

Results and discussion. The Figure shows a gradual decrease of respiratory rate with developing dehydration. The panting produced by a local POA heating (from 39.2 ± 0.1 to $40.6 \pm 0.1^\circ\text{C}$) also diminished until it was completely blocked after 3 days. After rehydration of the animals by allowing them a free access to water for 2 h, the respiratory rate increased and the panting response to a central thermal stimulation was restored.

Food intake in the course of dehydration was considerably decreased. For this reason an additional series of experiments was made in which during 3 days of a free access to water, the daily supply of food was reduced to amounts consumed by the animals during the water-

deprivation period. No changes of respiratory activity were observed in this group of rabbits.

The ear temperature (mean \pm SE) increased in response to a local POA heating from 34.8 ± 0.4 to $36.2 \pm 0.2^\circ\text{C}$ ($p < 0.001$) in controls and from 33.4 ± 1.0 to $35.8 \pm 0.6^\circ\text{C}$ ($p < 0.01$) in dehydrated animals.

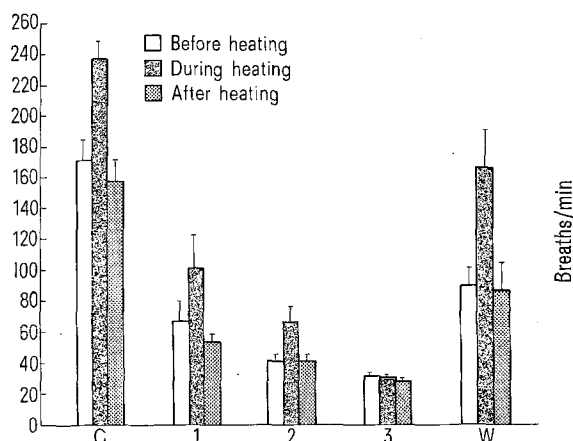
At the end of 10-min heating the rectal temperature decreased from 39.0 ± 0.1 to $38.8 \pm 0.1^\circ\text{C}$ ($p < 0.001$) in normally hydrated rabbits and from 39.2 ± 0.1 to $39.0 \pm 0.1^\circ\text{C}$ ($p < 0.01$) in water-deprived animals.

It should be stressed that respiratory movements in dehydrated rabbits were always well coordinated and the breathing rate increased in response to arousing stimuli (e.g. a sudden noise). It seems therefore that it was not impaired function of the respiratory system but rather a reduced sensitivity of the heat loss center to a thermal stimulation and/or a blocking of conduction of impulses from POA to the respiratory centres which were responsible for the inhibition of panting in dehydrated rabbits. This conclusion agrees with the opinion of EKBLOM et al.⁶ that a decreased rate of sweating in dehydrated humans is due to a reduced central influence upon sweat glands rather than to a primarily impaired secretory function of the latter.

Résumé. Chez les lapins déshydratés par privation d'eau pendant 3 jours, on constate la disparition de la polypnée produite par la stimulation thermique de l'hypothalamus antérieur, tandis que la réaction vasodilatatrice cutanée est conservée.

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Mean respiratory rates (\pm SE). C, control; 1, 2, 3, days of water deprivation; W, after 2 h of free access to water.

The Effect of Unilateral and Bilateral Lesions in the Locus coeruleus on the Levels of 3-Methoxy-4-Hydroxyphenylglycol (MHPG) in Neocortex

Studies with the histochemical technique of FALCK et al.¹ indicate that fibres arising from catecholamine-containing cell bodies in the brainstem have a widespread distribution in the mammalian central nervous system^{2,3}. Ungerstedt has presented evidence⁴ that the noradrenaline-containing terminals in the neocortex originate from cell bodies in the ipsilateral locus coeruleus, a small nucleus in the floor of the fourth ventricle (A6 cell body group of DAHLSTRÖM and FUXE²). We have recently modified⁵ the gas chromatography method of BOND⁶ to detect 3-methoxy-4-hydroxyphenylglycol (MHPG), the major metabolite of noradrenaline in rat brain^{7,8}, and developed a stereotaxic method for locating electrodes in the region of the locus coeruleus⁹. In this preliminary communication, we report the effects of unilateral and bilateral lesions of the locus coeruleus on the neocortical levels of MHPG which we take to represent an index of the turnover of noradrenaline (NA) in that region.

Methods. Eighteen female albino rats were anaesthetised with halothane and immobilized in a Kopf stereotaxic apparatus. A unipolar varnished steel electrode was located in the region of the locus coeruleus in 12 rats according to the technique of Crow, et al.⁹. An electrolytic lesion was made by passing a charge of 40 m Coul through the electrode tip to an anal cathode. In 6 animals the lesion was made on the left side, and in 6 bilaterally. In

6 further animals (controls) burr holes were drilled in the skull bilaterally and the dura removed but no electrode was inserted. 3 weeks after operation the brains were removed, the brainstems sectioned and stained by the Kluver-Barrera technique, and the neocortical portion of the prosencephalon prepared for assay of MHPG.

Results. Two rats in the group with bilateral lesions died shortly after recovery from anaesthesia. In the remaining animals, the electrolytic lesion had ablated the nucleus locus coeruleus on the appropriate side. The results of the neocortical assay for total MHPG (Table)

¹ B. FALCK, N.-A. HILLARP, G. THIEME and A. TORP, J. Histochem. Cytochem. 10, 348 (1962).

² A. DAHLSTRÖM and K. FUXE, Acta physiol. scand. 62 suppl. 232 (1965).

³ N.-E. ANDÉN, A. DAHLSTRÖM, K. FUXE, K. LARSSON, L. OLSON and U. UNGERSTEDT, Acta physiol. scand. 67, 313 (1966).

⁴ U. UNGERSTEDT, Acta physiol. scand. Suppl. 367, 1 (1971).

⁵ D. S. WALTER and D. ECCLESTON, Biochem. J., in press.

⁶ P. A. BOND, Biochem. Med. 6, 36 (1972).

⁷ E. MANNERINO, H. KIRSCHNER and B. S. NASHOLD, J. Neurochem. 10, 373 (1963).

⁸ S. M. SCHANBERG, J. J. SCHILDKRAUT, G. R. BREESE and I. J. KOPIN, Biochem. Pharmacol. 17, 247 (1968).

⁹ T. J. CROW, P. J. SPEAR and G. W. ARBUTHNOTT, Brain Res. 36, 275 (1972).

show that on the side of the unilateral lesions, and on both sides in those rats with bilateral lesions, there was a very marked reduction in the cortical content of the noradrenaline metabolite.

Discussion. These results show that histologically confirmed lesions of the nucleus locus coeruleus cause a marked fall in the turnover of noradrenaline in the ipsilateral neocortex. This supports the suggestion arising from histochemical studies⁴ that a noradrenaline-containing system with a very wide distribution in the neocortex arises from a small nucleus in the mid-pons. This finding would be consistent with the view that electrical self-stimulation obtained from electrodes placed using the same stereotaxic co-ordinates, and with their tips close to the locus coeruleus, is due to the activation of a noradrenergic-system⁹, and this may provide a clue to its function¹⁰. It is also of interest that in the group of rats with bilateral lesions (but not in either of the other 2 groups) we observed a striking behavioural syndrome

of marked hyperkinesia and repeated jumping which appeared within 2 h of recovery from anaesthesia and lasted for 4 h. Lesions of catecholamine-containing pathways are probably followed by amine release from degenerating terminals¹¹. ANDEN described a form of hyperkinesia characterised by large jumps after administration of catapresan and apomorphine in rats and postulated that noradrenaline receptor stimulation was involved¹².

Résumé. Des lésions électrolytiques, soit unilatérales soit bilatérales, ont été pratiquées dans des cerveaux de rats, dans la région du locus coeruleus. Trois semaines après, la teneur en 3-méthoxy-4-hydroxyphénylglycol (MHPG) des deux cortices cérébraux a été analysée par chromatographie à gaz. Les lésions unilatérales ont réduit la teneur en MHPG du cortex ipsilatéral, et après les lésions bilatérales la réduction eut lieu dans les deux cortices.

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Electrical Ablation of locus coeruleus

	N	L. H. Cortex (ng)	R. H. Cortex (ng)
Control rats	6	45 ± 16	42 ± 12
Unilateral (L-sided) lesions	6	17 ± 9 ^a	47 ± 11
Bilateral lesions	4	20 ± 10 ^a	17 ± 4 ^b

^a $P < 0.005$ vs control. ^b $P < 0.01$ vs control. ^c $P < 0.025$ vs control.

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¹⁰ T. J. CROW, *Nature* 219, 736 (1968).

¹¹ U. UNGERSTEDT, *Acta physiol. scand. Suppl.* 367, 49 (1971).

¹² N.-E. ANDEN, in *Amphetamines and Related Compounds* (Eds. E. COSTA and S. GARATTINI; Raven Press, New York 1970), p. 447.

Increased Hexokinase Activity in Red and White Skeletal Muscle after Denervation

Red and white skeletal muscles exhibit differences in their metabolism and in their response to denervation. Oxidative enzymes predominate in red muscles while glycolytic enzymes predominate in white muscles. Denervation tends to eliminate these differences by causing a greater fall of the predominant group of enzymes in the involved muscle¹.

The initiation of glycolysis requires the phosphorylation of glucose by the enzyme hexokinase. It might therefore be expected that hexokinase activity would display a pattern similar to that of other enzymes associated with glycolysis, being more active in white than in red muscles and undergoing a decrease in activity after denervation. The opposite pattern for hexokinase activity was found

in the present study. No other enzyme associated with glycolysis has been reported to exhibit this behavior.

Methods. 24 male albino rabbits underwent unilateral transection of the sciatic nerve. Unoperated animals were used as controls. The soleus (a red muscle) and the gastrocnemius (predominantly white) were removed and homogenized at 4°C. Hexokinase activity was measured according to the method of SHARMA et al.² as modified by

¹ E. L. HOGAN, D. M. DAWSON and F. C. A. ROMANUL, *Arch. Neurol.* 13, 274 (1965).

² C. SHARMA, R. MANJESHWAR and S. WEINHOUSE, *J. biol. Chem.* 238, 3840 (1963).

Hexokinase activity in normal and denervated soleus and gastrocnemius muscles of the rabbit

Muscle type	Control	Denervated ^a Weeks after denervation		
		2	4	8
Soleus	987 ± 133	1,150 ± 137	1,390 ± 161	1,970 ± 188
Gastrocnemius	280 ± 42	470 ± 59	784 ± 89	1,330 ± 147

Values indicate mmoles of glucose-6-phosphate formed per kg of non-collagenous protein/h of incubation. The control and each of the denervated groups consists of 8 animals, and the values represent the means ± standard errors. ^aAll the differences between the denervated and the control muscles are significant for $p = 0.01$.