All the modifications mentioned are practically irreversible, even if only 2 min after exchanging the isotonic KCl by isotonic KIO_3 the side pools are again filled with isotonic KCl. Only extreme durations of action potentials may be reduced by a small percentage after returning to KCl solution.

Discussion. The results indicate that IO_3^-, which among other actions is known to oxidize cystine to 2 molecules of the corresponding sulfonic acid and to oxidize disulfide bonds in insulin[7], probably reacts with a key molecule located inside of the sodium pathway across the membrane, controlling inactivation of the sodium system. Applied to the external surface of the nodal membrane, however, IO_3^- has almost no action, except for a small increase of run down of the sodium and potassium system of the membrane[8]. This finding corroborates the view of ROJAS and ARMSTRONG[9] who, from their finding of reduced inactivation in squid axons perfused with pronase, concluded that some protein located at the inside of the excitable membrane controls inactivation of the sodium system. IO_3^-, however, bears many advantages compared to pronase. It can be applied electrophoretically through micropipettes and its mode and site of action should not be too difficult to elucidate.

Furthermore, the possibility of working with 'open' sodium 'channels' will greatly enhance the possibilities to study the action of chemical and physical agents on the sodium system with simple voltage clamp systems.

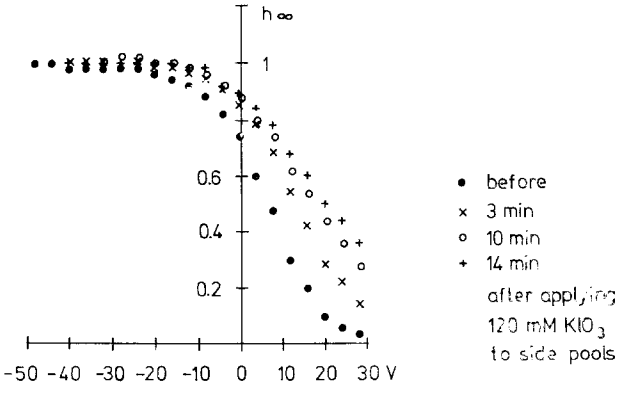

Fig. 3. h_∞ curves obtained before and after exchanging the isotonic KCl in the side pools by isotonic KIO_3. The results were obtained 'on-line' with a program developed for normal inactivation using prepulses (60 msec duration) from V = −50 to +30 mV. Note flattening of curves indicating reduced inactivation. Exp. 31 motor fibre *Rana esculenta*.

Zusammenfassung. Iodat (IO_3^-)-Ionen hemmen den Inaktivierungsvorgang des Natriumsystems, falls sie intraaxonal durch Diffusion vom abgeschnittenen Ende einer markhaltigen Froschnervenfaser her ans Innere der Schnürringmembran gelangen. Mit der Spannungsklemme erhält man dann in TEA-Ringer eine Strom-Spannungskurve des Natriumsystems auch mit lang dauernden Potentialänderungen. In der Stromklemme lassen sich unter diesen Umständen Aktionspotentiale mit Dauern bis zu 1 min registrieren.

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Muscarinic Mediation of the Biphasic Temperature Response to Intrahypothalamic Injections of Carbachol in the Cat[1]

There is considerable evidence that in several species acetylcholine may be a neurotransmitter at those synapses within the hypothalamus which are involved in the control of body temperature[2]. In the cat, injections of microgram quantities of acetylcholine or carbamylcholine (carbachol) into the anterior hypothalamic/preoptic (AH/PO) region of the brain evoke thermoregulatory changes which are dose-dependent[3]. Typically, low doses cause only a rise in body temperature and high doses, a fall. Intermediate doses produce a biphasic effect: a fall followed by a rise. To explain this dual effect on body temperature, it was postulated that the AH/PO region of the cat contains two partially overlapping cholinergic systems, one mediating heat gain and the other, heat dissipation[3]. Since both acetylcholine and carbachol possess strong muscarinic and nicotinic agonistic activity, it is possible that neurotransmission might be muscarinic in one of these systems and nicotinic in the other. The present experiments were carried out to examine this possibility.

Materials and methods. Using pentobarbital anesthesia and aseptic technic, 22 G stainless steel guide cannulae were implanted just above the AH/PO region in male cats weighing 2.5–3.7 kg. Two weeks were allowed for recovery from surgery. Through a 28 G injection cannula, sterile, pyrogen-free, isotonic solutions of drugs dissolved in an artificial cerebrospinal fluid were injected unilaterally in a volume of 1.0 µl at a depth of 1.5 mm below the guide tips.

During each experimental session, the cats were isolated in a temperature-controlled cabinet (20 °C ± 0.5 °C) and restrained in a stock-like device to which they had been previously accustomed. Colonic temperature, ear skin temperature and respiratory rate were monitored continuously throughout the session. These parameters were allowed to stabilize for at least 1 h before an intracerebral injection was performed.

The following drugs were used: carbamylcholine chloride, nicotine dihydrochloride, oxotremorine base or sesquifumarate salt, l-hyoscyamine hydrochloride and mecamylamine hydrochloride.

Results and discussion. In confirmation of a previous report[3], intrahypothalamic injections of 0.01 *M* to 0.03 *M* carbachol into AH/PO loci produced biphasic

[1] Supported in part by Grant No. NS11175-01 from the National Institutes of Health, U.S. Public Health Service.
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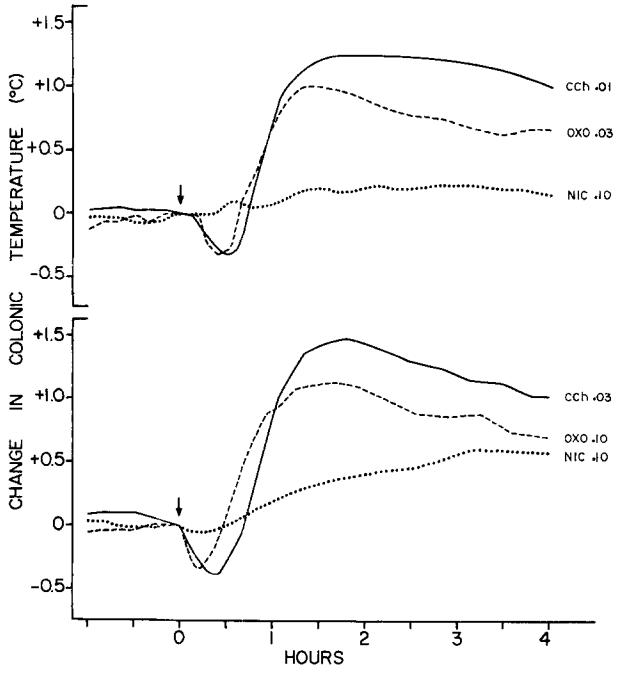
thermoregulatory responses. To determine whether the dual responses might be mediated by muscarinic and nicotinic systems within the AH/PO region, similar injections of nicotine and oxotremorine, specific nicotinic and muscarinic agonists, respectively, were performed. Nicotine, injected in concentrations ranging from 0.01 to 0.3 *M* produced either no effect or a delayed and gradual increase in temperature which bore no resemblance to the response to carbachol. Similar delayed, gradual temperature increases have been observed after control injections of artificial cerebrospinal fluid and may be attributable to pyrogen contamination or a pyrogenic tissue factor released by mechanical disturbance of the injection site. Oxotremorine, on the other hand, produced thermoregulatory effects which were remarkably similar to those evoked by carbachol, although somewhat higher doses were required. The thermoregulatory effects of injections of carbachol, nicotine and oxotremorine injected into 2 different AH/PO sites are illustrated in the Figure.

Further analysis of the nature of the biphasic carbachol response was carried out using 1-hyoscyamine, a specific muscarinic receptor antagonist and mecamylamine, a specific nicotinic receptor antagonist. One of these substances was injected into a site 20 min prior to the injection of a dose of carbachol which, when administered alone into the same site, evoked a biphasic response. At 6 sites, pre-injection of 0.012 *M* 1-hyoscyamine produced a 60–70% reduction in the magnitude of both the falling and the rising phase of the response evoked by 0.03 *M* carbachol. This reduction was significant at the 0.05 level. However, pre-injection of mecamylamine at a concentration of 0.13 *M*, 10 times the concentration of 1-hyoscyamine used, produced only a 29% reduction of the falling phase ($P > 0.05$) and failed to affect the rising phase. Injection of 1-hyoscyamine or mecamylamine alone had no consistant effect on body temperature, although mecamylamine occasionally produced a small increase.



Changes in colonic temperature evoked by injections into 2 sites within the AH/PO region of 1.0 µl of various molar concentrations of carbachol (CCh) nicotine (NIC) and oxotremorine (OXO).

These findings suggest strongly that both the fall and the rise in temperature produced by acetylcholine or carbachol injected into the AH/PO region of the cat brain are due to an action on muscarinic or muscarinic-like receptors and that stimulation of nicotinic receptors is not involved. The biphasic effect on body temperature evoked by injection of carbachol at some AH/PO loci is unlikely to be a result of sequential excitation and inhibition (or vice-versa) of a single muscarinic pathway because injection of a muscarinic antagonist at these same sites – which would presumably produce inhibition of function – failed to produce any major change in body temperature. Moreover, injection of carbachol at some sites within the AH/PO region evoked only one unitary effect, either a fall or a rise in temperature[3]. The most parsimonious explanation of these findings is that the AH/PO region of the cat contains partially overlapping heat gain and heat loss pathways, both of which are muscarinic in nature. Biphasic responses would occur when muscarinic agonists are injected into areas of overlap.

With respect to its lack of nicotinically sensitive synapses in the AH/PO heat loss pathway, the cat apparently differs from the rat and rhesus monkey. In these latter species, nicotinic stimulation of the AH/PO region evokes a decrease in body temperature[4,5]. However, the possibility that nicotinic synapses involved in heat loss may exist in the posterior hypothalamus or lower brain stem of the cat cannot be dismissed. Indeed, 2 recent reports that nicotine injected into the cerebral ventricles of the cat support this possibility[6,7].

Résumé. On a examiné la nature du changement biphasique de la température rectale produit par une injection de carbamylcholine dans l'hypothalamus du chat. Les phases d'augmentation et de diminution de la réponse ont été causées par des recépteurs hypothalamiques muscariniques.

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Pheromone and Host Odor-Stimulated Potentials in *Dendroctonus*

Electrophysiological investigations of antennal olfactory responsiveness to pheromones and host odors have been reported for several insect species[1]. Antennal olfactory response can be measured through action potentials from one to a few receptor cells[2] and through the electroantennogram (EAG)[3]. In general EAG records consist of the summation of several receptor potentials from olfactory receptors. However, with the indifferent electrode in the head of the insect, muscle potentials often appear in the records[3]. When the recording and