Prevention of DOCA saline hypertension by central 6-hydroxydopamine; role of saline intake

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Destruction of central noradrenergic neurones by intracisternal (i.c.) injection of 6-hydroxydopamine (6-OHD) prevents the onset of renal hypertension in rabbits, (Chalmers, Dollery, Lewis & Reid, 1974) DOCA saline and spontaneous hypertension in rats (Haeusler, Finch & Thoenen, 1972). Central noradrenergic neurones may initiate the rise in arterial pressure in experimental hypertension. However, since food and water appetite is diminished in animals treated with central 6-OHD, an alternative explanation might be that these animals are salt depleted and show less rise in arterial pressure for this reason. Breese, Cooper & Smith (1973) noted DOCA saline rats treated with i.c. 6-OHD consume less saline than intact DOCA saline rats.

We have investigated the role of saline consumption in the effect of i.c. 6-OHD on this type of hypertension by restricting saline intake in a group of rats implanted with DOCA (30 mg pellet). Rats in this group D (n = 10) were given saline equivalent to the average consumption of rats in group C (n = 10) which had been pretreated with intraperitoneal pargyline (40 mg kg) and i.c. 6-OHD (200 μg x 2) and implanted with DOCA. Two control groups were used, a normotensive group A (n = 8) without DOCA implant and an hypertensive group B (n = 7) with DOCA implant. All rats were uninephrectomized and given only 0.9% saline to drink.

At 5 weeks after implantation of DOCA the systolic arterial pressures in the groups were: A 140.4 ± 3.5, B 200.4 ± 6.9, C 150.1 ± 3.3, D 190.9 ± 5.4 (mmHg ± SEM). Saline consumption in Group C was significantly diminished throughout, and during the 5th week the consumption in Group C was 29.3 ± 5.0 ml/100 g/24 hrs compared with 44.1 ± 6.1 ml/1000 g/24 hrs in Group B. However, restriction of Group D to this intake did not prevent the hypertension.

Hence although saline intake is diminished in rats centrally depleted of noradrenaline, this is not the explanation for the failure to develop hypertension. Central noradrenergic neurones play a more direct role in maintaining arterial pressure.

References

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Loss of noradrenergic and dopaminergic terminals in the chronically isolated cerebral cortex of the cat.

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The increased epileptogenicity of chronically isolated cortex is most probably a consequence of denervation. One possibility is that denervation suppresses inputs of extracortical origin that normally exert a tonic inhibitory control on cortical excitability. Amongst the transmitter candidates for such an inhibitory control other than GABA, the authors have studied catecholamines (CA) in the cat cerebral cortex.

The synthesis of ^{3}H-noradrenaline (NA) and ^{3}H-dopamine (DA) from ^{3}H-tyrosine estimated in slices of the suprasylvian gyrus and of the cerebellar cortex revealed that the ^{3}H-DA/^{3}H-NA ratio was higher in the cerebral cortex than in the cerebellum. The uptake of ^{3}H-DA estimated in homogenates of the suprasylvian cortex was not only partially blocked by desipramine but also by benztropine (blocker of CA uptake in dopaminergic terminals). These data suggest that catecholaminergic innervation in the cerebral cortex of the cat can be attributed to dopaminergic as well as noradrenergic terminals and are in agreement with recent biochemical and