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Adrenovascular Lesions from Neurogenic Stress Modified by Suppression of Nervous Centres in Rat

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Adrenovascular lesions (hemorrhages and/or edema) caused by neurogenic stress, are modified by suppression of different nervous centres. Spinal transection at Th5 abolishes the adrenovascular response to neurogenic stress. Destruction of the anterior or posterior hypothalamus decreases this vascular response; the greatest effect was obtained by destruction of the hypothalamus medius or by hemidecortication. This effect was bilateral but more manifest contralaterally in cases with unilateral destruction. These results show that the adrenovascular reaction to neurogenic stress is regulated by the central nervous system, mainly by the hypothalamus and cerebral cortex.

Key words: Adrenal, Adrenal lesions, Neurogenic stress.

In a previous paper (11), the adrenovascular alterations caused by neurogenic stress in the rat and its modifications by different adrenal neurotomies were described. Vagotomy did not diminish the adrenovascular lesions, while splanchnicotomy practically abolished them. Since this influence of the sympathetic system on the adrenal glands is regulated by the central nervous system, it has been considered of interest to investigate the nervous centres more directly involved in such regulation. To this end different centres were lesioned: the spinal cord (transection at Th5), unilateral diathermocoagulation of the hypothalamus anterior, medius or posterior, and hemidecortication, the adrenovascular reaction subsequent to a neurogenic stress being compared with that of a control group.

Materials and Methods

Male Wistar rats of 230-250 g b.w., were housed in cages in a room at a constant temperature (21 ± 2 °C) and with a nyctameral light-dark cycle. Water and food were given *ad libitum*. According to the experiments, the rats were distributed into 6 groups: 1) control; 2) spinal tran-

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section (Th5); 3) diathermocoagulation of the right hypothalamus anterior; 4) Similarly with the hypothalamus medius; 5) the hypothalamus posterior; and 6) right hemidecortication. Each one of these groups was divided into two subgroups of animals: 5 rats were stressed 90 min before decapitation while the other 5 were not. The neurogenic stress was provoked by restraining the animals during 5 min and pinpricking them on the dorsum. Before surgical intervention the rats were anesthetized with nembutal (30 mg/kg) and the surgical techniques were those habitual in such cases. For the electrocoagulation of the hypothalamus, the skull of the rats, fixed in a stereotaxis apparatus, was drilled in appropriate points (1).

After a recovery time of 10 days, the rats were decapitated, the adrenals and encephalon were quickly removed and fixed in 10 % formalin. They were processed for inclusion in paraffin, cut (7 μm) and stained: the adrenals with hematoxylin-eosine and Masson's trichromic, and the brains with hematoxylin-eosine and cresyl-violett.

The spinal transection was checked exploring the motility and pain perception in the caudal extremities and, at necropsy, by examination with a surgical microscope of the transected myelomere.

The serial sections of the brain permitted a reconstruction of the hypothalamic lesions or, in the cases of hemidecortication, the deep cortical ablation. All cases with incorrect lesions were rejected.

To objetify the vascular changes that appeared in the different experiments, the area of the capillary bed and that of the hemorrhage as well as the area of the adrenal cortex was measured. The ratio vascular area/cortex area is expressed in percentages.

Results

Control group-neurogenic stress. — The neurogenic stress provoked an intense adrenovascular reaction: generalized vasodilatation and, in some areas, edema and hemorrhages. The vascular alterations were more intense in the zona fasciculata interna (ZFI) and in the zona reticularis (ZR). As a consequence of the vascular alterations the ZR appeared as a compressed zone. The average of the hemorrhagic area was 2.1 % of the cortex surface and that of the capillary bed 5.7 %.

Spinal transection at Th5. — The animals recovery was rapid and, with suitable care, without scars or infections in the anesthetized skin. The adrenal glands of these rats did not show any vascular alteration, and neither did the other 5 that were stressed (fig. 1). Capillary bed 1.3 %.

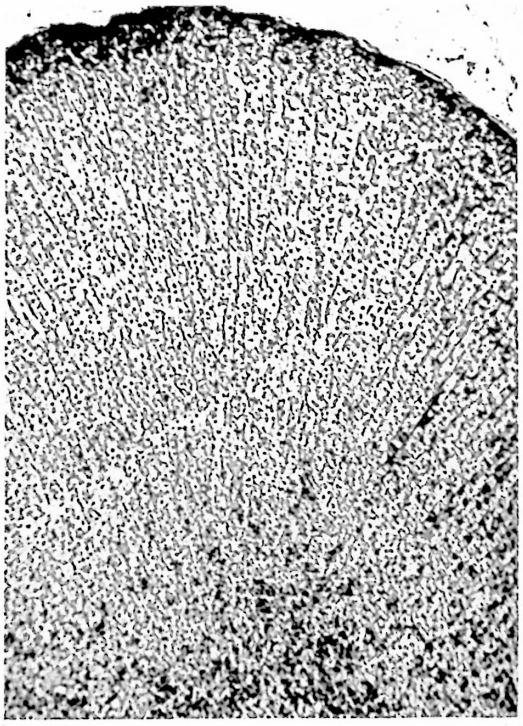


Fig. 1. *Adrenal cortex of a stressed rat with spinal cord transection.*
There is no vascular response to stress. Hematoxylin-eosine (× 70).

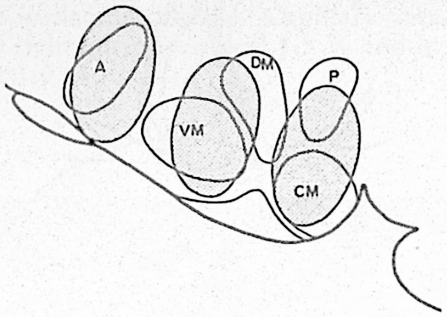
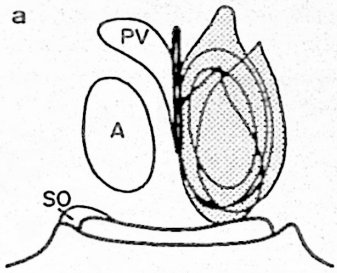


Fig. 2. *Schematic representation of a parasagital section (0.25 mm lateral) of the rat's hypothalamus, with the 3 destroyed areas (anterior, middle and posterior hypothalamus).*

Diathermocoagulation of the right hypothalamus anterior. — The area destroyed included: nucleus hypothalamicus anterior, n. paraventricularis and the middle third of the n. supraopticus (fig. 3). This destruction did not alter the vascular pattern of the adrenals. The stressed animals, on the contrary, showed a clear adrenovascular reaction, although of lesser intensity than in the stressed controls (group 1). This reaction, more manifest in the ipsilateral gland, was characterized by vasodilatation, in some cases by edema in ZFI and ZR, and in the right adrenal by spots with erytrocytic extravasation (fig. 4). The area of the capillary bed in the right adrenal cortex was 3.1 % and in the left one 2.9 %.

Diathermocoagulation of the right hypothalamus medius (fig. 4). — The nuclei eliminated were: arcuatus, ventromedialis and the ventral part of the dorsomedialis. The adrenals of the unstressed rats did not show vascular alterations. In the stressed animals the adrenovascular reaction was very limited (fig. 4b), and only a slight vasodilatation was observed in the ipsilateral gland. Capillary area: 1.8 %.

Diathermocoagulation of the hypothalamus posterior (fig. 5). — The lesion destroyed the right half of the corpus mammillare and the n. hypothalamicus posterior. The suppression of these nuclei did not cause adrenovascular alterations in the unstressed animals. The stressed rats



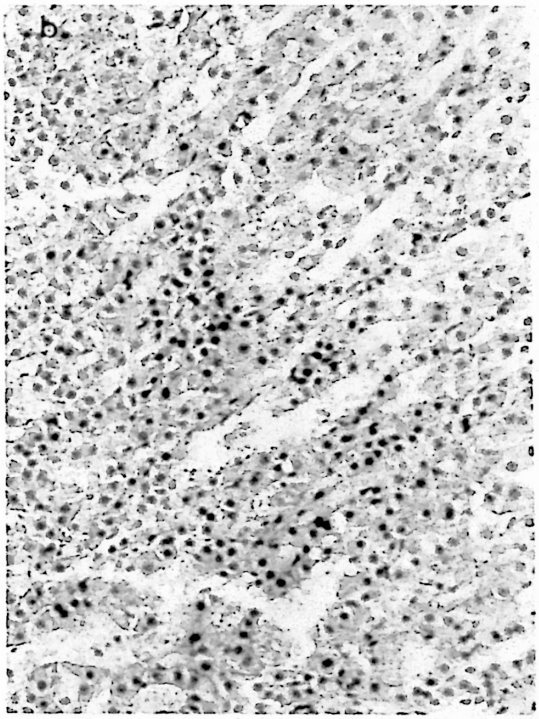


Fig. 3. *Electrocoagulation of the hypothalamus anterior.*
Schematic representation of a coronal section of the anterior hypothalamus of the rat. On the left side are represented the nuclei, and on the right side the lesions of the stressed rats of this group. b) Left adrenal cortex of one of these rats. Shows vasodilatation and erythrocytic extravasation. Hematoxylin-eosine (× 190).

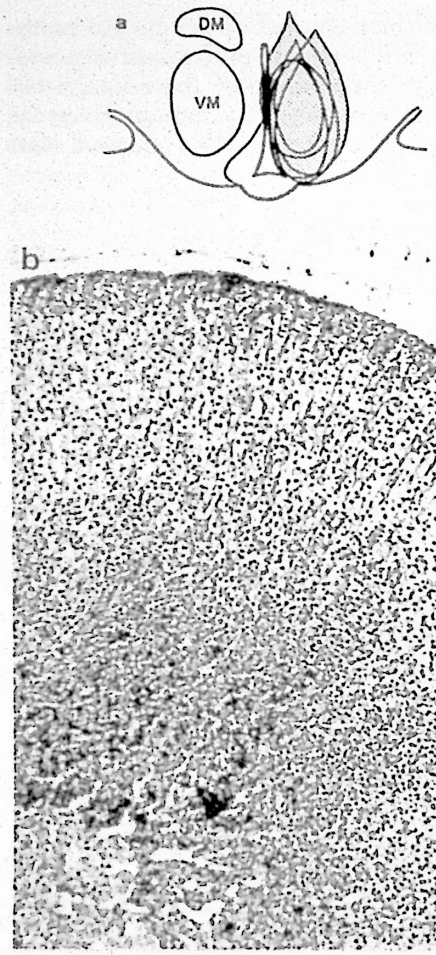


Fig. 4. *Electrocoagulation of the hypothalamus medius.*
Coronal section of the rat's middle hypothalamus. b) Left adrenal cortex of a stressed rat of this group. It can be noticed the absence of vascular alterations. Hematoxylin-eosine (× 70).

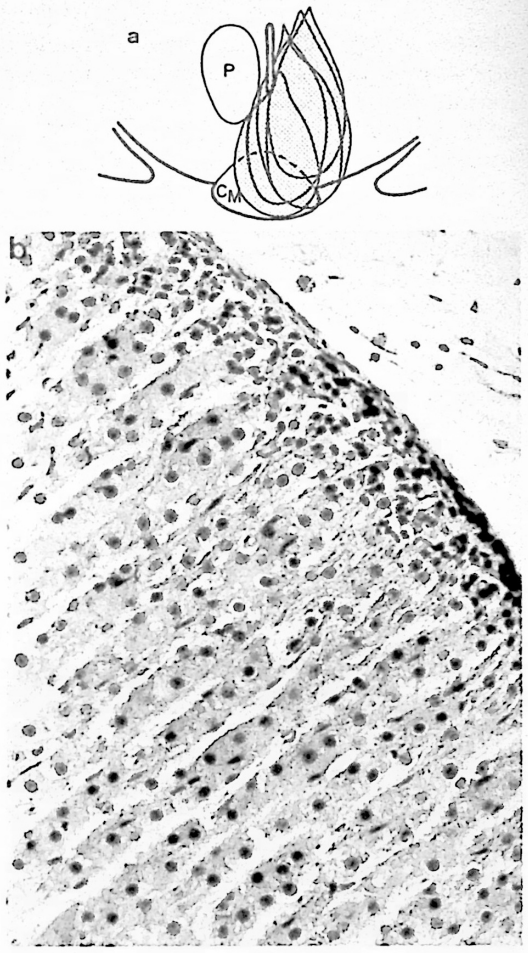


Fig. 5. *Electrocoagulation of the hypothalamus posterior.*
Coronal section of the rat's posterior hypothalamus. Left side, nuclei; right side, extension of the lesions. b) Left adrenal cortex of a stressed rat of this group. There is vasodilatation and edema. Hematoxylin-eosine (× 250).

showed, however, vasodilatation and edema in the ZFI and ZR, mainly in the ipsilateral adrenal (fig. 5) and, in one case, a small erythrocytic extravasation was observed. This adrenovascular reaction was smaller than that observed in the animals with destruction of the hypotalamus anterior. The capillary area was 4.7 % and the hemorrhage one 0.3 % in the right, and 4.1 % and 0.5 % respectively in the left adrenal.

Right hemidecortication (fig. 6). — Simple hemidecortication did not provoke vascular alterations in the adrenals; neither did the 5 stressed rats show adrenovascular alterations (fig. 6b). Only a slight vasodilatation in the ZR was observed in

the ipsilateral adrenal. Capillary area, in the right adrenal cortex, 1.5 % and in the left 1.0 %.

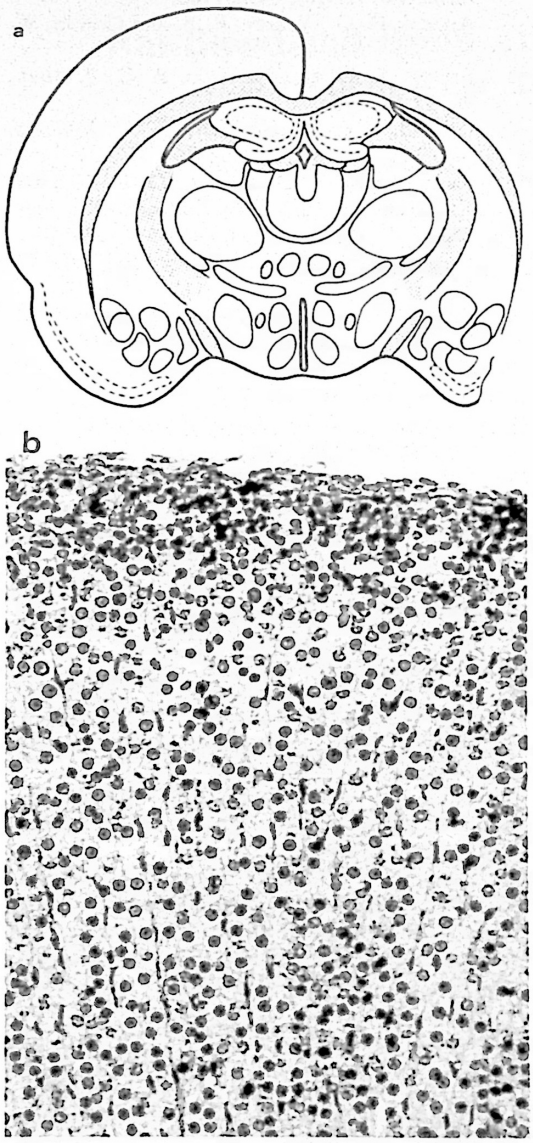


Fig. 6. *Hemidecortication of the right hemisphere.* Line drawing that shows the extension of the hemidecortication in group 6. b) Left adrenal cortex of a contralateral hemidecorticated and stressed rat. No vascular changes can be noticed. Hematoxylin-eosine (× 250).

Discussion

The effectiveness of the neurogenic stress employed in generating the adrenovascular reaction seems evident from the present results, and was discussed in a previous paper (11). The time elapsed between the action of the stress and the appearance of the adrenovascular reaction is very short (3, 15) making a 90 min delay prior to decapitation advisable as the adrenal lesions were more apparent at this time (11).

Spinal transection at Th5. — The suppression by spinal transection of the adrenovascular reaction in the stressed animals suggests that the control of this reaction is supraspinal, since the adrenal spinal centre is located caudal to Th5 (6, 9). Thus, as the two supraspinal centres more related to the adrenal function are the hypothalamus and cerebral cortex, successive elimination of the hypothalamus and the cortex of the right hemishpere was carried out. Since large destructions of the hypothalamus alter multiple functions which could interfere with results, unilateral lesions were produced either in the hypothalamus anterior, medius or posterior. Unilateral lesions, on the other hand, have enabled us to learn if the descending pathway is uni- or bilateral, and in the latter case if it has an ipsi or contralateral predominance.

Partial destruction of the hypothalamus. — The results obtained with partial destruction of the hypothalamus showed that the hypothalamus medius is the area most directly related to the adrenovascular control. The hypothalamus anterior and posterior also have an influence on the adrenovascular reaction to neurogenic stress but to a lesser degree. This agrees with the data reported by neuroendocrinologists (8, 10, 17, 21, 27) according to which the principal adrenocorticotropic centres are located in the hypothalamus medius. The

effect of these partial lesions of the hypothalamus is more evident on the contralateral side, i.e., the adrenovascular alterations are more manifest on the side of the neural lesion. This side difference also indicates that the pathway is neural rather than humoral, for if the hypothalamic influence on the adrenal vessels were exerted through the adenohypophysis, then there would be no difference between the right and left adrenal gland.

Hemidecortication. — Unilateral ablation of the cerebral cortex suppressed the adrenovascular reaction in the contralateral adrenal gland and clearly diminished it ipsilaterally which is in agreement with results reported by REINOSO (23). This cortical influence was stronger than that of the hypothalamus medius, supporting the hypothesis that the cortical control is at least partially exerted directly, without intervention of the hypothalamus, by means of direct projections to the reticular nuclei (16, 18, 22, 25) and to the autonomic centres of the brain stem and spinal cord (12, 14, 19). The existence of a direct corticospinal pathway, however, does not exclude the possibility that a part of the cortical action on the adrenovascular response to neurogenic stress could be carried out through the hypothalamus, since the cortico-hypothalamic projections are abundant (2, 4, 5, 7, 24, 27).

Resumen

Las alteraciones adrenovasculares provocadas por un estrés neurógeno se modifican al eliminar diferentes centros nerviosos: se suprime esta reacción al seccionar la médula espinal a nivel T5, al electrocoagular el hipotálamo medio y tras la hemidecorticación. Cuando la lesión es unilateral, el efecto sobre las suprarrenales es bilateral, pero con predominio contralateral. Estos resultados ponen de manifiesto el efecto regulador de los centros supraespinales en la reacción adrenovascular provocada por un estrés neurógeno.

Palabras clave: Suprarrenal, Lesiones suprarrenales, Estrés neurógeno.

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