The thirsty mind of the fruit fly: from osmosensation to water-seeking motivation

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To maintain body water homeostasis, the nervous system has to sense the water level in the body and drive water-seeking behavior when the body is dehydrated. To understand the neural mechanisms underpinning body-water sensing and water-seeking motivation, we investigate the nervous system of the fruit fly, where genetic tools permit the interrogation of neural circuits at single-cell resolution. We identified a pair of LHLK neurons in the fly brain that is activated by dehydration and releases the neuropeptide leucokinin to promote water-seeking behavior. LHLK neurons respond to dehydration by sensing the elevation of extracellular osmolality. This osmosensation requires the mechanosensory channel Pickpocket 26 (PPK26), the fly homolog of mammalian acid-sensing ion channels (ASIC). Leucokinin promotes water-seeking behavior by inhibiting two types of dopaminergic neurons in the mushroom body (MB), a computational center in the fly brain. These dopaminergic neurons encode the strength and specificity of the water-seeking motivation. Our study provides mechanistic insights into the neural basis of thirst, a primary desire conserved among almost all animals.