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Does the Effect of AVP on Hypothalamic Neurones Support its Proposed Role in Endogenous Antipyresis?

J. MORAVEC, Fr.-K. PIERAU[1]

Faculty of Science, Charles University, Prague and [1]MPI, Kerckhoff-Institut, Bad Nauheim, FRG

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Summary

The effect of AVP on unit activity and temperature sensitivity was tested in hypothalamic slices of the rat. The results demonstrate that AH/PO neurones in vitro react to AVP by significant changes of both static discharge and temperature sensitivity supporting the idea of direct modulation of thermoregulatory neurones by AVP.

Key words

Hypothalamic neurones – Temperature sensitivity – Fever – Arginine-vasopressin

The existence of endogenous antipyretic substances has been documented in a number of studies. Arginine-vasopressin (AVP) is one of the most frequently studied drug in this respect. The results published so far show, however, that AVP can affect body temperature in both directions depending on the route and site of administration. Since data about the effect of AVP on the thermosensitivity of AH/PO neurones are completely lacking, we performed an *in vitro* study on AH/PO slices from normal rats. Single unit activities were recorded extracellularly at 38 °C and the thermosensitivity was tested at sinusoid temperature changes ranging from 35 to 41 °C (duration 6 min, i.e. about 2 $^{o}C.min^{-1}$). Thermal coefficients (in term of $imp.s^{-1}.^{o}C^{-1}$) were calculated using a computer program for piecewise linear regression analysis.

The experimental protocol was as follows: after the unit had been isolated, the control static discharge was recorded for 10 min. Then the control temperature sinus (TS) was performed. In the 20th min of the experiment, AVP was applied and static discharge (SD) was recorded for 15 min, then another TS (1. TS after AVP) was performed. Static discharge following 1. TS was recorded up to the 45th min after AVP application (65th min of the experiment) when 2. TS after AVP was recorded. Thus, the control thermosensitivity, and thermosensitivity 15 min and 45 min after the application of AVP were determined.

In the course of the study the effect of AVP on the static discharge (SD) was tested at 38 °C in 62 neurones (25 warm sensitive, 30 insensitive, and 7 cold sensitive). Forty-two neurones (68 %) reacted to AVP with a transient increase of SD. These transients were characterized either by one peak (type 1 reaction) or by two or more peaks (type 2 reaction). Type 1 reaction was observed in 15 neurones (24 % – 9 warm sensitive and 6 insensitive). Type 2 reaction appeared in 27 neurones (44 % - 8 warm sensitive, 16 insensitive and 3 cold sensitive).

Thermosensitivity (expressed as TC) before and after the application of AVP could

be test in 56 of the neurones (23 warm sensitive, 27 insensitive and 6 cold sensitive). Generally, the temperature sensitivity within the range of 35-41 °C was changed after AVP in all three types of neurones.

The results obtained in the experiments can be summarized as follows:

1. At temperatures above 38 °C there are two criteria by which the warm sensitive neurones can be divided into two groups according to the changes of their thermosensitivity.

*a) Localization of the neuron*e

-the majority of warm sensitive neurones in MPA between bregma level -0.40 and -1.30 increased their thermosensitivity resulting in an average increase of more than 60 %;

-the majority of warm sensitive neurones of all the other groups (according to location) decreased their thermosensitivity resulting in an average decrease of 30-50 %.

b) Type of SD reaction to AVP

-the neurones with type 1 reaction (one peak) increased their thermosensitivity by 27-111 % on the average;

-the neurones with type 2 reaction (two or more peaks) decreased their thermosensitivity by 30-36 % on the average.

2. The thermoinsensitive neurones did not change their temperature coefficient after AVP at temperatures above 38 °C significantly, except for the neurones in PVN which increased their thermosensitivity by about 100 % on the average.

3. The cold sensitive neurones increased their cold sensitivity after AVP at temperatures above 38 °C by about 133 %.

4. Generally, in all groups the changes of thermosensitivity, if any, at temperatures below 38 °C were of opposite direction to those observed at temperatures above 38 °C.

5. The effect of AVP on the thermosensitivity of hypothalamic neurones tends to be long-lasting (more than 45 min) and appears to be biphasic.

The results of the present study demonstrate that AH/PO neurones *in vitro* react to AVP by significant changes of both static discharge and temperature sensitivity and support the idea of a direct modulation of thermoregulatory neurones by AVP. The extent to which the activity of different types or groups of neurones contribute to the thermal response of the individual is not known. It also remains an open question whether the contribution and/or the proportion of individual types and groups of neurones is changed during fever. Experiments on slices of febrile rat, are certainly necessary for further evaluation.

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J. Moravec, Faculty of Science, Charles University, CS-128 44 Prague 2, Viničná 7