

Action of imipramine on 5-hydroxytryptaminergic transmission and on 5-hydroxytryptamine uptake in the snail (*Helix pomatia*) brain

G. A. COTTRELL

Wellcome Laboratories of Pharmacology and Physiology Department, The University of St. Andrews, Fife, Scotland

Direct synaptic connexion is made between the giant 5-hydroxytryptamine (5-HT)-containing cell (GSC) of each cerebral ganglion of the snail and two repeatably identifiable neurones in each buccal ganglion (Cottrell, 1970, 1971). Transmission from the GSCS to the appropriate buccal cells is impaired with reserpine and blocked with LSD-25 at a concentration of 10^{-4} g/ml (Cottrell, 1970a, b). Directly applied 5-HT lowers membrane resistance and depolarizes the innervated buccal cells. Thus 5-HT is most probably used as a transmitter substance by the GSCS.

A potent inhibitor of the uptake of 5-HT by blood platelets is the tertiary amine antidepressant imipramine. Da Prada & Pletscher (1968) showed that this compound at a concentration of 3×10^{-5} M reduced 5-HT uptake by as much as 80% in intact platelets.

Experiments have been performed to test the effect of imipramine on the synaptic links between the GSCS and the buccal cells described. Imipramine markedly potentiated transmission between the cells. The effect was observed as an increase in the rate of membrane depolarization (made up of summed excitatory potentials) after adding imipramine (3.5×10^{-5} M).

Biochemical studies have shown that labelled 5-HT, at a concentration of 3.6×10^{-8} M in snail saline, is taken up by the 'brain' *in situ* and *in vitro*. Furthermore, this uptake was antagonized by about 80% by 3.5×10^{-5} M imipramine (Table 1).

TABLE 1. Effect of imipramine (3.5×10^{-5} M) on the uptake of 5-HT: (A) by the intact 'brain' *in situ* when perfused for 5.5 h with 60 ml of saline, containing 3.6×10^{-8} M 5-HT, by way of the cephalic aorta; and (B) by the isolated suboesophageal ganglia immersed for 5 h in 2 ml of saline solution containing 3.6×10^{-8} M 5-HT

Experiment and number	Temperature	Uptake of C-14 5-HT (ng)		Percentage inhibition of uptake by imipramine
		Without imipramine	With imipramine	
A ('Brain' perfused <i>in situ</i>)				
1	35°C	60	13	78
2	20	25	3.6	85
3	20	27	5	81
4	20	24	4.2	83
B (Isolated desheathed suboesophageal ganglia)				
5	20	4.6	1	78
6	20	11	2.1	80
7	20	17	2.3	86

These data provide direct evidence that the uptake of 5-HT is an important factor in terminating transmitter action at the 5-hydroxytryptaminergic synapse.

REFERENCES

- COTTRELL, G. A. (1970a). Direct postsynaptic responses to stimulation of serotonin-containing neurones. *Nature, Lond.*, **225**, 1060–1062.
 COTTRELL, G. A. (1970b). Actions of LSD-25 and reserpine on a serotonergic synapse. *J. Physiol., Lond.*, **208**, 28–29.
 COTTRELL, G. A. (1971). Synaptic connections made by two serotonin-containing neurones in the snail (*Helix pomatia*) brain. *Experientia*, **27**, 813–815.
 DA PRADA, M. & PLETSCHER, A. (1968). Isolated 5-hydroxytryptamine organelles of rabbit blood platelets; physiological properties and drug induced changes. *Br. J. Pharmac.*, **34**, 591–597.