CYCLIC GMP EFFECTS ON NEURONAL THERMOSENSITIVITY AND FIRING RATE IN RAT HYPOTHALAMIC TISSUE SLICES

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The rostral hypothalamus contains temperature sensitive and insensitive neurons, and this region plays an important role in thermoregulation and fever. It is possible that endogenous signals modify the activity of these neurons by intracellular cyclic nucleotides. Previous *in vitro* studies in our laboratory found that cyclic AMP increased the firing rate and thermosensitivity of hypothalamic warm sensitive neurons; however, cAMP had little effect on temperature insensitive neurons. The present study tested the responses of hypothalamic neurons to a different cyclic nucleotide, cGMP. Extracellular action potentials were recorded in hypothalamic tissue slices prepared from male, Sprague-Dawley rats. Each rat was killed by decapitation, the brain was removed, and a block containing the hypothalamus was cut. Horizontal tissue slices (350 microns thick) were sectioned and transferred to a recording chamber perfused with an oxygenated (95% O_2-5% CO_2), 300 mOsm/kg nutrient medium. The experimental medium was similar to the control medium but contained 8-bromo-cGMP (5-100 μM), a membrane permeable cyclic GMP analog. The perfusion medium and tissue slices were maintained at 36°-37°C using a thermoelectric assembly that also allowed periodic warming and cooling to characterize neuronal thermosensitivity. Single unit activity was recorded at various hypothalamic locations, including the preoptic area and anterior hypothalamus. Each neuron was characterized according to its thermosensitivity; i.e., its change in firing rate (Hz or imp/sec) during a change in tissue temperature. Neurons with a thermosensitivity of at least 0.8 imp/sec/°C were considered to be warm sensitive. Neurons having lesser thermosensitivities were grouped into subpopulations of temperature insensitive neurons; i.e., low-slope temperature insensitive neurons were less than 0.2 imp/sec/°C, while moderate-slope temperature insensitive neurons were at least 0.2 imp/sec/°C but less than 0.8 imp/sec/°C. Each neuron's spontaneous firing rate and thermosensitivity were tested before, during and after 8-bromo-cGMP perfusion. Low concentrations of 8-bromo-cGMP did not affect the firing rates of most warm sensitive neurons but either increased or decreased the firing rates of many temperature insensitive neurons. On the other hand, 8-bromo-cGMP did not affect the thermosensitivity of low-slope temperature insensitive neurons but either increased or decreased the thermosensitivity of many warm sensitive and moderate-slope temperature insensitive neurons. In addition to neuronal thermosensitivity, cGMP also affected neuronal responses to CO_2. Some neurons changed their firing rates when CO_2 concentration was increased to 10% (from a control concentration of 5% CO_2), and 8-bromo-cGMP altered this response to CO_2. In general, it appears that both cGMP and cAMP modify thermosensitivity in those neurons that are highly sensitive or moderately sensitive to temperature. In terms of firing rates, however, cGMP has its predominant effect on the least thermosensitive neurons, while cAMP primarily affects the most thermosensitive neurons.

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