The Effect of PGE$_2$ on Activity and Thermosensitivity of Hypothalamic Neurones in Rat Brain Slices

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Summary

Using brain slices the effect of prostaglandin E$_2$ (PGE$_2$) on neurones from different locations of the rat hypothalamus was analysed. PGE$_2$ (150 ng), when injected into the perfusion chamber, influences all hypothalamic neurones studied. The pattern of firing rate changes after PGE$_2$ is variable, but the depressive effect predominates - 72% of neurones decrease their firing rate in long-term experiments. PGE$_2$ also lowers the thermosensitivity of warm sensitive neurones and increases the thermosensitivity of temperature insensitive neurones.

Key words

Neuronal thermosensitivity - Prostaglandin E$_2$ - Hypothalamus - Rat

The effect of PG E$_2$ on neural activity in hypothalamic slices has been studied by several authors (Boulant and Scott 1986, Watanabe et al. 1987, Ono et al. 1987, Morimote et al. 1988). The results obtained were inconsistent. Ono et al. (1987) observed that warm-sensitive neurones were inhibited more than the nonthermosensitive ones. Morimoto et al. (1988) found that PG E$_2$ inhibited neurones in the ventromedial hypothalamus, but stimulated neurones in the PO/AH. No final conclusions can be made from these data. The effect of PG E$_2$ on thermosensitivity of neurones has not yet been studied under in vitro conditions.

In this study, unit activity was recorded in tissue slices of the brain stem, prepared from Wistar strain rats, weighing 200 g. Several slices (400 μm thick) containing the anterior and posterior hypothalamus and the septal area, were obtained by using a razor blade slicer. The slices were allowed to recover for one hour in carbogen bubbled artificial cerebrospinal fluid (ACSF) at 37 °C. For extracellular recordings the slices were transferred to a small chamber (volume 0.5 ml), continuously perfused with carbogenated ACSF with a velocity of 2.5 ml/min. The temperature was measured at the slice surface by a small thermocouple and kept at 38 °C by means of a Peltier device. Periodical temperature stimulation between 35 and 41 °C at the slow speed of 0.02 °C/s (to minimalize possible dynamic temperature effects) were usually applied twice to test the temperature sensitivity of the recorded neurones. Temperature stimulation was repeated 15 and 45 min after drug administration. PG E$_2$ (Sigma) was applied as bolus injection (150 ng/0.15 ml) into the inlet of the perfusion chamber. Single unit activity was extracellularly recorded with glass covered platinum wire microelectrodes. Action potentials and temperature were recorded and/or stored on an oscillograph, a chart recorder and magnetic tape and also fed into a computer for on-line data evaluation.

Warm- and cold-sensitive neurones were defined by a minimal temperature coefficient (TC) of 0.6 imp/s/°C with a positive sign for warm sensitivity and a negative sign for cold sensitivity. The
temperature response curve of each neurone was evaluated by relating the firing rate to slice temperature. In case of nonlinearity of the frequency temperature relationship, ranges with different sensitivities were estimated by selecting those two subsets of data points for which piecewise linear regression analysis gave the minimum sum of least squares for the entire set of data points. The intersection of the two regression lines determined the threshold temperature for a given neurone.

Prostaglandin E₂ (PG E₂) administration (150 ng) into the perfusion medium influenced the firing rate at 37 °C (tonic activity) of all neurones, independently their previous spontaneous activity, thermosensitivity or localization in the brain.

The time course of changes in tonic activity at 37 °C in individual experiments after PG E₂ was highly variable. Fig. 1 summarizes schematically different patterns of changes in firing rate and their relative occurrence. Evidently, the depressive effect of PG E₂ predominated. Temporal increases in firing rate were recorded in 28 % of experiments, only.

The brain neurones studied (n = 28) exhibited different temperature sensitivity. 68 % of neurones showed a linear relationship between temperature and firing rate, while 32 % of neurones were "non-linear". About 55 % of "non-linear" neurones exhibited the "hockeystick" relationship between temperature and firing rates, with the "breaking point" between 38.1-40.6 °C, i.e. above the normal body temperature. At temperatures above the "breaking point", most of the neurones appeared to be warm-sensitive. At temperatures below the "breaking point" they exhibited low temperature sensitivity. Few "non-linear" neurones were warm-sensitive at temperatures below 36.5–39.9 °C and temperature insensitive, or cold sensitive, above this range of temperatures.

Out of 19 "linear" neurones, 42 % were warm-sensitive (0.6 imp./s/ °C) and 58 % were temperature-insensitive. No cold-sensitive neurones were discovered among the "linear" neurones studied.

PG E₂ influenced the temperature sensitivity both of "linear" and "nonlinear" neurones. In warm-sensitive neurones, PG E₂ lowered the temperature coefficients, while in temperature-insensitive neurones PG E₂ tended to increase it (Fig. 2). Prostaglandin E₂ also influenced the character of the relationship between firing rate and temperature. About 50 % of "non-linear" neurones became "linear" after PG E₂, while PG E₂ induced a "non-linear" relationship between temperature and firing rate in 21 % of "linear" neurones.
elevation of the thermoregulatory "set point" during fever.

Fig. 2
Changes in temperature coefficients of "linear" neurones due to PG E\textsubscript{2} administration as related to their original thermosensitivity.

Fig. 3
Percentage of warm sensitive and temperature insensitive "linear" neurones before and 15 min and 45 min after PG E\textsubscript{2} administration.
References


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