ATP Excites Mouse Vomeronasal Sensory Neurons

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In many mammals, the vomeronasal organ (VNO) is a specialized chemosensory structure that is located at the caudal tip of the nose and important for a variety of social and sexual behaviors. Distributed throughout the sensory epithelium of the VNO are bipolar vomeronasal sensory neurons (VSNs) that respond to pheromones and odors by activation of metabotropic V1R and V2R receptors (Yang & Delay, 2010). In the main olfactory epithelium (MOE), extracellular nucleotides such as ATP attenuate odor responses in mouse olfactory sensory neurons (OSNs) and promote progenitor cells to differentiate into new OSNs (Hegg *et al*., 2003; Jia *et al*., 2009). However, little is known about such paracrine regulation of the VNO. In the rat, ionotropic P2X3 and metabotropic P2Y2 receptors are expressed in the sensory epithelium of the VNO (Gayle & Burnstock, 2005). Thus, we sought to show whether extracellular nucleotides such as ATP modulate excitability in mouse VSNs. To address this question, we performed perforated patch clamp experiments with isolated VSNs using gramicidin as the pore-forming agent. The majority of VSNs under voltage-clamp and current-clamp conditions exhibited an inward current and action potentials to 30 μM ATP respectively (n=15/18). The inward current was dose-dependent (n=4/4, in μM: 1, 10, 30, 50, 100) with extensive variability at higher concentrations of ATP (n=11/11, in μM: 30, 50, 100). Preliminary results suggested that this was not due to the catabolic conversion of ATP to adenosine by ectoATPases and subsequent activation of metabotropic A1 or A2 receptors since no responses were observed to 30μM adenosine (n=0/3). To determine if the effects of ATP were mediated by P2X or P2Y receptors, VSNs were incubated in the selective P2X antagonist PPADS for 5 min before co-application of PPADS and ATP. PPADS (5 μM) significantly blocked the inward current to 30 μM ATP which, after a 25 min wash, returned close to baseline (n=3/3, $p < 0.05$, paired samples t-test). In light of this finding, we hypothesize that the responses may be partially mediated by P2X receptors. Physiologically, ATP may be released from pannexin or connexin30.3 hemichannels expressed in the sensory epithelium of the VNO and enhance the excitability of VSNs (Zheng-Fischhofer, 2007). Experiments are currently underway to address this and other possible ATP release mechanisms present in the VNO.