Electrotonic Conduction in Molluscan Nerve Cells

It has often been assumed that in vertebrate[1] and invertebrate[2] neurons the influence of local potentials is restricted to a limited region of the cell. However, evidence from *Aplysia* giant neurons[3] suggests that the space constant of these cells is large. Consequently, electrotonic conduction may be an important method in conveying information. The purpose of the present note is to show that in molluscan neurons graded potentials initiated at distant axonal sites are electrotonically conducted to the cell soma; and to suggest that potentials occurring at distant locations may have an important influence on integrative regions of these cells.

The experiments were conducted on the isolated gastro-oesophageal ganglion of the nudibranch mollusc, *Anisodoris nobilis* (MacFarland), immersed in a circulating pool of sea water cooled to 10 °C. The ganglion contains 1 giant cell whose axon runs for a distance of 1.5–2.5 cm in the medial branch of the gastro-oesophageal nerve. The cut end of this and other nerves were drawn into fluid-filled stimulating pipettes, and short duration (1–2 msec) stimuli were applied between the nerve containing pipette (nerve electrode) and an adjacent pipette in the pool (bath electrode). Two independent 3 *M* KCl filled micropipettes, 1 for stimulating and the other for recording, were inserted under direct vision into the soma of the giant cell through the intact ganglionic connective tissue.

The response of the giant cell following stimulation of the medial branch of the gastro-oesophageal nerve was dependent on the polarity of the stimulus. When the bath electrode was made a cathode, the cell was invaded antidromically. When the bath electrode was an anode, a short latency hyperpolarization of the soma occurred. This hyperpolarizing potential was characterized by a number of properties that suggested it represented an electronically conducted potential: (1) its amplitude was dependent on the intensity of the stimulus (Figure 1A); (2) its latency was dependent on the distance of the nerve stimulating electrodes from the cell soma (compare Figure 1B to 1C); (3) it was only obtained following stimulation of the nerve containing the axon of the giant cell, and (4) hyperpolarization of the soma membrane to a level 70–80 mV below resting potential had very little effect on its amplitude.

As there was a detectable latency between the stimulus and the hyperpolarizing potential (Figure 1C), and as it only occurred following stimulation of the nerve branch containing the axon of the cell, the possibility that the potential represents an undesired coupling between the stimulating and recording systems can be eliminated. The finding that the contractile properties of the sheath can be abolished by a brief fixation of the ganglion and nerve in a weak solution of glutaraldehyde[4] without affecting the amplitude of the potential indicates that an electrical response of the sheath is not involved. Further, the finding that the potential is not affected by the abolition of spike generation in the ganglion and its nerve by the addition of procaine to the bath rules out the possibility that the potential represents a postsynaptic response of the giant cell.

If the response is an electrotonic potential, its duration should be dependent on the duration of the stimulating pulse. Extension of the duration of the stimulating pulse from 2 msec to 1 sec shows that the potential reaches its full amplitude (for the stimulus intensity used) when the pulse is extended beyond the time constant of the cell, and has a duration that is dependent on the duration of the stimulus (Figure 2). The long duration of the response, that occurs even when brief shocks are used, is consistent

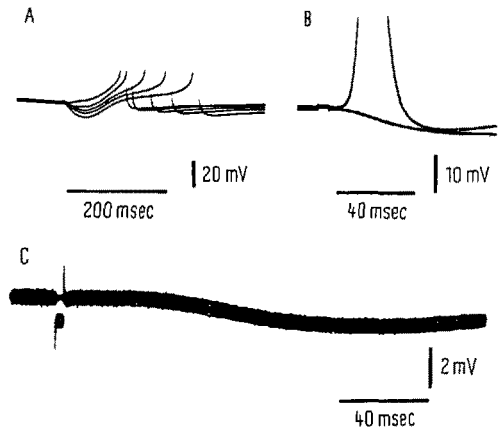

Fig. 1. Response of gastro-oesophageal giant cell to short duration stimulation of the medial branch of the gastro-oesophageal nerve. In (A) superimposed traces of the hyperpolarizing potential elicited by different intensities of peripheral nerve stimulation. In (B) superimposed traces of antidromic response and hyperpolarizing potential response of giant cell evoked by opposite polarities of peripheral nerve stimulation (stimulus applied to nerve 3.8 mm from soma). In (C) hyperpolarizing potential evoked by a stimulus applied to the nerve 12.5 mm from the soma of the giant cell.

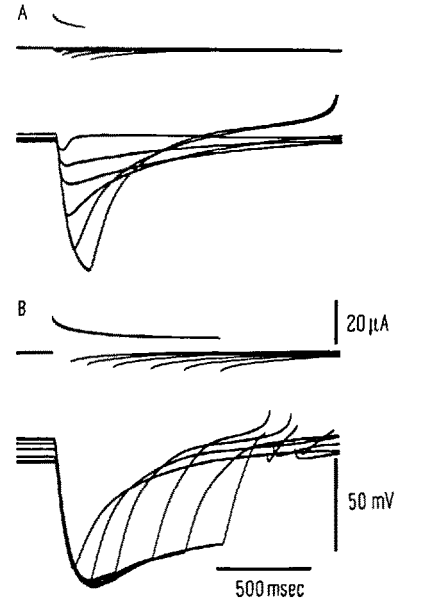

Fig. 2. Effect of stimulus duration on the amplitude of the hyperpolarizing potential of the gastro-oesophageal giant cell. In (A) and (B) superimposed traces of the hyperpolarizing potential elicited by different durations of stimulation; current shown in top trace, cell potential in bottom.

[1] J. C. Eccles, in *Structure and Function of the Cerebral Cortex* (Eds. D. B. Tower and J. P. Schadé; Elsevier Pub. Co., Amsterdam 1960), p. 192.
[2] T. H. Bullock and C. A. Horridge, in *Structure and Function in the Nervous System of Invertebrates* (W. H. Freeman and Co., San Francisco 1965), chapter 3.
[3] L. Tauc, J. gen. Physiol. *45*, 1077 (1962).
[4] M. Mirolli and A. L. F. Gorman, Comp. Biochem. Physiol. *24* (1968) in press.

with the finding that the giant cell has a long time constant. A short duration pulse applied to a distant location on the cell (axon) would appear both lengthened and reduced in amplitude at the soma[5].

The results are of interest for 2 reasons: first, the presence of electrotonically conducted potentials, if undetected, can introduce a serious source of error in the analysis of complex responses observed in cells following stimulation of peripheral nerves. Second, in the specific case we have studied, the synaptic region of the gastro-oesophageal giant cell is dispersed along the main axon and along dendritic-like axonal branches which extend into the neuropile of the neighboring buccal ganglion[6]. We suggest that the extensive electrotonic conductive properties indicated by our results may have physiological significance by allowing synaptic events occurring at regions distant from the integrative center of the neuron to influence the activity of the cell without the involvement of all-or-nothing conducted activity.

Zusammenfassung. Nach Axon-Reizung eines Mollusken-Riesenneurons sind zweierlei Potentiale zu beobachten: eine antidromische Zacke und eine schnelle Hyperpolarisation, was bedeutet, dass das hyperpolarisierende Potential ein durch die Reizung induziertes und über das Axon geleitetes elektrotonisches Potential darstellt.

A. L. F. GORMAN and M. MIROLLI

Laboratory of Neuropharmacology, Division of Special Mental Health Research Programs, IRP, MH, Saint Elizabeths Hospital, Washington (Washington D.C. 20032, USA),
19 February 1968.

[5] W. RALL, in *Neural Theory and Modeling* (Ed. R. F. REISS; Stanford Univ. Press, Stanford 1964), p. 77.
[6] M. MIROLLI and A. L. F. GORMAN, unpublished results.

Interaction of Spinal and Hypothalamic Thermodetectors in Body Temperature Regulation of the Conscious Dog

Thermosensitivity of the spinal cord has been derived from the findings that selective cooling within the vertebral canal causes shivering and cutaneous vasoconstriction[1], while selective heating is followed by suppression of shivering, vasodilatation and thermal panting[2]. These experiments have further shown that the diverse effector mechanisms participate in the thermoregulatory responses to varying extents, which are dependent on the general thermal state of the animal. Therefore, some cooperation between cutaneous, hypothalamic[3] and spinal cord thermodetectors must exist. To find out in what way this cooperation is achieved, the temperatures of the spinal cord and of the hypothalamus have been varied independently in unanaesthetized dogs at different ambient temperatures.

Methods. In 2 dogs weighing 14 and 19 kg, thermodes of polyethylene tubing and a thermistor probe were implanted chronically into the peridural space of the vertebral canal. Additionally, implantation of 6 thermodes of stainless steel tubing and of 1 thermistor probe into the anterior hypothalamus was performed stereotaxically under X-ray control after having filled the third ventricle with contrast medium[4]. After recovery from the surgical procedure, 21 experiments were carried out in the conscious animals at constant ambient air temperatures between 10 and 30 °C, in which the hypothalamic and vertebral canal thermodes were perfused with cold or warm water of constant temperatures between 20 and 48 °C. Temperatures in the rectum, in the anterior hypothalamus and the vertebral canal were recorded. To estimate heat production and evaporative heat loss, oxygen consumption and respiratory rate were determined. Skin temperatures of the paws and thermal conductivities of the skin at one ear and at the pastern joint of one hindleg were recorded to disclose variations of cutaneous blood flow.

Results. The Figure demonstrates 3 sections out of 1 experiment which was performed at an ambient air temperature of 20 °C. The first part contains the thermoregulatory responses of the animal to selective spinal cord cooling and to subsequent selective cooling of the anterior hypothalamus; both cooling periods were performed by perfusing the peridural thermode, and the hypothalamic thermodes respectively, with water of 25 °C at a rate of flow of 45–55 ml/min. Cooling of the spinal cord was followed by cold shivering and by increase in heat production which amounted, in average, to 80% of the precooling level. Cutaneous blood flow was reduced during spinal cord cooling, as indicated by the decreasing thermal conductivity of the skin of the hind leg.

Selective cooling of the anterior hypothalamus led to stronger shivering resulting in a mean increase in heat production for 140%. Additionally, cutaneous vasoconstriction of the ear is indicated by the decreasing thermal conductivity.

This part of the experiment shows that the thermoregulatory responses to spinal cord cooling and to hypothalamic cooling correspond to each other. From the greater responses to hypothalamic cooling it cannot be concluded safely that spinal thermosensitive structures play a minor role as compared with the hypothalamic thermodetectors. The distribution of the spinal thermodetectors is unknown; it must be taken into account that a considerable amount of thermally inert tissue is cooled by the peridural thermode.

The second part of the Figure demonstrates the thermoregulatory response to simultaneous cooling of the spinal cord and the anterior hypothalamus. The intensity of cooling was the same as before. Maximum shivering was elicited by this combined cooling. Oxygen consumption was elevated to an average value of 18.7 ml/min/kg, i.e. 210% above the resting level, with a peak value of 25 ml/min/kg. Cutaneous blood flow was markedly reduced, both on the ear and on the hindleg. Rectal temperature rose for 0.6 °C within 10 min. Apparently, the spinal and hypothalamic thermodetectors act together in pro-

[1] E. SIMON, W. RAUTENBERG, R. THAUER and M. IRIKI, Pflügers Arch. ges. Physiol. *281*, 309 (1964).
[2] C. JESSEN, K.-A. MEURER and E. SIMON, Pflügers Arch. ges. Physiol. *297*, 35 (1967).
[3] H. T. HAMMEL, J. D. HARDY and M. M. FUSCO, Am. J. Physiol. *198*, 481 (1960).
[4] D. M. HUME and W. F. GANONG, Electroenceph. clin. Neurophysiol. *8*, 136 (1956).