The Influence of Ambient Temperature on Thermoregulatory Responses to Intraventricularly Injected Monoamines in Sheep, Goats and Rabbits

Having found that an injection of noradrenaline (NA) into the cerebral ventricles of the cat caused a fall in body temperature, while a similar injection of 5-hydroxytryptamine (5-HT) caused a rise, FELDBERG and MYERS[1] proposed that the control of body temperature (Tb) is mediated through the controlled release of endogenous hypothalamic monoamines. There is now much supporting evidence for this thesis[2,3] but species apparently differ greatly in the effects upon thermoregulation when the monoamines are introduced into the cerebral ventricles or the anterior region of the hypothalamus[4]. FINDLAY and THOMPSON[5] found that changes in Tb of the ox are ambient temperature (Ta) dependent, and that both NA and 5-HT can cause a fall in Tb at different Ta. Little attention has been paid to the influence of ambient conditions in the majority of studies of the effects of hypothalamic monoamines upon thermoregulation, and apparent species variations could possibly be related to Ta.

Materials and methods. We have examined the effects of injections of NA and 5-HT into the lateral cerebral ventricles of sheep, goats and rabbits during exposure to a wide range of ambient temperatures upon several thermoregulatory parameters, and have compared these effects with those which might be predicted from a simple model of the neuronal connections between thermosensors and thermoregulatory effectors.

Cannulae were introduced into the lateral cerebral ventricles by aspetic surgery under general anaesthesia. In sheep and goats a modified Collison-type cannula was used[6,7]. In rabbits the technique and cannula assembly of MONNIER and GANGLOFF[8] was employed. At the same time a re-entry tube was secured against the wall of a carotid artery in sheep and goats for the subsequent recording of para-carotid temperature. At least one week was allowed for recovery before experiments were begun.

Tests were made with unanaesthetized animals in a climatic chamber. Successive tests on individual animals were made at intervals of not less than 3 days. Trunk skin, ear skin, rectal and paracarotid temperatures were registered at frequent intervals using a multipoint recorder. Respiratory excursions and thigh muscle EMG were sampled at intervals of 5 min using a polygraph recorder. NA (British Drug House) and 5-HT creatinine sulphate (May and Baker) were injected into the lateral ventricles of sheep and goats in volumes of up to 0.2 ml containing 100–250 µg of one or the other amine (base); in rabbits the corresponding quantities were 0.05 ml containing 20–75 µg NA or 40–85 µg 5-HT (base). Not more than 2 injections were made during a 6 h experimental period. Chamber temperature was held constant at 5, 10, 20, 30, 35 or 40 °C (± 1°) throughout anyone experiment. The sheep were tested first with fleece intact and again after shearing which was necessary to elicit shivering at 0 °C Ta.

Results and discussion. Table I summarizes the responses to intraventricular injections of NA. At high Ta, panting, which is a major avenue of heat loss in the 3 species, was always depressed and Tb rose. At a low Ta shivering, if present, was depressed and Tb fell. At a moderate Ta (20 °C for goats and rabbits, 10 °C for sheep with fleece, and 30 °C for sheared sheep) when the animals were neither shivering nor panting at the time of the injection, NA had little effect on Tb.

Table II summarizes the responses of intraventricular injections of 5-HT. In all 3 species 5-HT had little or no immediate effect upon Tb at high ambient temperatures,

Table I. Intraventricular noradrenaline

	Function	10 °C	20 °C	30 °C	40 °C
Sheep with fleece	resp. freq.	slow	moderate ▼	rapid ▼	rapid ▼
	shivering	—	—	—	—
	ear temp.	(c)	—	(d)	(d)
	body temp.	↑	▲	▲	▲
Sheared sheep	resp. freq.	slow	slow	slow	rapid ▼
	shivering	▼	▼	—	—
	ear temp.	(c)	(c)	—	(d)
	body temp.	▼	▼	—	▲
Goats	resp. freq.	slow	slow	rapid ▼	rapid ▼
	shivering	▼	—	—	—
	ear temp.	(c)	(c)	(d)	(d)
	body temp.	▼	↑	▲	▲
		5 °C			35 °C
Rabbits	resp. freq.	slow	moderate ↓	rapid ▼	rapid ▼
	shivering	▼	—	—	—
	ear temp.	(c)	↓	(d)	(d)
	body temp.	▼	↑	▲	▲

Table II. Intraventricular 5-hydroxytryptamine

	Function	10 °C	20 °C	30 °C	40 °C
Sheep with fleece	resp. freq.	slow	moderate ↑	rapid ↑	rapid
	shivering	—	—	—	—
	ear temp.	▲	▲	(d)	(d)
	body temp.	▼	▼	—	—
Sheared sheep	resp. freq.	slow	slow	slow	rapid
	shivering	▼	▼	—	—
	ear temp.	(c)	(c)	▲	(d)
	body temp.	▼	↓	↓	—
Goats	resp. freq.	slow	slow ▲	rapid ▲	rapid ▲
	shivering	▼	—	—	—
	ear temp.	↑	▲	(d)	(d)
	body temp.	▼	▼	▼	↓
		5 °C			35 °C
Rabbits	resp. freq.	slow ▲	moderate ▲	rapid ▼	rapid ↑
	shivering	▼	↓	—	—
	ear temp.	↑	▲	(d)	(d)
	body temp.	▼	▼	↓	—

Tables I and II. ▲, an increase in the function or temperature; ▼, a decrease in the function or temperature; ↑ ↓, a small change in a few individuals; (c) ear vessels constricted, no change as a result of injection; (d) ear vessels dilated, no change as a result of injection; —, function or temperature unchanged by injection.

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but resulted in a fall in Tb at low ambient temperatures. In goats at moderate Ta and in rabbits at both moderate and low Ta there was an increase in respiratory frequency and vasodilatation of the ears. Shivering, when present, was depressed. In sheep an increase in respiratory frequency did not always occur, and was only brief if it did. The ears of unshorn sheep vasodilated when 5-HT was injected at a low Ta, but in the sheared sheep the ears remained vasoconstricted. At high Ta (35 or 40 °C), when Tb was little affected by 5-HT, respiratory frequency was already high and ear blood vessels already dilated, so little or no further increase in heat loss was possible.

The hypothalamic action of the monoamines is presumably synaptic and a simple representation of the neuronal connections between thermosensors and thermoeffectors, which allows for reciprocal inhibition between heat production and heat loss functions (Figure) has been used in an attempt to analyse these effects of NA and 5-HT upon the hypothalamic control of Tb. A substance which activates either the pathway from cold receptors to heat production effectors, or from warm receptors to heat loss effectors, would be expected to cause reciprocal inhibition if it acted at the first synapses ('a' or 'b') but not if it acted at the second ones ('c' or 'd'). Also, an injected excitatory substance would be expected to be most effective in changing body temperature when the synapse at which it acts is not already being maximally activated by the drive from the thermosensors. The local injection of a substance which excites at synapse 'a', for example, would be expected to be more effective at low ambient and/or deep body temperature when heat loss could be increased and heat production reduced, than when heat loss was already maximally activated and heat production maximally inhibited.

An inhibitory substance which is released naturally as a consequence of the stimulation of the thermosensors would act, in this model, at the second synapses, and it could be either specific, inhibiting only heat production or heat loss when locally applied, or non-specific, inhibiting which ever pathway is active at the time of its application.

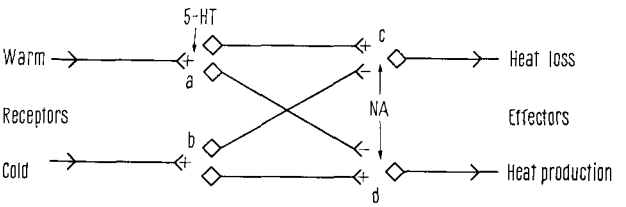
The observed effects of NA and 5-HT injected intraventricularly on temperature regulation are readily expressable in terms of this model. NA reduced heat loss and caused a rise in Tb at high Ta, and reduced heat production and caused a fall in Tb at low Ta. These responses are those expected of a nonspecific inhibitory substance acting at synaptic sites 'c' and 'd'. The overall effect of intraventricular 5-HT was to increase heat loss and to reduce heat production, and was therefore most effective at a low Ta when both these responses contributed to the fall in Tb, and least effective at a high Ta when there could be little further increase in heat loss and little or no decrease in heat production. These are the responses predicted for a specific excitatory substance acting at synapse 'a'.

The findings of FINDLAY and THOMPSON[5] reveal that in oxen 5-HT also appears to act as if it excites synaptic site 'a' specifically. They reported 5-HT to cause a fall in Tb at high Ta. NA caused a fall in Tb at low Ta and could have acted at site 'd'. However, NA was not injected at a Ta higher than 30 °C, so there is no evidence as to whether NA would inhibit heat loss at a higher Ta and so cause a rise in Tb in the ox.

Thus in terms of the model, which is obviously a grossly oversimplified concept, the monoamines NA and 5-HT do not act reciprocally at all ambient temperatures in sheep, goat, rabbit and ox. NA has the effects of a non-specific inhibitor which depresses the activity of both the heat production and the heat loss effectors, and can result in either a rise or fall in Tb, while 5-HT has the effects of a specific excitatory substance which increases the activity of heat loss effectors and depresses the activity of heat production effectors, and can thus only result in a fall in Tb.

If, then, in these species NA is not the excitatory substance which is complementary to 5-HT there may be another naturally occurring substance which performs this function. Preliminary studies[9] suggest that in sheep this could be acetylcholine.

The effects upon Tb of intraventricular NA and 5-HT in the sheep[10,11], goat[12], rabbit[13,14] and ox[15] have been reported to be similar, but not identical. The differences, it would now seem, could be due to differences in test conditions. However, the cat[1], dog[16] and monkey[17,18] are reported to react similarly to each other but quite differently from the other 4 species. It is therefore essential to know what influence Ta has upon the thermoregulatory effects of intraventricular or intra-hypothalamic monoamines in these species, and whether they can be interpreted in terms of the model.



A simple neuronal model to represent the reciprocal inhibition of heat production effectors when heat loss is increased in response to a warm stimulus, and the converse situation when the sheep is exposed to a cold stimulus.

Zusammenfassung. Zur Erklärung der Effekte auf die Thermoregulation in Schafen, Ziegen und Kaninchen bei verschiedenen Umwelttemperaturen von intraventrikulären Injektionen von Noradrenalin (NA) und 5-Hydroxytryptamin (5-HT) wurde ein einfaches Neuronenmodell vorgeschlagen. Diese Monoamine entfalten nicht in allen Situationen eine reziproke Wirkung. 5-HT führt zu einem Anstieg des Wärmeverlustes und einer Hemmung der Wärmebildung. NA hemmt sowohl Wärmeverlust wie auch Wärmebildung[19].

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