

Taste Damage: Previously Unsuspected Consequences

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Inhibition within the taste system

Taste damage, taste intensification and taste phantoms

Studies using anesthesia provide insights into oral phantoms. The chorda tympani nerve is accessible for anesthesia at two sites. First, the chorda tympani leaves the tongue with the lingual nerve (CN V) and the two travel through the pterygomandibular space. The inferior alveolar nerve, which conveys pain from the lower teeth, passes through the same space; thus dental anesthesia abolishes taste and touch as well as pain. Secondly, the chorda tympani passes through the middle ear after separating from the lingual nerve, so injection of an anesthetic just under the skin near the ear drum anesthetizes taste but not touch. Using both procedures, we showed that anesthesia of the chorda tympani intensifies tastes evoked from the contralateral rear of the tongue, the area innervated by the glossopharyngeal nerve (Lehman *et al.*, 1995; Yanagisawa *et al.*, 1998). This finding supports the earlier evidence of Halpern and Nelson (1965) for central inhibitory connections between the chorda tympani and glossopharyngeal nerves. This inhibition acts as a constancy mechanism: when one nerve is damaged, its input to the central nervous system (CNS) is reduced, releasing inhibition on other taste structures and thus compensating for the loss of input from the damage.

During our anesthesia experiments, about half of the subjects developed taste phantoms typically localized to the contralateral rear of the tongue (Yanagisawa *et al.*, 1998). This suggested that clinical taste phantoms (i.e. dysgeusia) might be the result of localized taste damage. Indeed, we have found taste damage in patients reporting taste phantoms (Bartoshuk *et al.*, 2002).

Taste damage, oral pain intensification and oral pain phantoms: burning mouth syndrome (BMS)

Anesthesia of the chorda tympani intensifies the burn of capsaicin on the contralateral anterior tongue (Tie *et al.*, 1999), indicating that taste input normally inhibits trigeminal input centrally. Taste inhibition could protect eating behavior in an animal suffering pain from tongue damage; it could also aid animals in eating plants defended by natural mechanisms such as capsaicin or thorns.

The intensification of oral burn is related to the genetic ability to taste PROP (6-*n*-propylthiouracil). Some individuals (nontasters) are 'taste blind' to PROP, while to others (tasters) PROP tastes bitter. The development of new psychophysical procedures (Hall *et al.*, 1975; Marks *et al.*, 1988; Bartoshuk *et al.*, 2004) has permitted quantification of this bitterness. Tasters are further subdivided into supertasters (those perceiving the most intense bitter) and medium tasters (those perceiving less intense bitter) (Bartoshuk *et al.*, 1994). Anesthesia of the chorda tympani produced the greatest intensification of contralateral oral burn from supertasters (Tie *et al.*, 1999).

We suspect that interactions between taste and oral pain are responsible for BMS (Grushka, 1987). Patients with BMS report intense oral pain in the absence of visible pathology. In a series of

BMS patients, we found severe taste damage. In addition, the intensity of the peak oral pain correlated with the density of fungiform papillae; that is, patients with BMS were primarily supertasters (Grushka and Bartoshuk, 2000). According to Grushka, interactions between taste and pain may extend to other facial pain. For example, patients with atypical odontalgia (pain appearing to originate from healthy teeth) showed taste damage (Grushka *et al.*, 2002).

GABA (gamma-aminobutyric acid) and taste inhibition

Grushka *et al.* (1998) discovered that the majority of BMS patients experienced relief using clonazepam, an agonist to the inhibitory neurotransmitter GABA, which is found in taste pathways (Davis, 1993; Wang and Bradley, 1993; Smith and Li, 2000). If BMS results because taste damage produces a loss of the inhibition normally exerted on central structures mediating oral pain, then a GABA agonist might be expected to counter that loss of inhibition and thus relieve the oral pain phantom.

Does taste inhibition operate more generally than previously understood?

Taste input may inhibit a variety of activities incompatible with eating (Bartoshuk and Snyder, 2002). The first evidence for this idea came from a study showing that women with pregnancy hyperemesis show taste damage (Sipiora *et al.*, 2000). Interestingly, many folk remedies for the nausea of pregnancy involve taste. For example, ginger combats nausea systemically (Smith *et al.*, 2004), but when consumed as a folk remedy, the patient benefits from stimulation of taste as well. Clonazepam has also been associated with anti-nausea effects (Shindo *et al.*, 1995).

Berger's clinical insights have played an important role in the development of these ideas. She noted that nausea, cough and hiccups are among the clinical problems afflicting cancer patients at the end of life. Cancer patients typically undergo therapies that damage taste (Duffy *et al.*, 2002). Taste stimulation (e.g. eating ginger, sucking a lemon, eating candies) is anecdotally associated with the treatment of these symptoms and GABA agonists have therapeutic value (Dicpinigaitis *et al.*, 2000; Smith and Busracamwongs, 2003). Given that taste is also thought to play a role in preparing the gastrointestinal tract for the arrival of food (e.g. cephalic phase responses) (Teff, 2000), damage to taste may have gastrointestinal consequences.

The evidence above suggests ways to harness the inhibition produced by the taste system for clinical benefit either by stimulating taste or potentiating central inhibition with clonazepam or other GABA agonists. The role of PROP status may also be important clinically; nontasters may produce less inhibition.

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