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SHORT COMMUNICATION

Effect of pyrogallol on the catecholamine content of the rabbit brain

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THERE have been many reports about the metabolic pathways of catecholamines (CA). Several investigations have indicated that O-methylation of CA precedes deamination *in vivo*, and that monoamine oxidase (MAO) plays only a minor role in the inactivation of infused epinephrine. Circulating norepinephrine in the rat is also metabolized predominantly by catechol-O-methyl transferase (COMT).[1, 2, 3] The weak *in vitro* activity of COMT in rat brain relative to that of MAO, and the fact that the CA content of brain was increased after intraperitoneal injection of iproniazid (a MAO inhibitor), but was not influenced by the intraperitoneal injection of pyrogallol (a COMT inhibitor), suggest that MAO plays a major role in the metabolism of CA in the brain.[4] We also observed that a significant increase in the CA content of rat brain was produced by the intraperitoneal injection of a new MAO inhibitor, 1037(1-benzyl-2 (4:5-tetramethylene-3-insoxazolylcarbonyl) hydrazine),[5] but that the intraperitoneal injection of pyrogallol failed to increase the CA content of brain.

The present experiments were on rabbits (males, weighing about 2 kg), which received intracisternal and intracarotid injections of pyrogallol. The intracarotid injections of pyrogallol (25 mg/kg, twice before killing) produced a slight decrease in the brain CA content from the mean value for saline treated controls (Table 1). A volume, not exceeding 0·2 ml of

TABLE 1. EFFECT OF INTRACAROTID INJECTION OF PYROGALLOL ON THE NOREPINEPHRINE CONTENT OF RABBIT BRAIN

Injected material	Animal No.	Norepinephrine content (μg/g)	
		Brain stem	Brain cortex
Saline	1	0·179	0·054
	2	0·207	0·050
	3	0·130	0·054
	4	0·073	0·093
	mean	0·147	0·063
Pyrogallol	1	0·125	0·041
	2	0·115	0·045
	3	0·103	0·054
	4	0·088	0·051
	mean	0·108	0·048

Two injections of pyrogallol (25 mg/kg) into carotid arteries of rabbits were made at 60 min and 30 min before decapitation. Norepinephrine in brain was extracted with 0·4 N perchloric acid and then fractionated with a Duolite C-25 column[10] and estimated by the trihydroxyindole method.

pyrogallol dissolved in sterile 0·9% NaCl solution was injected into the cisterna of rabbits. At dosage of 10 mg/kg at 60 min and 30 min before killing, intracisternal injection of pyrogallol caused a marked increase in the brain CA content (Table 2). These results suggest that pyrogallol may not be able to pass through the blood-brain barrier and that COMT also plays a significant role in the metabolism of CA in the brain.

Centrally administered pyrogallol resulted in the disappearance of spontaneous activity and marked ataxia. There was diminished muscular tone, so that the rabbits lay on their sides or abdomens and were unable to crouch, sit or walk. Their respiration was very rapid during the first 30 min after the injection. Drowsiness and vomiting were not observed. These effects lasted for about 2 hr. Control rabbits, which received 0·2 ml of sterile 0·9% NaCl solution into the cisterna did not show the above

TABLE 2. EFFECT OF INTRACISTERNAL INJECTION OF PYROGALLOL ON THE NOREPINEPHRINE CONTENT OF RABBIT BRAIN

Injected material	Animal No.	Norepinephrine content (μg/g)	
		Brain stem	Brain cortex
Saline	1	0·153	0·090
	2	0·148	0·064
	3	0·128	0·062
	4	0·136	0·062
	5	0·129	0·066
	6	0·132	0·072
	mean	0·137	0·069
Pyrogallol	1	0·585	0·136
	2	0·575	0·177
	3	0·304	0·082
	4	0·280	0·099
	5	0·206	0·142
	6	0·234	0·152
	7	0·230	0·078
	mean	0·345	0·124

Two intracisternal injections of pyrogallol (10 mg/kg, volume less than 0·2 ml) were given to rabbits at 60 min and 30 min before decapitation.

symptoms. The behavioural effects of epinephrine, norepinephrine and 5-hydroxytryptamine injected into the cerebral ventricles and the cisterna have been described by several investigators.[6, 7, 8, 9] It is of great interest to note that the effects of pyrogallol were very similar to those of centrally administered epinephrine and norepinephrine. The present communication suggests that COMT as well as MAO must be taken into consideration in the metabolism of the CA in the brain. More detailed studies are now in progress.

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