

NEURONS IN THE PREOPTIC AREA EXPRESSING C-FOS DURING COLD/WARM EXPOSURE AND PROJECTING TO THE PERIAQUEDUCTAL GREY

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The Preoptic area (PO) plays a key role in body temperature regulation by integrating information about local brain and other body temperatures, and by sending efferent signals to various effector organs. This area contains thermosensitive neurons, which change their activities with change in local brain temperature. In rats thermoregulatory skin vasodilation is elicited mainly by the activation of warm-sensitive neurons, since glutamate injection into the PO elicits vasodilation and procaine injected there elicits vasoconstriction. On the other hand shivering and non-shivering thermogenesis seem to be controlled by the inhibitory signals of warm-sensitive neurons (Kanosue *et al.*, 2000). Skin vasodilative neurons are located in the midbrain periaqueductal grey (PAG), especially in its rostral part (rPAG) (Zhang *et al.*, 1997). And recently we found that the caudal PAG (cPAG) contains neurons generating excitatory signals for non-shivering thermogenesis. However, the direct connections between the PO and the PAG in terms of thermoregulation has not been well documented. In the present study, we investigated the distribution of neurons in the PO activated by cold/warm exposure and projecting to the rPAG or cPAG. Male crj- Wistar rats (300- 350 g; Charles River Japan, Osaka Japan) were used. Under the anaesthesia with sodium pentobarbital (50 mg/kg, *i.p.*), retrograde tracer, cholera toxin- b (CTb) was injected into the rPAG (0.4 mm from midline, 5.2 mm to bregma and 6.4 mm below the skullface) or the cPAG (0.8 mm, 8.4 mm, 6 mm). After one week recovery period, rats were exposed to warm ($T_a = 33\text{ }^\circ\text{C}$) or cold ambient temperature ($T_a = 10\text{ }^\circ\text{C}$) for 2.5 h and then perfused under deep anesthesia for the immunohistochemical analysis of c-Fos protein and CTb. When CTb injection was centered in the rPAG, many cells double-labeled with Fos and CTb were observed in the median preoptic nucleus (MnPO) and the lateral part of the medial preoptic area (MPOL) in the warm-exposed rats but not in the cold-exposed rats. On the other hand, when the tracer injection was centered in the cPAG, double-labeled cells were seen in the lateral preoptic area (LPO) in the cold-exposed rats but not in the warm-exposed rats. These results suggest that different groups of PO neuron are activated by warm- or cold-exposure and project to the rPAG or the cPAG, respectively. These projections would form a part of the efferent pathway for the control of heat loss or heat production.

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