en évidence un rôle direct du thymus sur l'hypophyse. En effet, la thymectomie néonatale entraîne une dégranulation des cellules somatotropes, la surface de l'ergastoplasme est augmenté, le volume relatif de l'appareil de Golgi est augmenté et celui des mitochondries diminué. Ces modifications peuvent correspondre à une augmentation de la synthèse de l'hormone de croissance. Cette hypothèse est confirmée par l'élévation du taux plasmatique de GH que nous avons dosée chez les animaux thymectomisés. Nous avions d'ailleurs déjà montré que la synthèse d'ADN hypophysaire était augmentée après thymectomie[2].

Ces modifications cytologiques sont corrigées par les injections d'extrait thymique. Cependant, après cette opothérapie de substitution, nous constatons que le nombre de granules contenus dans les cellules somatotropes est supérieur à celui du témoin, alors que le taux de GH est inférieur à la normale. On peut penser que l'extrait thymique agit de façon synergique avec la GH comme Comsa[11] et nous mêmes[2] l'avions précédemment suggéré. Dans cette hypothèse l'animal thymectomisé recevant l'extrait aurait besoin d'une quantité plus faible de GH pour obtenir le même effet. L'extrait thymique agirait ainsi en bloquant la sécrétion de GH.

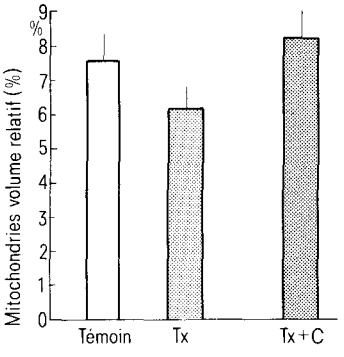

Fig. 5: Etude du volume relatif des mitochondries dans les cellules somatotropes. Influence de la thymectomie néonatale (Tx); opothérapie de substitution réalisée par l'extrait de Comsa (Tx+C).

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Effects of thyroid state on brain stem responses to iontophoretic noradrenaline[1]

J.A. Gonzáles-Vegas and Dolores Fuenmayor

Escuela de Bioanalisis, Facultad de Medicina, Universidad Central de Venezuela, Caracas (Venezuela), 13 January 1978

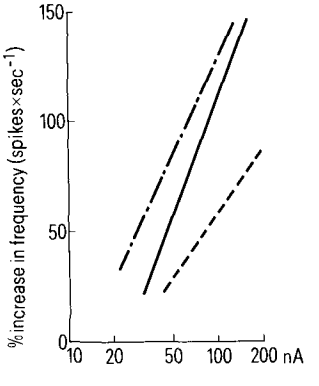
Summary. Responses to iontophoretic NA were increased in hyperthyroid rats and decreased in hypothyroid animals. No effect was observed on acetylcholine and glycine responses tested in the same way.

It has been suggested that thyroid hormone levels can influence the actions of catecholamines (CA) both at the peripheral target organs[2,3] and in the brain. Thus intraventricular administration of noradrenaline (NA) enhances motor activity in hyperthyroid rats[4], and injection of apomorphine (a dopamine agonist) to guinea-pigs made hyperthyroid results in an increased production of stereotypies as compared to untreated controls[5]. More recently Fregly et al.[6] have shown decreased beta receptor responsiveness in hypothyroid rats. This and other clinical evidence has led to the suggestion that thyroid hormone could alter the sensitivity of adrenergic receptors[7].

It was decided to investigate this possibility, at the single unit level in the brain, by studying changes in the responses to iontophoretically applied NA, in animals in which the thyroid state was altered. The technique of microiontophoresis was used in order to avoid the complications involved in the systemic administration of drugs.

Materials and methods. Male Sprague-Dawley rats of 250–350 g were divided into 3 groups. One served as a control group, 1 group received daily injections of triiodothyronine (150 µg i.p.) for 10 days, and the remaining group of rats were made hypothyroid either surgically or by administration of methimazole in drinking water. The thyroid function was assessed by measuring oxygen consumption and weight gain as compared to untreated controls.

The rats were anaesthetized with urethane (1 g/kg i.p.) and held in a stereotaxic frame, after drilling the overlaying bone, the cerebellum was removed by suction in order to expose the floor of the i.v. ventricle where all recordings were made (1–3 mm anterior to obex; 1–2 mm lateral to the midline; and 1–3 mm depth). 5 barrelled micropipettes containing the following drugs as 10% solutions were used: noradrenaline HCl pH 5.0; acetylcholine chloride pH 6.0; glycine pH 3.0, and NaCl 2 M was used in the remaining barrel to test for current artifacts. Conventional techniques were used to record from the central barrel of the assembly. Spikes were voltage-gated, counted, and the firing frequency over 1 sec epochs was displayed in a pen recorder as a frequency histogram. Special care was taken to ensure constant retention currents and a fixed interval between drug applications, to avoid introducing experimental arti-



Response to iontophoretically applied NA. Dose-response lines corresponding to: Control (——), hypothyroid (----) and hyperthyroid (-·-·-·-) groups; Regression lines were calculated by the least square method. Control group, $r=0.92$ $p<0.01$; hypothyroid, $r=0.75$ $p<0.05$; Hyperthyroid, $r=0.97$ $p<0.01$. Ordinate: percent increment above control frequency. Abscissa: current in nA.

facts[8] and prevent the development of tachiphylaxis. In addition, in some experiments the same electrode was used to record from control and from experimental animals, in an effort to compensate for changes due to different transport numbers in different pipettes. All recordings were made from 120 spontaneously active, unidentified brainstem neurones.

Results and discussion. NA responses were qualitatively similar to those previously described[9], but excitation was found more frequently than inhibition, so the former response was used in this study. Once a responsive unit was found, NA was applied at several currents, and a similar schedule was used with all the drugs tested. Threshold and maximal responses were not investigated. The averaged firing frequency measured in the minute preceding a 30 sec application, was compared to the maximum frequency attained after the application, and this was expressed as a percentage increase above the control frequency. Dose-response curves were constructed by drawing regression lines, using all data points obtained for a particular drug, from all animals in a group.

The figure shows the response to NA. The dose-response lines corresponding to experimental animals are displaced significantly in relation to control animals, suggesting decreased responsiveness in hypothyroid animals and increased responsiveness in hyperthyroid rats. A similar analysis of acetylcholine and glycine responses did not show any significant change (data not shown).

The present results are similar, at the single unit level, to those already quoted[2-6] which have used different paradigms of CA action, and suggest that this could be a general action of thyroid hormone in adrenergic systems. It is premature to speculate on the exact mechanism of action by which this effect is brought about, but experiments (to be reported elsewhere) show that acute administration of thyroid hormone by microiontophoresis does not produce the same effect, so it would appear that chronic administration is necessary to produce the change described. It is interesting to note that thyroid hormone can be taken by nerve terminals[10], and Dratman[11] has proposed that thyroid hormone could also act as an amino acid analog of tyrosine, whose uptake and subsequent metabolism by nerve tissue could lead to the formation of false transmitters, and these in turn could produce post-synaptic supersensitivity if released in sufficient amounts. Alternatively a certain level of thyroid hormone may be necessary for adequate synaptic function, levels above or below leading to hypersensitivity or hyposensitivity respectively.

The results reported could also have some bearing upon the explanation of the enhancement of the antidepressive action of imipramine produced by thyroid hormone[12], as CA have been involved in the pathogenesis of depression[13].

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PRO EXPERIMENTIS

Influence of hydrocortisone on cytopathic effect of Newcastle disease virus and stability to freezing of vescicular stomatitis virus[1]

R. Pompei, M.A. Marcialis, O. Flore, A. Pani, M.E. Marongiu and P.E. Manconi

Institutes of Microbiology II and Hygiene II, University of Cagliari, via G.T. Porcell 12, I-09100 Cagliari (Italy), 5 January 1978

Summary. The presence of hydrocortisone in virus-infected cell cultures leads to enhancement of the syncytia forming ability of Newcastle disease virus and to production of vescicular stomatitis virus particles which loose their infectivity upon storage below 0 °C.

In the course of investigations on the effects of steroid hormones on virus growth and cytopathology, it has been observed that hydrocortisone enhances the ability of Newcastle disease virus to form syncytia and leads to production of vescicular stomatitis virus particles which are inactivated when stored below 0 °C. Preliminary data from these researches are referred to herein.

Materials and methods. Hydrocortisone hemisuccinate was furnished by Sigma. Virus strains were Newcastle disease virus (NDV) and vescicular stomatitis virus (VSV), both used in previous researches[2]. Experiments were carried out on aneuploid HEp2 cells (ATCC, Rockville), grown in Eagle's minimum essential medium (MEM) brought at pH 7.3, and supplemented with 7% calf serum. 16-h-old cell monolayers (10^6 cells/sample) were infected with 10 virus plaque forming units (PFU) per cell for 1 h at 20 °C, washed 3 times in Hanks' balanced saline solution (BSS, pH 7.3) and incubated at 37 °C in Eagle's MEM (pH 7.3) containing 2% calf serum. Hydrocortisone was added to the infected cultures in decreasing concentrations, starting from the maximum non-cytotoxic dose (MNCTD) established as previously described[3]. Virus-induced cytopathology was evaluated by microscope examination of cell monolayers stained by Giemsa. To quantitize infectious virus yield, whole culture samples were sonicated (40 Hz for 1 min) and stored at either above or below 0 °C prior to being cleared of cell debris at 3000 rpm for 5 min. Appropriate dilutions of supernatants thus obtained were tested for the content in PFU by the agar method[4]. An error of about 23% was found for both viruses.

Results. Table 1 shows the results obtained from tests in which hydrocortisone was added to cell cultures soon after