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Is cortical dopamine only the precursor of noradrenaline?

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It has generally been assumed that the catecholamine nerve terminals in the rat cerebral cortex were noradrenergic (Ungerstedt, 1971). However, the dopamine (DA) concentration in this structure is comparable to that of noradrenaline (NA). To investigate whether cortical DA might play a role other than merely the precursor of NA in noradrenergic neurons, NA and DA were estimated biochemically in the cortex (Thierry, *et al.*, 1971) after electrolytic or chemical destruction of the ascending noradrenergic pathways. Groups of 8 Charles River male rats were killed 5 weeks after either bilateral electrolytic lesions of the locus coeruleus or microinjections of 6-hydroxydopamine (6-OH-DA) made laterally to the pedunculus cerebellaris superior (PCS), or after sham operations. Electrolytic lesions were made with high frequency current (100 KH_3, 2 mA. 10 s). 6-OH-DA (2 μg in one μl, protected with ascorbic acid) was injected locally into the PCS (1 μl/5 min). Lesions of the dorsal noradrenergic pathway (locus coeruleus) or combined lesions of the ventral and dorsal noradrenergic pathways (PCS) induced marked decreases in cortical NA content (Table 1), of 65 and 92%

TABLE 1. *Catecholamine levels in the rat cortex after either bilateral electrolytic lesions of the locus coeruleus or bilateral microinjection of 6-OH-DA made laterally to the pedunculus cerebellaris superior (P.C.S.)*

	Locus coeruleus		P.C.S.	
	Control	Lesion	Control	6-OH-DA
NA (μg/g)	0·280 ± 0·014	0·097 ± 0·001*	0·213 ± 0·021	0·017 ± 0·003*
DA (μg/g)	0·196 ± 0·024	0·151 ± 0·009	0·122 ± 0·007	0·140 ± 0·029

Results are the mean ± S.E.M. of data obtained with 8 rats.
*$P < 0·001$ when compared with control values.

respectively. Surprisingly, cortical DA concentration was not changed significantly after either type of lesion to the noradrenergic neuronal systems. These results strongly suggest that most cortical DA is not localized in noradrenergic nerve terminals and this may suggest the existence of dopaminergic neurons in the cerebral cortex.

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Pharmacological interactions between γ-hydroxybutyric acid and agents which modify cerebral γ-aminobutyric acid (GABA) metabolism

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γ-Hydroxybutyric acid (GHB) and imidazoleacetic acid (IMA) are both naturally occurring brain metabolites which, when administered to rats and mice at 400 mg/kg I.P.,

produce a characteristic hypnotic state (Marcus, Winters, Roberts & Simonsen, 1971), but which, at doses in excess of 1 g/kg, induce general seizures (Clifford, Taberner, Tunnicliff, Rick & Kerkut, 1972). In the present work we have injected rats with subhypnotic doses of GHB and IMA both simultaneously and at various time intervals and have determined the duration of the loss of righting reflex and the total sleeping time. Criteria for loss of righting reflex and sleeping time were as defined previously (Rick, Benton & Taberner, 1972).

Potentiation of the depressant behavioural effects occurred when 100 mg/kg IMA I.P. was given 30 min prior to 100 mg/kg GHB I.P. This potentiation did not occur when the drugs were administered in the reverse order. When 200 mg/kg GHB and 200 mg/kg IMA were given together, general seizures were induced in all the animals tested which lasted for over 3 hours.

Since we have shown that IMA can inhibit rat brain gamma-aminobutyric acid-2-ketoglutaric acid aminotransferase (GABA-T) (Clifford *et al.*, 1972) we have examined the effect of pre-treating animals with 12·5 mg/kg of amino-oxyacetic acid (AOAA), an established inhibitor of GABA-T, which induces large increases in the brain GABA level in various species (Wallach, 1961). Rats pretreated with 12·5 mg/kg AOAA I.P. slept for over two hours following an injection of 200 mg/kg GHB 30 min later. When the GHB was administered 2 or 4 h after the AOAA the animals slept for up to 4 h and showed loss of righting reflex for about 60 minutes. This effect was not observed with shorter time intervals between the injections.

In addition we have confirmed that pyrazole, a potent inhibitor of alcohol dehydrogenase, potentiates GHB sleeping time and loss of righting reflex (Taberner, Rick & Kerkut, 1972; Bessman & McCabe, 1972). Also, rats pretreated with 100 mg/kg pyrazole I.P. slept for over 4 h following an injection of 200 mg/kg IMA, suggesting that the effect of pyrazole on the inactivation of GHB might not be as specific as has been suggested. At the doses used, none of the drugs, GHB, IMA, AOAA or pyrazole induced sleep when administered alone.

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Effect of amino-oxyacetic acid on the accumulation of ^{3}H-γ-aminobutyric acid (^{3}H-GABA) by rat retina

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Retinae were dissected and incubated in Krebs bicarbonate medium at 37° C with radioactive amino acids as described previously (Starr & Voaden, 1972).

When retinae were incubated with ^{3}H-GABA (5×10^{-8}M) there was a rapid accumulation of radioactivity by the tissue, resulting in a maximum tissue medium ratio (dpm/g tissue: dpm/ml medium) of 50:1 for control retinae and 100:1 for retinae exposed to amino-oxyacetic acid (AOAA, 10^{-5}M). A double reciprocal plot of the initial velocity