at least 10 min, 5-HT (1 and 100 μM) depressed DRP amplitude by 6 ± 2% (n = 15) and 3 ± 1% (n = 7), respectively. No depression by 5-HT was observed in the presence of quipazine (1 μM) in 4 experiments.

In preliminary experiments, quipazine has been shown to antagonize contractions of rat fundus induced by 5-HT. Stomach strips were superfused at 37°C with Krebs solution. The dose-response curve to 5-HT was displaced to the right in a non-parallel manner, suggesting a non-competitive mode of antagonism. PT_{50} values were obtained by determining the negative log of the molar concentration of quipazine which reduced the maximal effect of 5-HT by 50%. This value is around 6.9.

References

GREEN, AR., YOUDIM, M.B.H. & GRAHAME-SMITH, D.G. (1976). Quipazine: its effects on rat brain 5-hydroxytryptamine metabolism, monoamine oxidase activity and behaviour. *Neuropharmacology*, **15**, 173–179.

HONG, E. & PARDO, E.G. (1966). On the pharmacology of 2- (1-piperanzinyl) quinoline. *J. Pharmac. exp. Ther.*, **153**, 259–265.

RODRIGUEZ, R., ROJAS-RAMIREZ, J.A. & DRUCKER-COLIN, R.R. (1973). Serotonin-like actions of quipazine on the central nervous system. *Eur. J. Pharmac.*, **24**, 164–171.

The mechanism of 5-hydroxytryptamine-induced pressor responses in ganglion-blocked anaesthetized dogs

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The cardiovascular actions of 5-hydroxytryptamine (5-HT) *in vivo* are complex. However, in ganglion-blocked anaesthetized dogs 5-HT produces dose-dependent vasopressor responses which are thought to result from stimulation of excitatory receptors for 5-HT in vascular smooth muscle (Stone, Wenger, Ludden, Stavorski & Ross, 1960; Saxena, Houwelingen & Bonta, 1971). We have carried out experiments to determine the nature of the receptors involved.

Male and female beagle dogs (7–10 kg) were anaesthetized with thiopentone (25 mg/kg i.v.) and barbitone sodium (300 mg/kg i.p.). Blood pressure and heart rate were recorded and drugs were administered via the right femoral vein. Ganglion-blockade was produced by mecamylamine (5 mg/kg i.v.).

5-HT (1–30 μg/kg i.v.) produced dose-related increases in arterial pressure and heart rate. The vasopressor action of 5-HT, but not of phenylephrine, was antagonised in a dose-dependent manner by the 5-HT antagonists methysergide (10–100 μg/kg i.v., Figure 1) and cyproheptadine (10–100 μg/kg i.v.). However, the 5-HT-induced vasopressor action was also antagonised by phentolamine (0.3–3.0 mg/kg i.v., Figure 1), reduced by bilateral adrenalectomy and abolished by syrosingopine pretreatment (0.5 mg/kg i.v. 48 h and 1.0 mg/kg i.v. 24 h previously).

We conclude that most, if not all, of the 5-HT-induced pressor response in ganglion-blocked anaesthetized dogs results from catecholamine release, of which a major component arises from the adrenal glands. This release process appears to be susceptible to blockade by methysergide and cyproheptadine and could therefore involve a D-receptor-mediated depolarization by 5-HT of the chromaffin cells in the adrenal medulla (see Douglas, Kanno & Sampson, 1967).

References

DOUGLAS, W.W., KANNO, T. & SAMPSON, S.R. (1967). Effects of acetylcholine and other medullary secretagogues and antagonists on the membrane potential of adrenal chromaffin cells: an analysis employing techniques of tissue culture. *J. Physiol. Lond.*, **188**, 107–120.

SAXENA, P.R., VAN HOUWELINGEN, P. & BONTA, I.L. (1971). The effects of mianserin hydrochloride on the vascular responses evoked by 5-hydroxytryptamine and related vasoactive substances. *Eur. J. Pharmac.*, **13**, 295.

STONE, A.C., WENGER, H.C., LUDDEN, C.T., STAVORSKI, J.M. & ROSS, C.A. (1960). Antiserotonin-antihistaminic properties of cyproheptadine. *J. Pharmac. exp. Ther.*, **131**, 73–84.

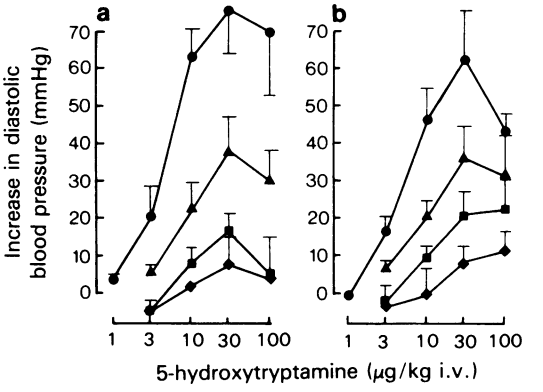

Figure 1 Mecamylamine-treated anaesthetized dog. Antagonism of the vasopressor effects of 5-HT by (a) methysergide (▲10, ■30 and ◆100 ug/kg i.v.) and (b) phentolamine (▲0.3, ■1.0 and ◆3.0 mg/kg i.v.). Control observations in the absence of antagonist (●). Each point is the mean value (± s.e. mean, n = 4).