

The following demonstration, presented to the British Pharmacological Society Meeting at Mill Hill (5th–7th January, 1977), appeared as a title only in the March 1977 issue of the British Journal of Pharmacology.

Do 5-HT neurones support self-stimulation?

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With electrodes implanted in certain areas of the brain, rats can be trained to press a lever to deliver electrical stimulation through the implanted electrode (Olds & Milner, 1954). This 'self-stimulation' behaviour presumably indicates that the electrode activates neural systems which have rewarding effects. Previous pharmacological and biochemical evidence suggests that activation of catecholamine-containing systems plays a crucial role in reward mechanisms. In particular it has been found that there are foci of self-stimulation sites at the level of origin of a major dopamine-containing system in the ventral mesencephalon (Crow, 1972) and a noradrenergic system in the nucleus locus coeruleus (Crow, Spear & Arbuthnott, 1972).

More recently it has been found that self-stimulation can also be obtained with electrodes implanted in the region of the median and dorsal raphe nuclei which comprise 5-HT containing cell bodies giving rise to ascending fibres which innervate large areas of the forebrain with tryptaminergic terminals. This finding raises the question of whether the neurochemical mechanisms of reward are more complex than previously suggested. With electrodes on the median raphe nucleus, Miliaressis, Bouchard and Jacobowitz (1975) have claimed that self-stimulation responding is selectively suppressed by administration of the 5-HT synthesis inhibitor *p*-chlorophenylalanine. In these experiments we have attempted to replicate this effect and to study the time course of inhibition following *p*-chlorophenylalanine. We also investigated whether the inhibition is a function of responding by including a rest-pause of 30 min in each test session.

The results (Figure 1) show that there is a modest

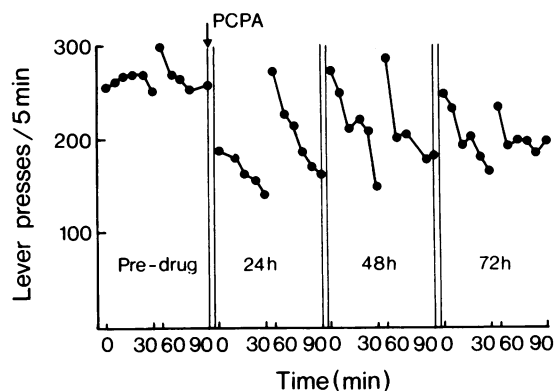


Figure 1

reduction in responding following *p*-chlorophenylalanine administration but that this effect is maximal at 24 h, when noradrenaline stores are known to be depleted, and that there is considerable recovery by 72 h when 5-HT depletion is greatest. The decline of responding during the test session, and recovery after the rest-pause are greater at 24 and 48 h than at 72 h, findings which also raise doubts as to whether 5-HT depletion is responsible for the inhibition of responding seen in these experiments.

Thus even though electrical self-stimulation can be obtained with electrodes located in the raphe nuclei the role of 5-HT neurones in reward processes appears doubtful.

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References

- CROW, T.J. (1972). A map of the rat mesencephalon for electrical self-stimulation. *Brain Res.*, **36**, 265–273.
- CROW, T.J., SPEAR, P.J. & ARBUTHNOTT, G.W. (1972). Intracranial self-stimulation with electrodes in the region of the locus coeruleus. *Brain Res.*, **36**, 275–287.
- MILIARESSIS, E., BOUCHARD, A. & JACOBOWITZ, D.M. (1975). Strong positive reward in median raphe: specific inhibition by para-chlorophenylalanine. *Brain Res.*, **98**, 194–201.
- OLDS, J. & MILNER, P.M. (1954). Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. *J. comp. physiol. Psychol.*, **47**, 419–427.