. the skull was opened as in actual pinealectomy, and the confluence of the superior sagittal and transverse sinuses was opened which caused as much bleeding as in actual pinealectomy. 19 controls (C) were left intact. All animals had involuted testes at the beginning of the experiment, as ascertained by palpation, a method that has been shown to be reliable[8]. In 16 comparable hamsters, killed between January 8th and 12th, weight of both testes was 79.8 ± 2.1 mg (M ± S.E.) and weight of accessory glands was 19.9 ± 9.3 mg. On January 8th the animals were placed in light-tight chambers. 9 pinealectomized hamsters, the 9 sham-operated hamsters, and 10 of the untreated controls were exposed to long photoperiods (16 h light/24 h), while 13 pinealectomized hamsters and 9 untreated controls received short photoperiods (8 h light/24 h). After 36 days in these conditions, all hamsters were sacrificed and the weight of testes and accessory glands was determined.



Weight of both testes (above) and of accessory glands (below) from hamsters after 36 days in long (L = 16 h) or short (L = 8 h) photoperiods. P, pinealectomized; C, untreated controls; S, shamoperated. Open bars, absolute weight; hatched bars, relative weight; means and standard errors are given. Statistics (U-test). Testes: Absolute and relative weight of testes in group C and S in L = 16 h significantly higher than in all other groups ($p < 0.05$ to < 0.002) except for difference in absolute weight between P and S in L = 16 h ($p < 0.1$); differences between other groups not significant. Accessory glands: Absolute and relative weight of group C and S in L = 16 h significantly higher than in any other group ($p < 0.01$ to < 0.002), differences between other groups not significant.

There was development of testes and accessory glands in all groups, even in the untreated hamsters exposed to short photoperiods. This confirms earlier findings from which it had been concluded that the transition from physiological winter conditions with quiescent gonads to summer conditions with gonadal activity, is based on an endogenous mechanism, and can take place even in short photoperiods while long photoperiods accelerate the process[6–8].

The development of testes and accessory glands was significantly higher in control and sham-operated hamsters kept in long photoperiods than in all other groups (Figure). Contrary to expectation, pinealectomy inhibited the acceleration of gonadal development due to long photoperiods, rather than stimulated gonadal development in short photoperiods: under both light regimes the pinealectomized hamsters did not differ significantly from the short-day controls.

These findings contradict the assumption that light has only an inhibiting effect on the pineal, and suggest that the pineal is not only involved in testicular involution brought about by short photoperiods, but also participates in the mediation of the accelerating effect of long photoperiods on gonadal development. The fact that comparable results were obtained in 2 species as unrelated as the weasel[5], a mustelid, and the Djungarian hamster, a rodent, indicate that participation of the pineal in the mediation of stimulating effects by long photoperiods is a more general phenomenon, and not based on special physiological properties of a single group. The results also show that in experiments on the function of the pineal, not only the photoperiod in which the animals are kept, but also the phase of their annual cycle has to be taken into consideration, at least in seasonal breeders.

Zusammenfassung. Beim Hamster *Phodopus sungorus* verhinderte Pinealektomie die durch lange Photoperioden bewirkte Beschleunigung der Entwicklung von Hoden und Anhangsdrüsen. Die Befunde zeigen, dass die Epiphyse nicht ausschliesslich antigonadotroph wirkt, sondern auch an der progonadotrophen Wirkung langer Photoperioden beteiligt ist.

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Elevation of Rat Plasma Insulin by Intrathecal Pentobarbital

A controversy exists concerning the genesis of the hyperinsulinemia that accompanies the hyperphagia and obesity of rats with chronic lesions of the ventromedial hypothalamus. Some authors[1,2] have maintained that the hyperinsulinemia is secondary to the onset of hyperphagia, whereas others[3–7] have suggested that the hyperinsulinemia is a primary effect of the ventromedial lesion and therefore independent of hyperphagia. In the present experiment, the recently developed technique of intrathecal administration of anesthetic was applied to examine the functions of the hypothalamus. The technique has been reported to produce a reversible lesion of the ventromedial hypothalamus[8–15], an area which constitutes the walls of the ventral portion of the third ventricle of the brain and which is thus in contact with the cerebrospinal fluid. We observed a rapid and significant increase of plasma immunoreactive insulin (IRI) after the intrathecal administration of sodium pentobarbital that preceded eating by the rats and which therefore could not have resulted from it.

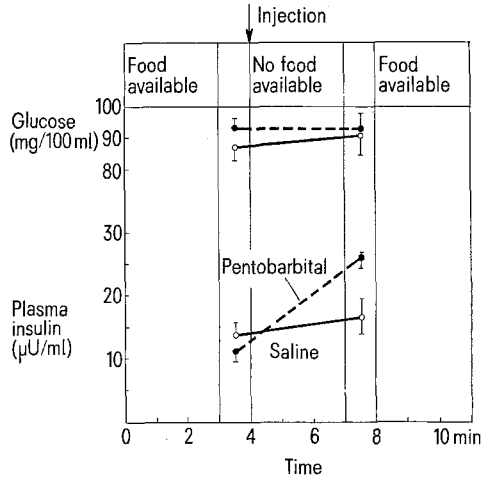
Materials and methods. Subjects were 10 female albino rats maintained on ad libitum food and water. They were each cannulated with a 4.5 mm 27 gauge needle stereotaxically implanted into the left lateral ventricle and cemented to the skull[16]. The coordinates were: With the nose bar 5 mm above the interaural line, 1.2 mm posterior to bregma and 1.5 mm lateral to the mid-saggital suture. After a 7-day recovery period, all rats underwent the

following procedure: A rat was removed from its home cage and placed for 3 min in a plastic chamber containing 2 fresh Purina Lab Chow pellets. The area of the floor of the chamber was approximately 2000 cm². Feeding (an episode in which the rat grasped and chewed a pellet for a period of time exceeding 10 sec) and other motor behaviors were recorded. The rat was then placed in a restraint and a blood sample (approximately 0.5 ml) was milked from the tip of its tail. The rat then received 15 µl of intrathecal physiological saline (Trial 1) or 15 µl of 50 mg/ml sodium pentobarbital (Trial 2) 48 h later. The rat was then replaced in the chamber for 3 min, this time with no food available. A second blood sample was then taken and the rat returned to the chamber for a third 3-min session, this time with food again available and with behavior being monitored. Plasma IRI[17] and whole blood glucose[18] determinations were made as previously described. The data were analyzed with *t*-tests (two-tailed).

Results. The blood data are summarized in the Figure. There were no consistent changes of IRI or glucose following intrathecal saline. Following intrathecal pentobarbital, there was a significant ($p < 0.01$) increase of IRI but no consistent change of glucose. Blood samples taken 48 h after the administration of the pentobarbital revealed that the IRI values had returned to normal.

No rat demonstrated feeding prior to the injection on either trial. There was also no feeding following the administration of the saline. However, following the administration of the pentobarbital, all but 2 of the rats demonstrated feeding. The other 2 had to be artificially respirated and so feeding was not possible. The feeding following pentobarbital persisted throughout the 3-min period for those animals which ate. These rats also exhibited instances of either motor ataxia, dis-coordination, or repetitive stereotyped movements following the administration of the pentobarbital, whereas no unusual motor behaviors were observed in any animal following the intrathecal saline. The altered motor behaviors following pentobarbital have been reported previously[8–12] and may have been due to penetration of the anesthetic into the caudate nuclei which also border the ventricles.

Discussion. The data clearly show that the administration of pentobarbital into the left lateral ventricle of awake rats transiently elevates plasma IRI levels and that this increase of insulin can be observed prior to the demonstration of the stimulus-bound feeding which also occurs. These findings are consistent with the hypothesis that this procedure produces a reversible lesion of the medial hypothalamus, an area which is thought to exert an inhibitory influence upon lateral hypothalamic areas[19–21] responsible for control of vagally-mediated insulin secretion[22] and feeding[23,24]. Traditionally, the ventromedial hypothalamic nuclei have been identified as the structures that exert this inhibitory influence[19–21]. However, recent evidence indicates that the ventral noradrenergic bundle is more essential for the inhibition of feeding[25,26], and presumably of insulin secretion as well. This might also explain the report of feeding following intrathecal pentobarbital in rats with lesions of the ventromedial hypothalamic nuclei[15]. Those authors concluded that all of the feeding-inhibitory area was not destroyed.



Mean immunoreactive insulin and blood glucose values at the first and second blood sampling intervals. The brackets represent plus and minus 1 standard error of the mean.

Zusammenfassung. Zufuhr von Natriumpentobarbital in den lateralen Ventrikel bei wachen Ratten ergab nach 3 min eine signifikante Erhöhung des plasmaimmunoreaktiven Insulins vor jeder Nahrungsaufnahme, im Vergleich mit Kontrollen. Die Resultate deuten an, dass die normalerweise gehemmte neurale Sekretion von Insulin durch ein intraventrikuläres Anästhetikum ausgelöst wird.

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[27] This research was supported by National Institutes of Health Grants Nos. AM 05498, AM 12829, and AM 17112.