L'étude sur l'aorte isolée montre un antagonisme de la PTH avec la PE qui est un α stimulant. Seule la phase lente de la contraction est sensible à la PTH, la phase rapide n'est pas modifiée.

L'hypothèse la plus vraisemblable paraît être l'intervention de PTH sur les mouvements de calcium extracellulaire. Au cours de notre étude les contractions de l'aorte sont provoquées par la PE qui est très spécifique des récepteurs α. D'après GODFRAIND[10] et confirmé par VAN BREEMEN[11], la contraction rapide dépendant d'un α stimulant met surtout en jeu la mobilisation du pool intracellulaire, avec passage des zones de stockage vers le milieu cytoplasmique. La phase lente nécessiterait l'intervention du calcium extracellulaire. Or il apparaît que seule la phase lente est sensible à la PTH. La diminution de l'influx du calcium extracellulaire aboutissant à une inhibition de la contraction serait en accord avec l'observation de PARSON[12] qui note chez le rat, 10 min après l'injection simultanée de PTH et de Ca^{47} une baisse de la teneur en calcium radioactif dans les tissus mous. Il semblerait donc que PTH empêche l'entrée du calcium extracellulaire dans les cellules des muscles lisses de l'aorte. De plus, RASMUSSEN[13] observe une augmentation de l'AMPc, dans les cellules rénales en présence de PTH et BORLE[14] sur des cellules rénales isolées montre qu'il existe une relation entre l'efflux de calcium et le taux d'AMPc. Il ne serait donc pas impossible que PTH ait le même effet au niveau de la fibre musculaire lisse[15]. En conclusion, notre expérimentation préliminaire fournit quelques éléments sur l'action encore mal connue de la parathormone au niveau de l'appareil circulatoire.

Summary. In rats, parathyroïd hormone (PTH) induced a rapid fall of arterial pressure due to vasodilatation. Contraction of isolated aorta produced by phenylephrine was decreased significantly after PTH. This antagonism acted only on the last part of contraction.

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[15] Nous adressons nos remerciements à Monsieur le Professeur J. C. STOCLET pour ses conseils tout au long de ce travail.

Mammalian Pineal Gland: 7-Day Rhythmic Activity?

It is well established that the mammalian pineal gland undergoes prominent circadian changes in function which are to a great extent dependent on environmental lighting conditions[1]. In the present study, we should like to report that there are indications which suggest that the pineal glands of rats kept in our laboratory exhibit, in addition to 24 h cycles, characteristic 7-day cycles. It is totally unclear, as yet, by which internal or external factors this rhythm is caused and whether or not it is just a peculiarity of rats kept under the environmental conditions of our laboratory. Nevertheless we feel that an early publication of our findings is indicated, because the changes observed on different days of the week are of such magnitude that they appear to be of more than academic interest. It appears particularly meaningful to us also that the indications for such a cycle have come from studies on an organ epitomized as 'biological clock'[2] or 'regulator of regulators'[3] in which such a rhythm is perhaps not unexpected.

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Amount of synaptic ribbon fields[a]

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Experiment I[b] (Nov./Dec.)	2.25 ± 0.24 (2)[d]	8.0 ± 1.5 (2)	5.0 ± 1.0 (2)	2.75 ± 1.75 (2)	3.25 ± 1.75 (2)	1.75 ± 0.24 (2)	0.75 ± 0.24 (2)
Experiment II[b] (May)	14.3 ± 3.09 (3)	4.2 ± 0.92 (4)	12.3 ± 2.62 (3)	11.0 ± 2.78 (3)	13.5 ± 1.89 (3)	11.8 ± 1.33 (3)	11.0 ± 3.82 (3)
Experiment III[c] (July)	5.3 ± 0.7 (3)	2.0 ± 0.8 (3)	5.0 ± 1.0 (3)	6.2 ± 1.6 (3)	5.0 ± 1.5 (3)	3.7 ± 1.4 (3)	4.2 ± 0.4 (3)

[a] Expressed as means ± standard error/unit area of pineal tissue, the unit area corresponding to an area of 17640 μm^2 (i.e. the tissue area lying within 10 apertures of electron microscopic specimen supporting grids). For each animal the ribbon fields lying in 20 apertures were counted. [b] Animals were kept under natural lighting conditions with additional artifical illumination from 07.00 to 19.00 h. [c] Animals were kept in a light-proof room with a lighting schedule of 12 h illumination (07.00 to 19.00 h) and 12 h darkness for 3 weeks prior to sacrifice. [d] Figures in brackets denote number of animals used. Statistical analysis: I: Mon + Tues vs Fri + Sat + Sun, $p < 0.01$. II: Mon vs Tues + Wed + Thurs + Fri, $p < 0.001$. III: Mon vs Tues + Wed, $p < 0.02$; Mon vs Sat + Sun, $p < 0.05$; Tues + Wed + Thurs vs Fri + Sat + Sun + Mon, $p < 0.1$.

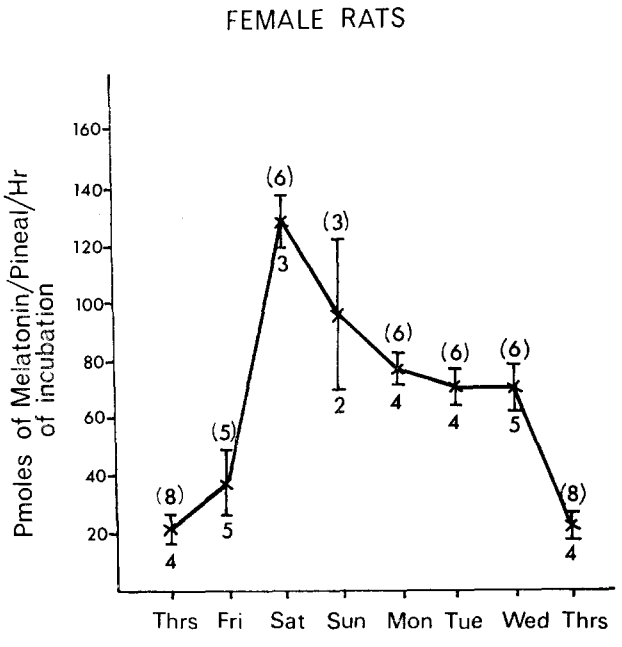

Fig. 1. HIOMT activity in pineal glands of female Wistar rats kept under natural lighting conditions with additional artifical illumination from 07.00 to 19.00 h. The animals were killed between 10.00 and 12.00 h and the glands were assayed individually on the same day using a slight modification of AXELROD, WURTMAN and SNYDER's method[4], in which the homogenization of individual glands was carried out in a medium of 1 ml 0.1 *M* phosphate buffer (pH 7.9) containing 500 µg of N-acetyl-serotonin. 50 µl aliquot of the homogenate was transferred to a test tube containing 0.05 µCi of S-adenosyl-L-(methyl-^{14}C) methionine (55 mCi/mmol) in a final volume of 100 µl. The reaction was stopped after 60 min incubation by adding 1 ml of 0.1 *N* sodium hydroxide (pH 12). The values given represent means ± S.E. The figures in brackets denote the number of animals used and those below the S.E.'s the number of weeks in which the experiments were carried out. Statistical analysis (Student's *t*-test): Thurs + Fri vs Sat + Sun + Mon $p < 0.001$; Tue + Wed vs Thurs + Fri $p < 0.001$. For further details see Figure 2.

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Clear evidence for the presence of 7-day rhythmic changes of pineal function was obtained by studying the activity of hydroxyindole-*O*-methyl transferase (HIOMT) which is a key enzyme in the formation of the pineal hormone, melatonin[1].

Figure 1 shows that, in the pineal glands of female Wistar rats kept under natural lighting conditions, HIOMT activity followed a characteristic pattern. HIOMT activity was highest on Saturdays and lowest on Thursdays, the Thursday values being 6 times lower than those on Saturdays. A gradual decrease in enzyme activity was noted between Saturdays and Thursdays, a striking increase occurred between Fridays and Saturdays.

Since HIOMT activity is supposed to be twice as high in metestrus and diestrus as in proestrus and estrus[5], the stage of the estrous cycle was taken into consideration. In Figure 2 it can be seen that the differences observed are not due to sampling animals of a particular stage of the estrous cycle on particular days of the week.

Female rats kept under a lighting schedule of 12 h illumination (07.00 to 19.00 h) and 12 h darkness showed an HIOMT pattern similar to that of the above animals, but with the highest peak on Sunday. Male rats (Figure 3) also revealed the characteristic weekly HIOMT pattern.

Indications that pineal function might vary according to the day of week was also obtained by studying the synaptic ribbons which, it has been suggested, might be involved in intercellular communication between adjacent pinealocytes[6,7], the main cellular constituent of the mammalian pineal gland. The results obtained in the present study are listed in the Table. It can be seen that 3 series of experiments yielded somewhat variable results. In the first experiment, the amount of ribbon fields showed a behaviour similar to that of HIOMT activity, but with a phase shift of 2 days. In the other two experiments, perhaps the most important finding was that the Monday values differed strikingly from those obtained on the other days of the week.

The comparison of the results obtained for HIOMT activity and the amount of ribbon fields reveals that the two parameters studied apparently follow different patterns. Nevertheless, both parameters support the view that pineal function may differ according to the day of week. At the present state of our knowledge, HIOMT activity represents a better parameter of pineal function than the amount of synaptic ribbons, and we therefore attach more importance to the HIOMT results. We feel that, after exclusion of any technical errors, the HIOMT

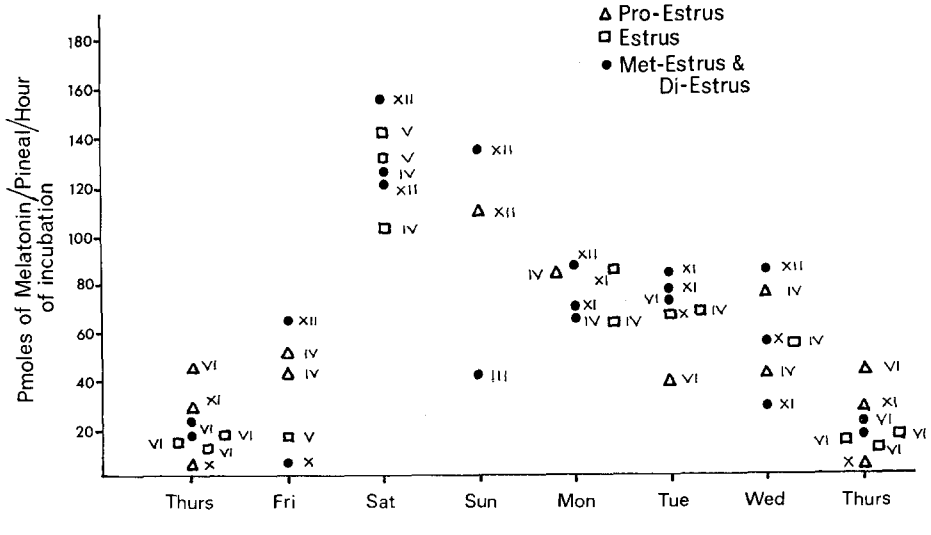

Fig. 2. HIOMT activity of individual animals (i.e. those used in Figure 1) taking into consideration the stage of the estrous cycle. The Roman numerals denote the month in which the experiments were carried out. Because of a fair number of borderline cases between Met-Estrous and Di-Estrous animals these two phases were pooled.

results have been so consistent over many weeks and months that they can well serve as a basis for a working hypothesis that rat pineal function exhibits a 7-day rhythmic activity.

We are aware that the postulate of a 7-day functional cycle is an unusual one. Admittedly, there is no known prominent geophysical counterpart for such a rhythm[8]. On the other hand, the results reported here do not represent the first hint for such a rhythm. Circaseptan rhythms in thermovariance[9] and 17-ketosteroid excretion[8] have been described in humans. The fact that the latter rhythm was not always synchronized with the weekly societal rhythm led to the speculation that a weekly component in physiologic function might have preceded the societal 7-day week and that the sizeable gap between circadian rhythms on the one hand and monthly and annual rhythms on the other might be reduced by about weekly rhythms and that this could facilitate the temporal integration of organisms[8].

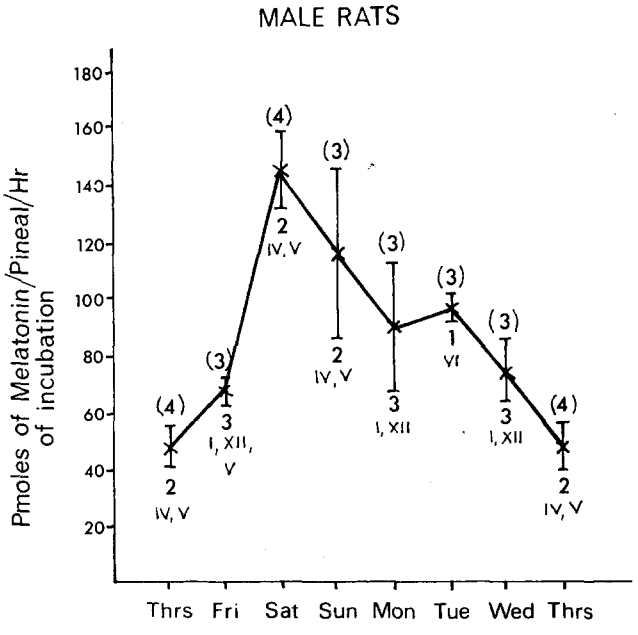

Fig. 3. HIOMT activity in pineal glands of male Wistar rats. For details see Figure 1, for the explanation of the Roman numerals Figure 2. Statistical analysis: Sat + Sun vs Wed + Thurs + Fri $p < 0.001$.

From our results we are inclined to conclude that, if the 7-day cycle in the rat pineal gland is not endogenous, it is probably the change in the environmental conditions over the weekend which has a profound and long-lasting effect on the organ. Such an interpretation is all the more likely because most pronounced changes occurred in relation to the weekend. Furthermore it is becoming increasingly apparent that factors other than environmental lighting affect pineal function as well[10,11]. Seasonal rhythms[11], the presence of β-receptors whose sensitivity undergoes characteristic changes[12] and the close association with the sympathetic nervous system[1] make the pineal an ideal target for external and internal stimuli which could easily lead to a superimposition of a 7-day functional cycle on 24 h cycles. In this context it is interesting to note that recently the HIOMT activity pattern during the estrous cycle in the rat has been described as the sum of the oscillations of at least 2 rhythms whose frequencies differ slightly[13]. Further studies are in progress to elucidate the factor(s) responsible for the 7-day cycle and to unravel its physiological significance.

Zusammenfassung. In der Zirbeldrüse männlicher und weiblicher Ratten deutet das Verhalten des an der Melatoninbildung beteiligten Enzyms Hydroxyindol-*O*-methyltransferase auf das Vorhandensein eines 7tägigen Funktionszyklus hin.

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Uncoupling of Heart Cells Produced by Intracellular Sodium Injection

It is known that the low intracellular calcium concentration in muscle cells is maintained by an active uptake by mitochondria and sarcoplasmic reticulum, and also by active extrusion of the ion through the surface cell membrane.

In other cells, like red blood cells, ATP is used directly to extrude calcium from the cell interior[1]. In excitable tissues, however, evidence has been obtained that the inward movement of Na^+ and probably the outward movement of K^+ provides energy for calcium extrusion[2,3]. In this case, the breakdown of ATP is indirectly involved, since it is essential for the maintenance of sodium gradient.

In cardiac muscle the stochiometric relationship seems to be the exchange of two sodium ions for one calcium ion[4]. Studies of BAKER and BLAUSTEIN[5], and BAKER et al.[3] showed, indeed, that a small raise in the intracellular sodium concentration of the squid axon, results in a large increase in the intracellular calcium concentration.

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