This Week in The Journal

Type I Taste Bud Cells Contribute to Salt Perception

Caitlin Baumer-Harrison, Martin A. Raymond, Thomas A. Myers, Kolbe M. Sussman, Spencer T. Rynberg, et al.

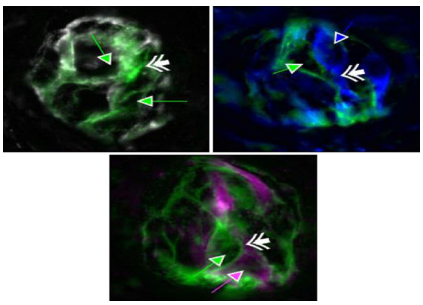
(see pages 7795–7810)

Taste perception is transduced by receptors and channels expressed in different types of taste bud cells. Sweet, umami, and bitter tastes are transduced by G-protein-coupled receptors expressed in Type II cells, whereas sour taste depends on proton influx into Type III cells. Perception of salty taste is more complicated. Perception of aversively high concentrations of NaCl may depend on the detection of anions by Type II or Type III cells, whereas appetitive responses appear to be mediated by amiloride-sensitive epithelial sodium channels (ENaCs), at least in rodents. All three types of taste bud cells express some ENaC subunits, but amiloride-sensitive sodium currents have only been detected in cells that are most likely Type I cells. But because these cells have generally been considered to be glia-like support cells, their role in salt perception has been doubted.

Baumer-Harrison, Raymond, et al. obtained strong support for the hypothesis that Type I cells contribute to appetitive responses to NaCl by expressing channelrhodopsin selectively in these cells. Photostimulation of channelrhodopsin-expressing cells on the anterior tongue evoked electrical activity in the chorda-tympani nerve, which innervates taste buds in that region. Tongue photostimulation also activated gustatory neurons in the rostral nucleus of the solitary tract (rNTS), where individual neurons can be categorized based on their responses to various tastants. Notably, rNTS gustatory neurons that showed the strongest amiloride-sensitive NaCl responses also responded more strongly than other cells to photostimulation of the tongue.

Remarkably, photostimulation also had behavioral effects in sodium-depleted mice. These mice preferred water with a low concentration of NaCl to plain water, and they similarly preferred illuminated water to nonilluminated water. In contrast, sodium-replete mice did not show a preference for NaCl or illuminated water over plain, non-illuminated water.

These results indicate that the activation of Type I taste bud cells leads to activation of NaCl-responsive neurons in the rNTS and can drive drink choices in sodium-depleted mice. This is consistent with the hypothesis that ENaCs in Type I cells mediate appetitive responses to NaCl. Future work should further test this hypothesis by determining whether inhibiting Type I cells blocks physiological and behavioral responses to NaCl.



In mouse fungiform taste buds, GAD65 (green) is expressed in cells that express NTPDase2 (a marker of Type I cells; gray), but not in cells that express PLCβ2 (a marker of Type II cells; blue) or CA4 (a marker of Type III cells; magenta), allowing selective targeting of Type I cells. See Baumer-Harrison, Raymond, et al. for details.

Microglial Exosomes Mediate Ethanol-Induced Neuron Death

Sayani Mukherjee, Miguel A. Cabrera, Nadka I. Boyadjieva, Gregory Berger, Bénédicte Rousseau, et al.

(see pages 7965–7979)

Ethanol damages the developing nervous system, with effects ranging from disruption of long-range communication to microencephaly and agenesis of the corpus callosum. These effects stem from impairment of neurogenesis, migration, neurite extension, myelination, and survival, which results partly from the activation of microglial immune responses and partly from the production of reactive oxygen species (ROS). Mukherjee et al. now report that these two pathological processes are related: immune molecules released by microglia increase ROS production in neurons, leading to neuron death.

Microglia, like other cell types, release vesicles called exosomes, which contain proteins and RNA and can be taken up by other cells. Because microglial exosomes can contain inflammatory cytokines, Mukherjee et al. hypothesized that they are responsible for ethanol-induced neuron death. They looked specifically at the effects of microglial exosomes on hypothalamic β-endorphin neurons, which are lost when newborn (equivalent to human third trimester) rat pups are treated with ethanol. Consistent with their hypothesis, markers of microglial exosomes were higher and their activity was greater in extracellular vesicles isolated from the hypothalamus of ethanol-treated pups than those from control pups, and treating pups with a drug that reduces exosome release attenuated loss of β-endorphin neurons in ethanol-treated pups.

Proteomic analysis of exosomes purified from cultured microglia revealed that ethanol exposure increased levels of many immune molecules, including the complement protein C1q. C1q helps initiate the complement signaling cascade that promotes inflammation, phagocytosis, and formation of the membrane attack complex (MAC), which induces cell lysis. Importantly, treating rat pups with ethanol increased hypothalamic levels of C1q, MAC proteins, and the apoptosis marker caspase-3. Moreover, a drug that lowers microglia levels reduced hypothalamic C1q expression in ethanol-treated rats. Finally, exosomes purified from ethanol-treated microglia increased ROS production and apoptosis in cultured hypothalamic neurons; these effects were blocked by C1q-neutralizing antibodies, and apoptosis was reduced by inhibiting ROS.

These and additional results suggest that ethanol exposure during development increases the release of C1q-containing exosomes from hypothalamic microglia. These molecules trigger formation of the MAC and production of ROS in β-endorphin neurons, leading to apoptosis. Whether similar mechanisms contribute to ethanol-induced neuronal death during the development of other brain areas remains to be determined.

This Week in The Journal was written by Teresa Esch, Ph.D.
https://doi.org/10.1523/JNEUROSCI.twij.40.41.2020