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Response of identified ventromedial hypothalamic nucleus neurones to putative neurotransmitters applied by microiontophoresis

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Recent physiological studies have indicated that the amygdala exerts a prominent excitatory influence on the majority of HVM neurones, and that HVM neurones have efferent connections to both hypothalamic (median eminence, anterior hypothalamic area) and extrahypothalamic (preoptic area, periaqueductal gray, amygdala and thalamus) areas (Renaud & Martin, 1975b). This study details preliminary results on the responsiveness of HVM neurones, identified through their afferent and efferent connections, to microiontophoretic application of substances which may act as neurotransmitter agents in this region.

Spike discharges from HVM neurones in pentobarbitone anaesthetized male Sprague Dawley rats were recorded with single 3.0 M NaCl filled micropipettes rigidly mounted to an adjacent multibarrelled micropipette filled with the following solutions:– monosodium L-glutamate (0.5 M, pH 7.0); gamma aminobutyric acid (0.5 M, pH 4.5); glycine (0.5 M, pH 3.5); histamine dihydrochloride (0.2 M, pH 4.0); dopamine HCl (0.2 M, pH 4.5); picrotoxin (5 mM, pH 7.5); strychnine sulfate (5 mM, pH 5.5); growth hormone release-inhibiting hormone or somatostatin (5 mM, pH 6.5); thyrotrophin releasing hormone (5 mM, pH 6.5); and luteinizing hormone releasing hormone (5 mM, pH 6.5).

The actions of these substances on the neural activity or excitability of HVM cells are summarized in Table 1.

Of the excitatory substances, the action of glutamate was brisk in onset and termination compared with the slow onset excitant action of histamine, an effect which outlasted the application by several seconds (Haas, 1974). The potent depressant action of GABA and glycine was rapid in onset and termination. Although these effects could be antagonized by picrotoxin and strychnine respectively, only picrotoxin applied either by microiontophoresis or by intravenous injection partially antagonized synaptic inhibition evoked by amygdala stimulation. Only depressant responses were observed with the three hypothalamic peptides tested. Selected HVM neurones displayed marked sensitivity to some peptides but not others (Renaud & Martin, 1975a; Renaud, Martin & Brazeau, 1975). The action of dopamine was never as potent as that of the depressant amino acids, but similar to the weaker depressant responses observed with some peptides.

More detailed study of HVM neurones with specific efferent connections, may indicate cellular populations with receptors for specific substances, and may help to define their biological significance in neural integration and regulation within this important hypothalamic centre.

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Table 1 Pattern of response (no. of cells)

	Increase	*Decrease*	*No response*	*Current range (nA)*
Glutamate	46	0	0	24-80
Histamine	12	20	5	3-25
GABA	0	18	1	5-20
Glycine	0	16	1	8-22
Dopamine	0	18	6	20-50
GH-RIH	0	28	8	5-80
LH-RH	0	13	5	10-30
TRH	0	46	20	10-30

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Failure of denervation to influence the high affinity uptake of choline by sympathetic ganglia

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The transport process responsible for the uptake of choline in the central nervous system possesses high and low affinity components (Yamamura & Snyder, 1973; Haga & Noda, 1973; Neal & Gilroy, 1975) and there is some evidence that the high affinity choline transport process may be associated with cholinergic nerve terminals (Kuhar, Sethy, Roth & Aghajanian, 1973).

In the present study we have attempted to obtain further information on the possible association of the high affinity choline uptake process with cholinergic nerve endings by comparing the kinetics of choline uptake in normal and denervated ganglia.

Superior cervical ganglia were dissected from anaesthetized rats, de-sheathed, and then incubated for various times at 25°C in Krebs bicarbonate Ringer containing [^{3}H]-choline (1 μCi/ml). The ganglia were then dissolved in Soluene (Packard) and the radioactivity determined by liquid scintillation counting. Unilateral decentralization of the ganglion was performed under halothane anaesthesia 12 to 17 days prior to excision of both ganglia.

Ganglia accumulated radioactivity when incubated with [^{3}H]-choline (1.8×10^{-7} M). This uptake was almost linear for 60 min at which time a tissue : medium ratio of approximately 9 was achieved. The effect of choline concentration on the uptake was studied over a concentration range of 0.2 to 600 μM. Since preliminary experiments indicated that uptake was linear over this concentration range for at least 20 min, incubations of this length were used to obtain estimates of the initial velocity of choline uptake. The kinetic data indicated that the uptake process for choline in ganglia was saturable and, as in brain, could be resolved into a high and low affinity process, with apparent *Km* values of 2.1 μM and 43 μM respectively. The uptake of choline at both high and low concentrations was unaffected by denervation of the ganglia and a paired comparison of ganglia (7 pairs) at the lowest choline concentration (0.2 μM) revealed no significant difference between the choline uptake in denervated ganglia and the contralateral controls (Tissue; medium ratios = 3.20 ± 0.23 and 3.68 ± 0.31 respectively). It is unlikely that this result was due to failure of the denervation since ganglia were taken to be denervated only if there was obvious ptosis and a failure of the palpebral fissure to respond to bipolar stimulation (2 Hz, 0.5 ms, 30 V) of the preganglionic nerve stump. Denervated ganglia in the same series, showed greatly reduced ChAc activity. Furthermore, stimulation of denervated ganglia regionally superfused as described by Bowery & Tulett (1975) failed to increase the efflux of radioactivity from the soma although similar stimulation of control ganglia caused large increases in the release of radioactivity. These results imply that in ganglia the high affinity choline uptake process is not restricted to cholinergic nerve terminals.

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