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Effect of reserpine on the transport of 5-hydroxytryptamine to the rat brain

Bulat & Supek (1967; 1968a) have surveyed previous work on the passage of 5-hydroxytryptamine (5-HT) across the blood-brain barrier, the subject of which has been a matter of dispute for some time, and have demonstrated the penetration of 5-HT through the blood-barrier 10 min after an intravenous injection. The concentration of 5-HT in the rat brain was directly dependent on dose.

The uptake of 5-HT by platelets against a concentration gradient has been reported (Stacey, 1961). Reserpine can affect platelet 5-HT in two ways: either by depleting the 5-HT or by inhibiting its uptake (Lahti & Platz, 1969; Alivisatos, Ungar & others, 1970). We have found a very low dose of reserpine (5 μg/kg) to have no depleting effect on endogenous 5-HT; however, the same dose of reserpine prevented a significant uptake of exogenous 5-HT by the platelets. Under these conditions we examined the transport of 5-HT to the brain of reserpinized rats.

Male Sprague-Dawley rats (190–220 g) were injected into the tail vein with 10 mg/kg of 5-HT creatine sulphate in saline. When reserpine was used, the animals received 5 μg/kg in 30% propylene glycol intraperitoneally 18 h before the 5-HT. Control animals were injected with saline or the propylene glycol. The animals were killed 10 min after the 5-HT injection by cutting the jugular vein, and blood samples were collected in siliconized containers using oxalate as an anticoagulant. 5-HT in platelet-rich plasma and platelets were extracted according to Crawford & Rudd (1962), except the re-extraction was with heptane and 0·01N HCl after which the aqueous phase was acidified to 3N with HCl (conc.). Extraction of brain 5-HT was according to Wiegland & Perry (1961). The fluorescence of 5-HT was measured on an Aminco-Bowman spectrofluorometer at 540 nm (activation 295 nm) using a Kodak screen (Wise, 1967).

In the perfusion studies, the animals were anaesthetized with ether after which the right carotid artery was tied off distally and a polyethylene tube inserted above the ligation; 10 ml of isotonic saline was then perfused into the artery. The same procedure was performed on the left carotid artery and the animals were then decapitated to remove the brain which appeared to be free of blood.

Reserpine neither depleted nor inhibited the uptake of endogenous 5-HT in blood platelets (Table 1). Furthermore, it exerted no effect on the concentration of endogenous 5-HT in the rat brain. After administration of 10 mg/kg of 5-HT, the absolute platelet content of 5-HT was significantly lower in reserpinized animals than in animals receiving no reserpine, indicating a blockade of 5-HT uptake in the platelets by the reserpine. This blockade, however, was not complete since the value obtained in reserpinized animals injected with exogenous 5-HT was much higher than that of the controls receiving reserpine only.

In animals injected only with 5-HT, the brain 5-HT content was significantly increased above the control values (Table 1). These results substantiated the findings of Bulat & Supek (1967; 1968a,b) that 5-HT does cross the blood-brain barrier.

Table 1. *Absolute contents of 5-HT in rat plasma, platelets and brains 10 min after injection of 5-HT* (10 mg/kg, i.v.). Each value represents mean ± s.e. Figures in parentheses are the numbers of animals.

Treatment	5-HT content in Platelet-rich plasma (μg/ml)	Platelet (μg/g)	Brain (μg/g)
Control	0·39 ± 0·01[1] (4)	0·37 ± 0·01[1] (4)	0·61 ± 0·01[1] (6)
Reserpine	0·37 ± 0 (4)	0·37 ± 0·01 (4)	0·62 ± 0·02 (6)
5-HT	2·86 ± 0·37 (4)	0·97 ± 0·04[2] (4)	0·82 ± 0·02[4] (6) 0·83 ± 0·06[6] (4)
5-HT after reserpine	2·32 ± 0·20 (4)	0·52 ± 0·04[3] (4)	0·96 ± 0·03[5] (6) 0·95 ± 0·18[6] (4)

[1] Same value was found for both saline and propylene glycol control groups.
[2] Differs from the 5-HT after reserpine group ($P < 0·001$).
[3] Differs from the control group ($P < 0·02$).
[4] Differs from the control group ($P < 0·001$).
[5] Differs from the control group ($P < 0·001$) from the 5-HT group ($P < 0·01$).
[6] Value obtained from the saline perfused brain.

When the same dose of 5-HT was given to reserpinized animals, the increase in brain 5-HT was even more pronounced. From the data it appears that reserpine pre-treatment significantly inhibits the platelet uptake of injected 5-HT, and thus increases the amount of 5-HT available for passage to the brain. Since the values of 5-HT obtained from the perfused animals did not vary from the non-perfused brain, the increase in the brain 5-HT content could not be attributed to the 5-HT carried over in the blood.

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