measurable due to tissue variation of enzyme concentration.

The fact that there is essentially no change in the absolute amount of the enzyme indicates that the increased activities recovered in the lower density range comes from the $NA_{1.178}$ particle. If this is the case, and since 80% of the DβH is bound to the vesicular membrane, then the vesicle must be transformed into lighter units by nerve stimulation – these lighter units possibly being fragments of the vesicular membrane itself.

When a vesicle containing pellet from the spleen was lysed by hypo-osmotic shock, and then subjected to density gradient centrifugation, the DβH activity was almost entirely confined to the 1.107–1.115 density range. This apparently membrane-bound DβH has the same density characteristics as some of the DβH present in the spleen after electrical stimulation, i.e. sedimentation to the density range 1.107–1.115. Additionally, when a vesicular pellet was incubated at 37°C for 30 min to empty it of its NA, the density of the DβH of these 'empty' vesicles was 1,150. These results show that it is not merely a loss of NA which causes the marked DβH density changes after electrical stimulation but that the vesicle is fragmented so that only the membrane remains.

It is apparent that $NA_{1.125}$ has lost more of its NA than the other particle (Figure 2). While it seems obvious from previous experiments[6–8] that $NA_{1.178}$ directly releases its NA (and DβH), the results reported here imply that both particles are involved in the release process. Whether they both release their NA directly into the extracellular space remains unresolved, however. It is equally possible that $NA_{1.125}$ acts as an emergency store of transmitter which is used to fill the other vesicles under stress conditions.

Of the several modes of NA release which have been suggested[10], the one to gain the most recent support has been that of exocytosis[6–8]. The present series of experiments offer additional support for this release mechanism in that it is the only one which could increase the amount of DβH containing membranes. Whether the release is by a true exocytotic mechanism i.e. a fusion of the vesicular and axonal membranes for a finite time, or by a reversed pinocytosis where the vesicle is incorporated into the axonal membrane, cannot be resolved by these experiments. In either case, however, the resultant increase in vesicular membrane in the nerve endings indicates that once having fused, the vesicle is replaced and not reused[11].

Résumé. Une stimulation électrique in situ de la rate du chien provoque l'apparition de membranes contenant de la dopamine-β-hydroxylase. Les membranes sont très probablement le résultat d'une fusion de la membrane axonale et de la membrane vésiculaire, pendant le processus de décharge. Une telle formation de membranes indique que les particules chargées de noradrénaline ne peuvent être utilisées qu'une seule fois.

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[11] This work was supported by a grant from the Fund for Interdisciplinary Research, Belgium. We thank Misses L. Feys, H. Geffens and M. Vanneste for valuable technical assistance.

Effects of Noradrenaline and Thyroxine on Cerebral Metabolism

It is well known that thyroid hormones regulate growth, differentiation and oxidative metabolism in various animals. There are many interrelationships between catecholamines and thyroid hormones[1,2]. The aim of this study is to show what effect noradrenaline, thyroxine and both together have on respiration of the rat cortex slices during ontogeny. Because it has been observed that the concentration of 10^{-4} *M* noradrenaline increases the oxygen consumption of some parts of the brain[3], only this concentration was used. Thyroxine-doses at the different stages of ontogeny were given approximately according to Tirri et al.[4].

Materials and methods. Sprague-Dawley rats were used as experimental animals. Litters were reduced to 8 animals. Half of them were injected s.c. with thyroxine once a day and the other half, injected with 0.9% NaCl, served as controls. Thyroxine was dissolved first in 0.1 *N* NaOH and then diluted with 0.9% NaCl saline. The animals were killed by decapitation, the brains were excised at 0°C and 0.3–0.4 mm thick slices were cut from the cortex. The oxygen consumption of the brain cortex slices was measured by conventional Warburg technique at 37°C using Krebs-Ringer phosphate saline (pH 7.2) with glucose (6 m*M*) as a medium. Pure oxygen was used as gaseous phase. Noradrenaline used in half of the experiments was tipped into the medium after the first manometric reading. Usually less than 120 sec elapsed from decapitation to cooling of the brain with saline and after 15–20 min the Warburg vessels were in the thermostat. The results were calculated on the basis of dry weight of the tissues and expressed as QO_2 (μl O_2 per mg dry weight per h) for the first three 30-min periods after the gassing and equilibration periods of 5 min and 10 min, respectively.

Results and discussion. It can be seen from Table I that noradrenaline (10^{-4} *M*) had no effect on the respiration of rat brain cortex slices during ontogeny. In an earlier study, it was observed that noradrenaline does not affect the respiration of the adult rat cortex slices[3]. However, noradrenaline increased the respiration of cortex slices in age groups of 20, 40 and 120 days in rats treated with thyroxine. It was generally observed that the stimulation of oxygen consumption caused by noradrenaline decreases as a function of time. Because 10 days was the only age

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Table I. The effect of noradrenaline ($10^{-4}M$) on the oxygen consumption (QO_2) of rat brain cortex slices during ontogeny

Age (days)		$QO_2 \pm$ S.E.M. (0–30 min)	Significance (p)	$QO_2 \pm$ S.E.M. (30–60 min)	Significance (p)
10	Control	12.8 ± 0.5 (6)	—	12.7 ± 0.5	—
	Noradrenaline	13.8 ± 0.8 (6)		13.1 ± 0.7	
20	Control	14.1 ± 0.3 (7)	—	13.9 ± 0.4	—
	Noradrenaline	13.9 ± 0.5 (7)		13.7 ± 0.4	
40	Control	13.5 ± 0.4 (10)	< 0.1	12.7 ± 0.4	—
	Noradrenaline	12.8 ± 0.4 (10)		12.7 ± 0.4	

–, not significant. Number of experiments in parentheses.

Table II. The effect of noradrenaline ($10^{-4}M$) on the oxygen consumption (QO_2) of thyroxine treated rat cortex slices during ontogeny

Age (days)		$QO_2 \pm$ S.E.M. (0–30 min)	Significance (p)	$QO_2 \pm$ S.E.M. (30–60 min)	Significance p	Dosis (μg T_4/kg)
10	Control	13.2 ± 0.5 (6)	—	13.0 ± 0.3	—	3×300
	Noradrenaline	12.5 ± 0.4 (6)		11.7 ± 0.9		
20	Control	13.4 ± 0.4 (8)	< 0.025	13.7 ± 0.5	< 0.1	3×300
	Noradrenaline	14.7 ± 0.3 (8)		15.4 ± 0.6		
40	Control	12.6 ± 0.3 (11)	< 0.01	12.6 ± 0.4	< 0.025	4×700
	Noradrenaline	14.7 ± 0.4 (11)		13.9 ± 0.5		
120	Control	11.2 ± 0.5 (9)	< 0.05	11.8 ± 0.4	< 0.1	5×800
	Noradrenaline	13.0 ± 0.4 (9)		12.9 ± 0.3		

–, not significant. Number of experiments in parentheses.

group in which noradrenaline caused no stimulation of respiration, it may be expected that thyroxine dosage was not optimal. Two different doses: 2×300 μg T_4/kg and 5×300 μg T_4/kg were also tested. Noradrenaline had no effect also in both of the cases.

KRISHNA et al.[1] detected (the dose of thyroxine was similar to that used in this study) that thyroxine increases the amount of adenyl cyclase in the adipose tissue of the adult rat. There is some evidence[5,6] that catecholamines stimulate the adenyl cyclase in the cortex. It is thus possible that the stimulated metabolism caused by increased 3′, 5′-AMP could explain the increased oxygen consumption.

If the control values in Tables I and II are compared with each other, the effect of thyroxine on the respiration of the cortex slices can be seen. FAZEKAS et al.[7] found that thyroxine increases the respiration of juvenile rat cortex slices, which could not be observed in the study in question. Perhaps it is the different thyroxine dosage that causes the difference in the results. RASKIN and FISHMAN[8] found that the Na-content of the brain tissue increases in case of hyperthyreosis, whereas the K-content is decreased. However, there was no difference in the activity of ATP-ase. Perhaps the result is due to a failure of methods because the lowered ATPase activity could explain the small decrease of respiration observed in this study.

Zusammenfassung. Bei mit Thyroxin behandelten Ratten verursachte Noradrenalin eine Stimulierung des Sauerstoffverbrauchs in Cortex-Ausschnitten. Der Wegfall dieser Beobachtung bei normalen Ratten weist auf die Wechselwirkung zwischen Noradrenalin und Thyroxin im Gehirngewebe hin.

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Effect of Oxyphenbutazone on Concentration of Penicillin in Serum

Non-hormonal antiphlogistic therapy with pyrazol derivatives has long been used successfully in the treatment of inflammatory processes, fever and pain. According to LEGLER and BRACHARZ[1], treatment with antiphlogistics of oxyphenbutazone type combined with antibiotics results in a higher antibiotic concentration in the serum. This increase has been ascribed either to inhibition of the tubular secretion[2], or to interaction of pyrazol derivatives