Selective protection of 5-hydroxytryptamine stores against the action of reserpine by treatment with 5-hydroxytryptophan

SIR,—Recently we have observed by means of repeated injections of *m*-tyrosine, given shortly before and after reserpine, that it is possible partially to protect the catecholamine stores of the mouse brain against the action of this alkaloid (Carlsson & Lindqvist, 1967). This protection was evident 24 hr after the injection of reserpine, long after the acute effects of *m*-tyrosine had worn off. At the same time the animals were protected against the gross behavioural actions of reserpine. Since *m*-tyrosine was unable to prevent 5-hydroxytryptamine (5-HT) depletion by reserpine, these results underline the importance of catecholamine depletion for the reserpine syndrome.

We have now observed that repeated injections of 5-hydroxytryptophan (5-HTP), given to mice shortly before and after reserpine, will protect 5-HT stores against the action of this alkaloid, while the catecholamine stores are left unprotected (Table 1). Thus, 24 hr after the injection of reserpine (3 mg/kg, i.p.) the brains of the 5-HTP-treated animals still contained about 60% of the normal 5-HT level, compared to 20% in the controls treated with reserpine alone. The catecholamine levels were about 10% of normal irrespective of 5-HTP treatment. It could be proved that here we are dealing with a true protection of 5-HT stores; if animals protected with 5-HTP as described above received a second injection of reserpine after 24 hr, the 5-HT level was rapidly reduced from about 60 to 20%. Further, it was found that animals given 5-HTP in the same dosage but no reserpine, had normal brain 5-HT levels after 24 hr.

TABLE 1. EFFECT OF REPEATED INJECTIONS OF 5-HYDROXYTRYPTOPHAN (5-HTP) ON THE RESERPINE-INDUCED MONOAMINE DEPLETION IN THE BRAIN Female white mice received 400 mg/kg DL-5-HTP subcutaneously. After 30 min reserpine (3 mg/kg) was injected intraperitoneally. Two additional injections of 5-HTP (200 mg/kg) were given after another 1½ and 3½ hr. Controls received the same dose of reserpine only. The animals were killed 24–28 hr after the injection of reserpine. (In two of the experiments a slightly different dosage schedule for 5-HTP was used.) In two experiments indicated in the Table the same dose of reserpine was given 24 hr after the first dose, and the animals were killed after another 4 hr. Data (μg/g) are single values, obtained from 3 to 9 pooled organs.

	5-hydroxytryptamine (μg/g)	Noradrenaline (μg/g)	Dopamine (μg/g)
5-HTP + reserpine	0·29, 0·28 0·25, 0·34 0·29	0·04, 0·04	0·09, 0·08
Reserpine	0·07, 0·06, 0·13	0·04, 0·05	0·07, 0·09
5-HTP + reserpine + reserpine (after24 hr)	0·10, 0·06	—	—

In spite of the efficient protection of 5-HT stores, the animals treated with 5-HTP and reserpine when examined 24 hr after the injection of the alkaloid, i.e. long after the acute 5-HTP effects had worn off, could not be distinguished from their controls treated with reserpine alone. Hypokinesia, inhibition of exploratory behaviour, hunched back posture and blepharospasm, were thus equally pronounced in both groups.

These experiments, as well as those of Carlsson & Lindqvist (to be published) indicate that the gross reserpine syndrome in the mouse is largely due to catecholamine depletion, whereas 5-HT depletion plays a minor role, if any. Needless to say the possibility remains that 5-HT depletion plays a role for less conspicuous effects of reserpine.

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