

INDOLEAMINES AND THERMOREGULATION IN THE RAT

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Feldberg and Myers (1963) were the first to suggest that 5-HT was an important neurotransmitter in central thermoregulatory pathways and other workers have supported that conclusion (Jacob and Girault, 1979). However an indoleamine that is not 5-HT may also play a thermoregulatory role (Bligh et al 1979, Cox et al 1983). The aim of this study was to seek evidence to support the existence of this indoleamine and to provide more information on the receptor with which it interacts.

Core temperature was measured at an ambient temperature of 20°C in Alderley Park Wistar rats (250 to 350g) using a rectal thermistor probe. Central injections or electrical stimulations were carried out using guide cannulae or electrodes previously implanted into the preoptic anterior hypothalamus or dorsal raphe nucleus respectively.

Intrahypothalamic injection of 5-HT caused a dose related hypothermia, ED₅₀ 52nmol (defined as the dose required to produce a response that was 50% of the maximum achievable), whereas tryptamine injected into the same site caused a hyperthermia, ED₅₀ 5.1nmol. Since d-Fenfluramine produces a hyperthermia that is 5-HT₂-receptor mediated (Blackburn et al 1985), we decided to determine whether tryptamine-hyperthermia was also 5-HT₂-receptor mediated. Intrahypothalamic injection of ICI 169,369, a 5-HT₂ receptor antagonist (Blackburn et al 1988), blocked responses to tryptamine, ID₅₀ 5.3nmol (defined as the dose of antagonist that reduced, by 50%, the response to a just submaximal dose of agonist), but was slightly more potent as an antagonist of 5-HT, ID₅₀ 2.7nmol. In contrast, methergoline, a compound with 5-HT₁-like receptor antagonist activity was more potent as an antagonist of tryptamine than of 5-HT (ID₅₀ 0.9 and 5.2nmol, respectively). Further, since ICI 169,369 is an antagonist at the 5HT_{1C} receptor (Growcott et al 1988), albeit with lower potency, then it is possible that it is this receptor subtype with which tryptamine interacts.

Finally, if these pharmacological responses to tryptamine have a physiological counterpart, it should be possible to activate an endogenous pathway to produce similar effects. The dorsal raphe nucleus contains cell bodies of ascending 5-HT pathways, but non 5-HT indoleamine cells have also been reported (Bjorklund et al 1971). Electrical stimulation of the dorsal raphe nucleus (25 Hz at 0.04mA), like tryptamine injection, caused a hyperthermia which was reduced by 65% by pretreatment with methergoline used in a tryptamine selective dose (2.5 mgkg⁻¹ i.p.).

Thus these results suggest that tryptamine-induced hyperthermia in the rat may be mediated via a receptor subtype similar to that currently designated 5-HT_{1C} and also that it may be mimicking the effects of an endogenous thermoregulatory pathway. However the chemical identity of the neurotransmitter in this pathway awaits elucidation.

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