Neural Correlates of Oral Irritation by Mustard Oil and other Pungent Chemicals:
A Hot Topic

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Together with taste and smell, oral sensations of touch, temperature, chemical irritation and pain play an important role in determining food flavor. Trigeminal sensations are mediated by sensory fibers innervating the oral mucosa that project via the lingual nerve to reach the brainstem trigeminal complex, with extensive terminations in subnucleus caudalis (Vc) (Carstens et al., 1995). Neurons in superficial laminae of dorsomedial Vc often respond to a wide range of thermal, mechanical and irritant chemical stimuli (Carstens et al., 1998).

Different pungent chemicals elicit distinct temporal patterns of oral irritation. Repetitive application of capsaicin elicits a progressive rise in irritancy (sensitization; Green, 1989), as do piperine and concentrated salts and acids. In contrast, nicotine, menthol and cinnamaldehyde elicit irritation that declines across trials (desensitization; for a review, see Carstens et al., 2002). These contrasting patterns are also observed in the responses of Vc neurons (Dessirier et al., 2000) and may depend on the relative strength of opposing excitatory and desensitizing processes that are initiated in trigeminal nerve endings by a particular irritant.

Recent molecular studies have uncovered the existence of six transient receptor potential (TRP) channels that account for thermal sensations from extreme cold to extreme heat (Jordt et al., 2003; Montell, 2003). Several of these also respond to irritant chemicals. Thus, TRPV1 (VR-1) is activated by noxious heat and capsaicin (Caterina et al., 1997), TRPM8 (CMR-1) by cooling and menthol (McKemy et al., 2002; Peier et al., 2002) and TRPA1 (ANKTM1) by intense cold, mustard oil, cinnamaldehyde, cannabinoids and other chemicals (Story et al., 2003; Bandell et al., 2004; Jordt et al., 2004).

Our laboratory is particularly interested in the sensory properties of mustard oil in relation to TRPA1.

In psychophysical experiments, lingual application of mustard oil (allyl isothiocyanate, 0.125%) elicited a desensitizing pattern of oral irritation and exhibited mutual cross-desensitization with capsaicin (Simons et al., 2003). Mustard oil similarly elicited a desensitizing firing pattern in Vc neurons recorded in anesthetized rats and cross-desensitized responses to pentanoic acid (Simons et al., 2004). However, mustard oil (1.25%) sensitized Vc responses to noxious heat, consistent with its well-known sensitizing effect on the skin. These contrasting effects of mustard oil (i.e. heat sensitization and chemical desensitization) are not consistent with peripheral or central sensitization, but might reflect a TRPA1-mediated enhancement of thermal gating of TRPV1 and an inhibition of chemical gating of TRPV1 (or other channels) co-expressed in the same trigeminal nerve endings.

TRPA1 is activated by intense cold, mustard oil and cinnamaldehyde (Bandell et al., 2004) and we routinely record from Vc neurons that respond to these stimuli as well as to noxious heat and capsaicin (but not menthol). An example is shown in Figure 1. TRPA1 exhibits desensitization to repeated cooling (Story et al., 2003). We observed a significant decline in successive responses of Vc neurons to repeated lingual cooling (3°C) at rapid (15 s) intervals (Figure 2A,C). Vc responses usually also exhibited desensitization to repeated application of mustard oil or cinnamaldehyde (Figure 2B). Moreover, cold-evoked responses were significantly reduced following application of mustard oil or cinnamaldehyde (Figure 2B,D), suggesting a TRPA1 chemically mediated cross-desensitization of thermal gating of TRPA1.

In conclusion, a substantial population of Vc neurons receives input from trigeminal afferents expressing TRPA1 and/or TRPV1, with some properties of TRPA1 being reflected in the responses of Vc neurons. It is curious that mustard oil, associated with a burning quality and intense cold, both apparently act via a common transduction mechanism. It is additionally puzzling as to how the nervous system can make qualitative discriminations based on input from neurons that respond to both noxious hot and cold stimuli. Nevertheless, the discovery of thermo- and chemosensitive TRP channels has certainly spiced up the field of trigeminal chemoreception.

Acknowledgements
Supported by NIH (DE 13685) and the California Tobacco-related Disease Research Program (No. 11RT-0053).

References


