this was accompanied by an increase in the anti-Parkinson effect of L-dopa. Since increased concentrations of 3-*O*-methyldopa have been shown to be associated with decreased SAM during administration of L-dopa (Ordonez & Wurtman, 1973) the possibility that a reduction in SAM may also be related to the anti-Parkinson effect of L-dopa should be considered.

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REFERENCES

AXELROD, J. (1971). *Science*, **173**, 598–606.
EISENFELD, A. J., AXELROD, J. & KRAKOFF, L. (1967). *J. Pharmac. exp. Ther.*, **156**, 107–113.
HORNYKIEWIEZ, O. (1966). *Pharmac. Rev.*, **18**, 925–964.
MESSIHA, F. S., HSU, T. H. & BIANCHINE, J. R. (1972). *J. clin. Invest.*, **51**, 452–455.
ORDONEZ, L. A. & WURTMAN, R. J. (1973). *Biochem. Pharmac.*, **22**, 134–137.
TAYLOR, K. M. & RANDALL, P. K. (1975). *J. Pharmac. exp. Ther.*, **194**, 303–310.
WURTMAN, R. J. & ROSE, C. M. (1970). *Science*, **169**, 395–397.

Actions of propranolol on 5-HT receptors of snail neurons

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The β-antagonist propranolol specifically interacts in low concentrations to block binding of 5-hydroxytryptamine (5-HT, serotonin) to a membrane fraction of rat brain homogenate, suggesting that it may block 5-HT receptors (Middlemiss, Blakeborough & Leather, 1977). Propranolol is known to have central effects in man, including anti-anxiety and anti-schizophrenia activity, and these effects could result from an action on 5-HT transmission (Green & Grahame-Smith, 1976).

To investigate further whether propranolol can in fact selectively effect transmission at serotoninergic (5-HT releasing) synapses, it is necessary to test the action of the drug on the intracellularly recorded electrical activity of neurons which receive a serotoninergic input. Such experiments are difficult in the mammalian brain for technical reasons. An alternative approach is to use a simpler preparation. One such preparation comprises part of the c.n.s. of the snail *Helix pomatia*, and also *Aplysia*, incorporating two readily located, symmetrical, giant 5-HT neurons and their follower neurons. Excitatory or inhibitory responses are recorded from different specified neurons when one of the 5-HT neurons is stimulated and the responses are mimicked with applied 5-HT (Cottrell & Macon 1974; Gerschenfeld & Paupardin-Tritsch 1974).

We have tested the effects of propranolol on the responses of these follower neurons to iontophoresed 5-HT, in *Helix pomatia*. Initial experiments showed that the drug antagonized the depolarizing responses to 5-HT (on the M cell) without affecting the 5-HT hyperpolarizing response. Even at 2×10^{-4}M, propranolol did not alter the input resistance or the firing pattern of the follower neurons, nor did it have any obvious local anaesthetic effect.

However, subsequent experiments showed that the same concentrations of propranolol also antagonized the depolarizing, but not the hyperpolarizing action of acetylcholine on other identified neurons. A similar effect was observed on dopamine responses. Further, unlike the binding studies of Middlemiss & others (1977) in which (−)-propranolol was approximately 60 times more potent than its (+)-isomer, blockade of the depolarizing 5-HT responses was equally effective with each isomer.

Thus propranolol does not act as a stereospecific, selective, 5-HT antagonist on these snail neurons. The effect of blocking depolarizing but not hyperpolarizing responses, may result from a direct action on transmitter activated, depolarizing, ionic channels, as has been suggested to account for a similar effect of curare on molluscan neurons (Carpenter, Swann & Yarowsky 1977).

It remains to be shown whether propranolol antagonizes iontophoresed 5-HT responses at neurons receiving serotoninergic input in the mammalian brain.

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REFERENCES

CARPENTER, D., SWANN, J. & YAROWSKY, P. (1977). *J. Neurobiol.*, **8**, 119–132.
COTTRELL, G. A. & MACON, J. (1974). *J. Physiol., Lond.*, **236**, 435–464.
GERSCHENFELD, H. M. & PAUPARDIN-TRITSCH, D. (1974). *Ibid.*, **243**, 457–481.
GREEN, A. R. & GRAHAME-SMITH, D. G. (1976). *Nature* **262**, 594–596.
MIDDLEMISS, D. N., BLAKEBOROUGH, L. & LEATHER, S. R. (1977). *Nature* **267**, 289–290.