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Introduction

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It is now over 30 years since Gaddum & Picarelli (1957) described and characterised tryptamine receptors in the periphery. The setting in which they were working was what to us now is an antique department of pharmacology whose most sophisticated equipment was a smoked drum to record the response of a variety of smooth muscle preparations to the extracts of tissue containing the sought after transmitters. Gaddum the Professor of Pharmacology was the ideas man, Crawford a brilliant though highly obsessional methodologist, and Amin an indefatigable Indian PhD student. That group (Amin *et al*, 1954) described the presence of 5-HT in brain. They had been looking for substance P but the contractile response of the preparations to the extracts of brain did not resemble that peptide but serotonin. In many ways that was an initiator of psychopharmacology which has progressed exponentially to the present day.

The 5-HT system of neurones in brain originally seen as rather primitive has emerged with great complexity especially in relation to its receptor population. It now appears that the M and D receptors they described are indeed now characterised as 5-HT_3 and 5-HT_2. Indeed the wide range of 5-HT receptors currently characterised (Tricklebank, 1987) would have surprised Gaddum himself; 5-HT has also been implicated in many diverse behaviours as well as the control of mood. It is difficult to see the common themes in obsessional behaviour, suicidal intent, bulimia, aggression, anxiety and appetite. The facilitation or inhibition of the repetition of specific behaviours might, however, as in for example, obsessive compulsive neurosis or bulimia, be one of these and lead to some understanding of the drugs currently available to the psychiatrist. Although the drugs discussed at this symposium are themselves highly specific in blocking the reuptake of 5-HT into the neurone; their efforts may be non-specific since they will depend on the increased concentration of the amine caused by reuptake inhibition at particular groups of receptors entering into play as the intrasynaptic and extrasynaptic level of 5-HT rises.

What is also becoming apparent is the potential for different doses of these drugs to have different effects. Low doses of clomipramine appear to be efficacious in panic disorder with a rapid onset whilst higher doses for a longer period appear to be necessary for the treatment of depression. This may, of course, reflect the concentration of 5-HT at receptor sites whose sensitivities to this amine differ. Long continued use of specific 5-HT reuptake inhibitors to cause down regulation of 5-HT_2 receptors may be necessary in the treatment of depression. These questions are addressed on a broad front in this symposium and are beginning to suggest answers to difficult clinical problems.

References

AMIN, A. H., CRAWFORD, T. B. B. & GADDUM, J. H. (1954) The distribution of substance P and 5-hydroxytryptamine in the central nervous system of the dog. *Journal of Physiology (London)*, **126**, 596–618.

GADDUM, J. H. & PICARELLI, Z. P. (1957) Two kinds of tryptamine receptor. *British Journal of Pharmacology*, **12**, 323–328.

TRICKLEBANK, M. D. (1987) Subtypes of 5-HT receptors. *Journal of Psychopharmacology*, **1**, 222–226.