COLD-GATED CHANNEL AS A THERMOSTAT AGAINST COLD

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Cooling of skin evokes afferent impulses in cold fibers, which would elicit heat production (HP) responses (e.g., shivering) and/or heat-gain (HG) behaviors. In physiology, it has been assumed that a cold fiber is a sensor to transduce *T* into the firing rate (FR) code, with which the brain detects *T*. If a cold fiber is a sensor, *T* and FR must be in a one-to-one ratio. However, due to threshold and overshoot responses in FR, *T* and FR are not in a one-to-one ratio, and a cold fiber may not be a sensor. In contrast, from the threshold responses in FR, we have proposed that a cold-receptor itself is a thermostat that compares *T* with the threshold temperature and elicits impulses to drive HP responses or HG behavior when *T* is below threshold. However, the machinery of the thermostat is not clear. The aim of this study is to clarify it by analyzing ionic basis of cold receptors with patch-clamp techniques in cultured cells of dorsal root ganglion (DRG) containing cell bodies of sensory fibers. Wistar rats (2-14 days old) were anesthetized by diethyl ether and decapitated to isolate DRG. After dissociation with collagenase and trypsin, DRG cells were plated on a coverslip and cultured in DMEM containing 10 % fetal bovine serum. After identifying cold-sensitive neurons with Fura-2 microfluorimetry, we performed patch-clamp recordings in these neurons (EPC-7, List). Data were acquired with MacLab (AD Instruments). In whole-cell current-clamp mode, cooling transiently elicited receptor potentials leading to brief impulse trains. Because *T* and these responses were not in a one-to-one ratio, these cold-sensitive neurons may not act as sensors, but act as thermostats. In whole-cell voltage-clamp mode, cooling transiently induced non-selective cation currents, underlying the receptor potentials. In outside-out patch mode, cooling-induced single channel currents were recorded, indicating that these channels were ionotropic receptors responding to cold directly without cytosolic soluble substances. We conclude that the cold-gated channel itself is a thermostat molecule acting against cold.

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