INVOLVEMENT OF THE PARABRACHIAL NUCLEUS IN COLD-INDUCED THERMOGENESIS IN THE RAT

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The parabrachial nucleus (PBN), an integrative site for the autonomic nervous system in the brainstem, is a target of neurons mediating cold information in the spinal dorsal horn. Many Fos-positive cells are observed in the PBN during cold exposure. These findings suggest the involvement of parabrachial neurons in the thermoregulatory system to maintain the body temperature in a cold environment. Thus, to test this possibility we investigated the effects of electrical stimulation of the PBN on O_2 consumption (VO_2) and those of electrolytic lesions of these regions on cold-induced thermogenesis. For stimulation experiments, male Wistar rats were anesthetized with urethan (1.2 g/kg, i.p.) and kept on a heating pad to maintain their body temperature at 36-37°C. A concentric electrode was stereotaxically inserted into the unilateral PBN region. Stimuli were 20 Hz monophasic square pulses with a duration of 0.5 ms and a strength of 10-40 μA for 5 min. VO_2 was measured by an open-circuit method. After the experiments, the stimulation site was verified histologically on the coronal section of the brain. Electrical stimulation of the PBN (20 μA) immediately increased VO_2 by 1.26 ± 0.11ml/min/kg$^{0.75}$ (n=4) within 5 min, and VO_2 returned to the baseline level within 25 min. The magnitude of thermogenesis increased with the intensity of the stimulus (10-40 μA). The effective site was located in and around the medial or lateral PBN. For lesion experiments, a monopolar stainless-steel electrode was inserted into the PBN under anesthesia with ketamine (50 mg/kg, i.p.) and 1% isoflurane in air. A battery-operated transmitter was implanted intraperitoneally in each rat to measure body temperature (T_b) and locomotor activity by a telemetry system. The measurement was performed at least 1 wk after the surgery. After the experiments, rats were anesthetized with Nembutal (50 mg/kg, i.p.) and the brain was fixed in formalin solution. The site and extension of lesion was examined histologically. Rats were placed in a metabolic chamber at the ambient temperature of 28.5 ± 0.1°C. The chamber was then cooled to 16.6 ± 0.6°C within 40 min and maintained at this temperature for 90 min. In rats with bilateral lesions in the PBN, cold stimulation elicited an integrated increase in VO_2 of 429.3 ± 40.5 ml/kg$^{0.75}$ (n=11), which was significantly smaller than that elicited in the sham rats (679.6 ± 35.0 ml/kg$^{0.75}$, n=7). Cold exposure had no effect on T_b of sham-operated rats but decreased that of PBN-lesioned rats by 2.14 ± 0.12°C (n=11). Both frequency and duration of locomotor activity during the cold exposure were similar between the PBN-lesioned and sham-operated rats. The present study showed that electrical stimulation of the PBN elicited thermogenesis and that lesions in the PBN attenuated the thermogenesis during the cold exposure and resulted in a marked hypothermia. Accordingly, the PBN is involved in the neural mechanism of heat production against a cold exposure.

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