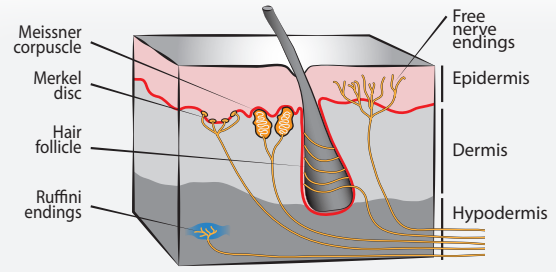
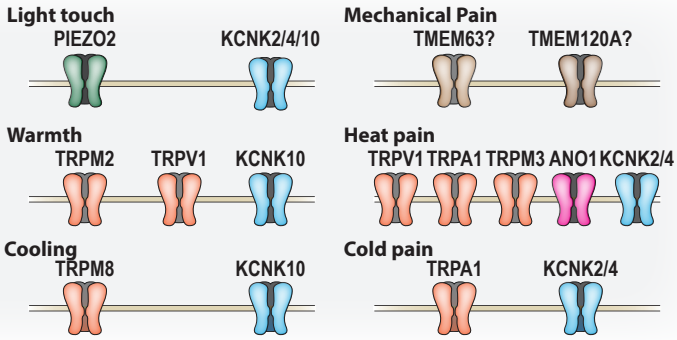
SnapShot: Orofacial Sensation

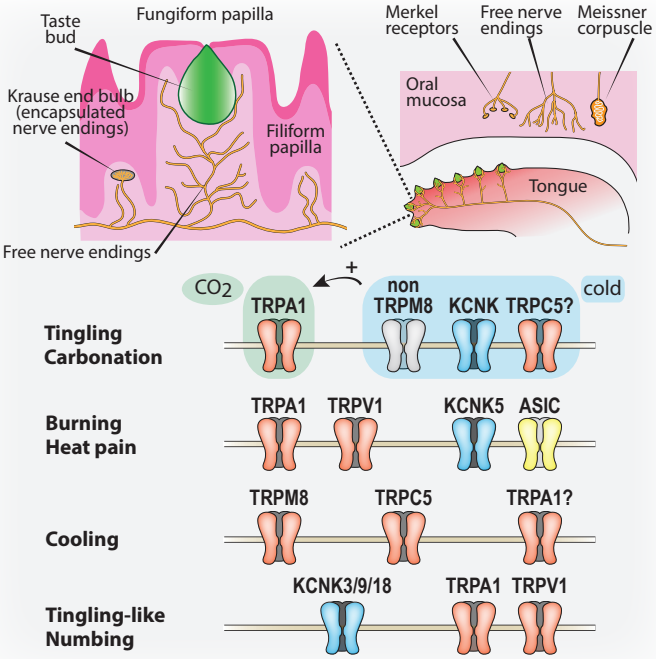
Patrick Delmas, Bertrand Coste

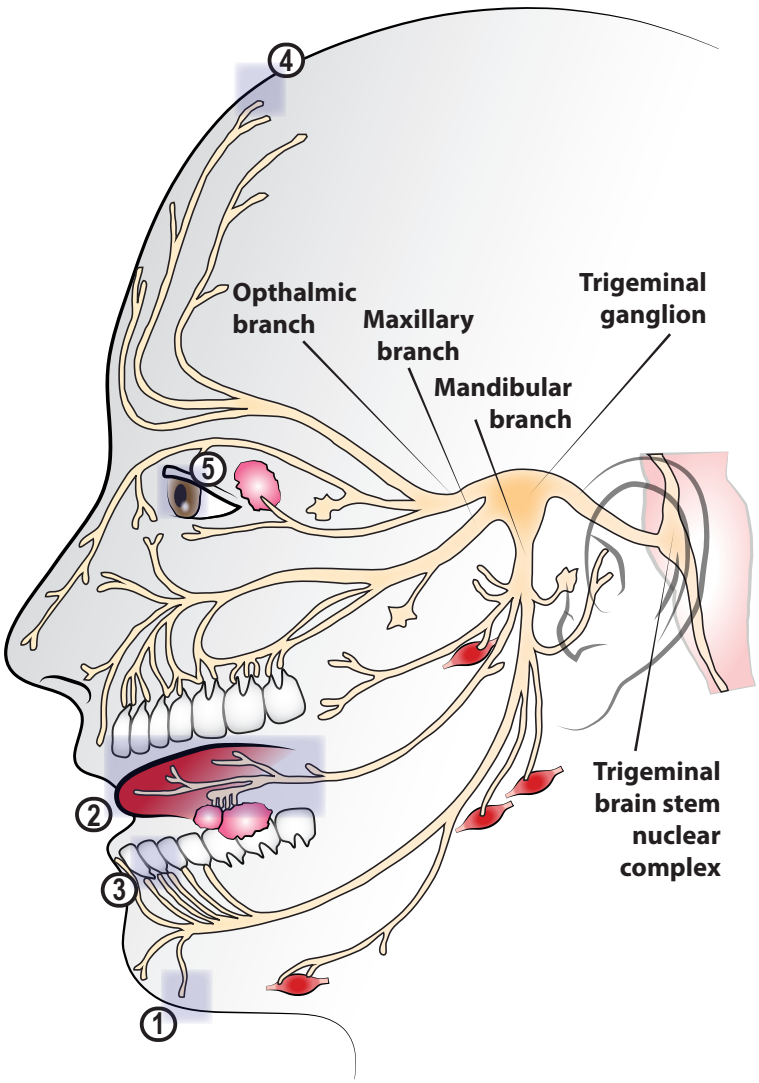
1- Skin / Touch, thermosensation and pain



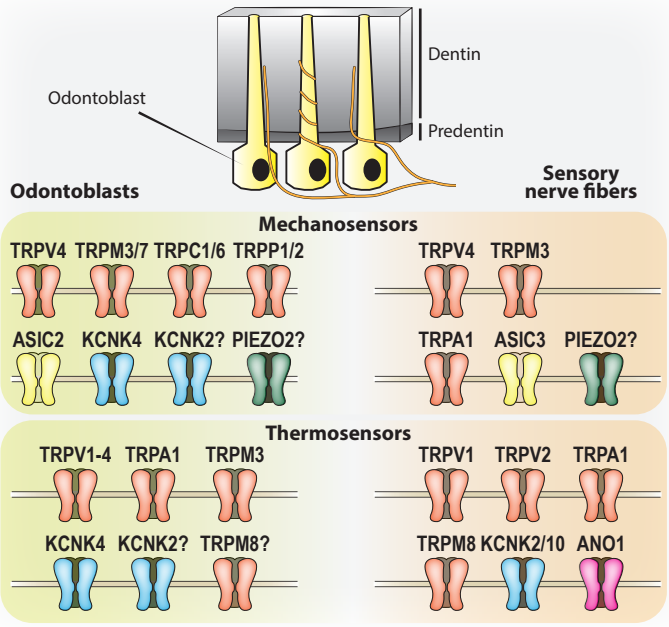


2- Tongue and oral cavity / Mouthfeel

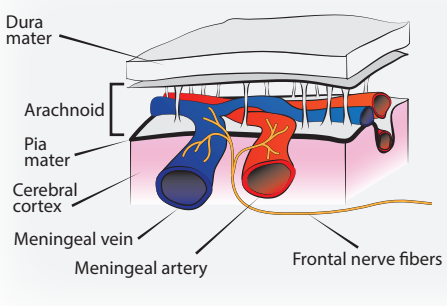


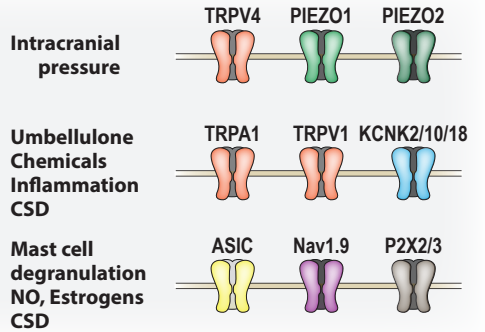


3- Tooth / Dental pain

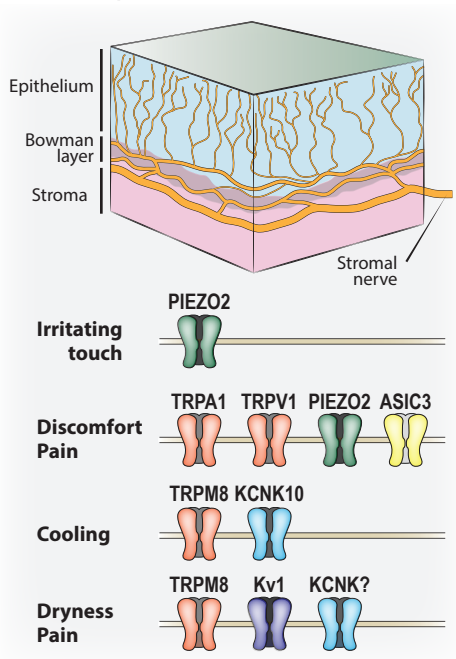


4- Meninges and large cranial vessels / Pain headache





5- Cornea / Pain



Cell SnapShot

OROFACIAL SENSATION

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Abstract

Ophthalmic, maxillary and mandibular branches of the trigeminal nerve provide sensory innervation to orofacial tissues. Trigeminal sensory neurons respond to a diverse array of sensory stimuli to generate distinct sensations, including thermosensation, mechanosensation, itch and pain. These sensory neurons also detect the distinct sharpness or pungency of many foods and beverages. This SnapShot highlights the transduction ion channels critical to orofacial sensation.

Facial skin sensations

Sensory messages from facial skin are mediated by different classes of afferent trigeminal nerve fibers distributed in the epidermis and dermis. Touch and pressure are sensed by mechanoreceptors, whilst thermoreceptors and nociceptors encode the sensations of temperature and pain, respectively. Facial muscles however are devoid of typical muscle spindle proprioceptors, therefore trigeminal corpuscle-like structures found in facial muscles may serve as proprioceptors (not illustrated). It is now well accepted that perception of a single stimulus requires several transduction channels and conversely, a given transducer channel may contribute to multiple modalities. Data extrapolated from hind paw skin studies suggests that heat-evoked pain response relies on functionally redundant TRPV1, TRPA1 and TRPM3 channels (Vandewauw et al., 2018). TRPA1 also functions as a noxious cold thermal sensor, activated below 17°C as well as a transducer of exogenous irritant compounds and neurogenic inflammation. TRPM8, which is activated by cold temperatures and menthol, mediates cooling sensation (Peier et al., 2008) in conjunction with the temperature-sensitive KCNK10 channels. The chanzyme TRPM2, which combines a thermo-TRP ion channel with an ADP ribose pyrophosphatase domain, along with TRPV1 and KCNK10, has emerged as a candidate for transduction of warmth (Tan and McNaughton, 2016). The mechanically-activated Piezo2 channel is the predominant transducer for light touch (Ranade et al., 2014). Transducers for mechanonociception and pleasant touch have yet to be identified.

Oral cavity and mouthfeel

The oral cavity is populated with encapsulated and free trigeminal nerve endings. These sensory fibers can be activated by mechanical forces and temperature and by a huge array of chemical agents. Chemically-sensitive nociceptors provide sensory signals that help avoid inhalation, ingestion or absorption of potentially threatening chemical and biological agents. Trigeminal innervation also plays a fundamental role in mouthfeel, which describes the physical or textural sensations caused by foods and beverages. Many compounds found in foods, beverages, and spices can chemically activate oral trigeminal nerve endings to convey sensations of heat, cold, touch, pain, tingling and numbing (Simons et al., 2019). Ion channels detecting oral chemesthetic agents include many TRP channels, proton-sensitive ion channels (ASICs, Waldmann et al., 2000) and potassium channels among others. Chemesthesis explains the pungent or sharp feel of many different foods and spices such as the burning sensation from chili peppers (capsaicin; TRPV1), black pepper (piperine; TRPV1, KCNK), ginger root (gingerols; TRPV1), Szechuan pepper (linalool; TRPA1, KCNK) and wasabi roots (TRPA1), the coolness of peppermint (menthol; TRPM8) and the tingling sensation associated with carbonated drinks (CO_2, carbonic acid; Wang et al., 2010) or Sichuan peppercorns (hydroxyl sanshool; KCNK). Importantly, the sensations evoked by many of these chemical agents show cross-interaction with temperature and mechanical stimuli. For example, cooling and touch (bubbles) introduce additional perceptual qualities to the tingling experience evoked by carbonated drinks; menthol potentiates cold sensations, while capsaicin sensitizes the perception of heat.

Tooth and pain

Teeth are innervated by a dense network of myelinated and unmyelinated trigeminal nerve fibers that converts external stimuli into pain. Sensory nerve fibers entering the dental pulp innervate the odontoblasts, which besides their role in dentinogenesis have important functions in sensory perception. It is therefore suggested that the experience of pain via exposed dentine involves both direct activation of transduction channels in nerve endings and interaction of odontoblasts with afferent fibers. The main causes of tooth pain include pulp infection and traumatic injury, which induce chemical and thermal changes in

dentinal fluid as well as fluid movements. Different families of ion channels present in dental primary afferent fibers and odontoblasts are known to transduce sensory stimuli into pain. The polymodal TRP and ASIC ion channels are necessary to initiate nociceptive signals in response to various stimuli such as stretch, heat, cold and changes in pH. TRP, KCNK2/10 and piezo channels expressed in dental primary afferent neurons have been hypothesized to be key contributors for the sense of temperature and dentinal fluid movement in teeth.

Cranial vessels and headhache

Cranial meninges are richly innervated by trigeminal afferent nerve fibers from the ipsilateral trigeminal ganglion. The only sensation evoked following stimulation of meningeal sensory afferents is pain, pointing to their important roles in headache pain processing. Although conveying pain signals, meningeal sensory afferents can be activated by punctuate probing and stroking, warming or cooling stimuli and by a variety of chemical stimuli, algesic agents and inflammatory mediators. Proinflammatory substances and cortical spreading depression (CSD) are pathophysiological conditions that sensitize meningeal nociceptors by acting at TRPV1, TRPA1, KCNK and Nav1.9 (Royal et al., 2019; Bonnet et al., 2019). TRPA1 can also be activated by volatile substances such as umbellulone, a headache-inducing monoterpene ketone found in the leaves of the tree Umbellularia californica, also known as the headache tree. Increased sensitivity of meningeal nociceptors contributes to the generation of primary headaches such as tension-type and medication-overuse headaches and migraine or trigemino-autonomic headaches.

Cornea and pain

The cornea is rich in sensory nerve supply derived from the trigeminal ophthalmic and maxillary divisions. Ocular sensory neurons can be classified as polymodal- and mechano-nociceptors, and cold thermoreceptors. Pain is associated with mechanical, chemical, and thermal heat stimulation of the ocular surface, while cold thermoreceptors detect wetness (Belmonte et al., 2017). Transduction of mechanical forces by corneal mechano-nociceptor endings involves Piezo2. TRPV1 and TRPA1 appear to be the main detectors of many exogenous irritants, chemicals, heat and inflammatory mediators in polymodal neurons. TRPM8 is critical in the sensing of temperature decreases by ocular cold thermoreceptor fibers. Many of these channels are involved in dry eye disease, where inflammation causes abnormal activity of cold thermoreceptors and sensitization of nociceptors, causing dryness sensations and pain.

References

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