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Central and Peripheral Lateral Inhibitory Effect of CO_2 on Sweet Perception

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Abstract

The gustatory system includes taste receptor cells organized in multicellular clusters and located within gustatory papillae. Taste cells, namely type I, II, and III cells, express specific receptors for different gustatory stimuli.

Type III cells secrete serotonin (5-HT), norepinephrine (NE) and GABA, that are inhibitory paracrine transmitters, acting on receptors on type II cells and exerting a negative feedback.

In this study we speculated whether the peripheral "lateral inhibition" mediated by type III taste cells onto type II taste cells, is present also at the central level between the areas activated in response to sweet and those in response to the carbonation.

Our data suggested that CO_2 modulates sweetness perception, reducing the perception of sweetness with a stronger reduction of sucrose processing.

Furthermore, the gustatory system seems responsive to CO_2, both at peripheral and central levels.

The sense of taste guides organisms to identify and consume nutrients avoiding toxins and indigestible materials. For humans, this means recognizing and distinguishing the "basic" tastes (sweet, umami, sour, salty, and bitter). There are likely additional qualities that might also be considered basic tastes.

Each taste quality is associated with different nutritional or physiological requirements or potential dietary hazards. Sweet indicates the presence of carbohydrates that serve as an energy source; salty regulates the intake of sodium and other salts, essential for maintaining the body's water balance and blood circulation; umami, the taste of l-glutamate and a few other l-amino acids, reflects a food's protein content; bitter guards against consuming poisons, many of which taste bitter to humans; sour signals the presence of dietary acids.

The five universally accepted basic tastes have specific receptors in oral, pharyngeal and laryngeal regions. Moreover, the expression of taste receptors has been recently reported also in the gastrointestinal tract and particularly in the gut, although their function in digestive and ingestive processing remains unknown[1].

In addition to the basic tastes, the taste system appears responsive to CO_2 but the presence of specific CO_2 peripheral receptors and central neural pathway is still debated[2].

The gustatory system includes taste receptor cells (TRCs) organized in multicellular rosette clusters labeled 'taste buds' and located within gustatory papillae. Taste cells, namely type I, II, and III cells, express specific receptors for different gustatory stimuli[3]. Sweet, umami, and bitter tastes are detected by 2 distinct families of G-protein-coupled receptors (GPCRs) on type II receptor cells. T1R taste receptor family is composed of 3 distinct members that heterodimerize to sense sweet (T1R2 and T1R3) and amino acids (T1R1 and T1R3)[3]. T2R taste receptor family include numerous divergent GPCRs that detect bitter substances. Conversely, sour and salty are sensed by ion channels[3]. The polycystic kidney disease channel expressed by type III cells has been proposed as the acid-sensing machinery detecting the sour[4]. CO_2 is also detected by sour-sensing cells; even though, the taste of carbonation is separated from acid detection because it is mediated by carbonic anhydrase 4, a glycosylphosphatidyl inositol-anchored enzyme tethered on these cells' surface[4]. This enzyme catalyzes the conversion of CO_2 into bicarbonates and protons, with the protons being the relevant signal[4].

Receptor cells respond to and transduce stimuli mediated by taste GPCRs (sweet, bitter, or umami) and secrete ATP to excite primary sensory afferent fibers. ATP also excites neighboring presynaptic (type III) cells. On the other hand, type III cells respond directly to sour taste stimuli and indirectly, via ATP, to sweet, umami, and bitter stimuli. Type III cells secrete serotonin (5-HT), norepinephrine (NE) and GABA, that are inhibitory paracrine transmitters, acting on receptors on type II cells and exerting a negative feedback[5]. One might speculate that 5-HT mediates "lateral inhibition" suppressing the output of adjacent receptor (e.g., sweet) (Figure 1).

The negative feedback loop may also participate in sensory by decreasing the afferent signal over time.

Contrasting with a growing knowledge on the peripheral perceptual mechanisms of taste, including the molecular dynamics of taste receptors, our knowledge of the central processing of taste is still largely incomplete[6].

The most credited candidates to the function of human primary taste cortex (hPTC) are the frontal operculum and the anterior insula (FO/AI).

A new, powerful tool to extend our knowledge of hPTC has been recently provided by fMRI, which is essential in conveying valuable information on the functional anatomy of other neural sensory pathways.

We recently showed with fMRI experiments that the presence of carbonation (carbonated versus non-carbonated beverages) produced a bilateral reduction of neural activity in the insular cortex[7].

By a different data analysis in this study we speculated whether the peripheral "lateral inhibition" mediated by type III taste cells onto type II taste cells, suppressing the output of adjacent receptor, is present also at the central level between the areas activated in response to sweet and those in response to the carbonation.

Behavioral data demonstrated that CO_2 is able to significantly reduce sweet-induced taste perception. Indeed, in the presence of carbonation, a sweet-induced perception of a 10% glucose solution was significantly reduced[7].

Furthermore, fMRI demonstrated that the presence of carbonation (carbonated versus non-carbonated beverages), independently of the sweetening agent (sucrose, As-Ac) produced a bilateral reduction (Figure 2) of neural activity in the insular cortex (IC)[7].

This central inhibitory effect seems to mirror the peripheral "lateral inhibition" operated by type III cells, responsible for the perception of CO2, on type II cells, responsible for the perception of sweet, via 5-HT, NA or GABA (Figure 1).

The finding of a reduction in brain activity in the gustatory regions in response to carbonation may also clarify the inhibitory pathway between type III putative CO_2 perception cells and type II sweet perception cells.

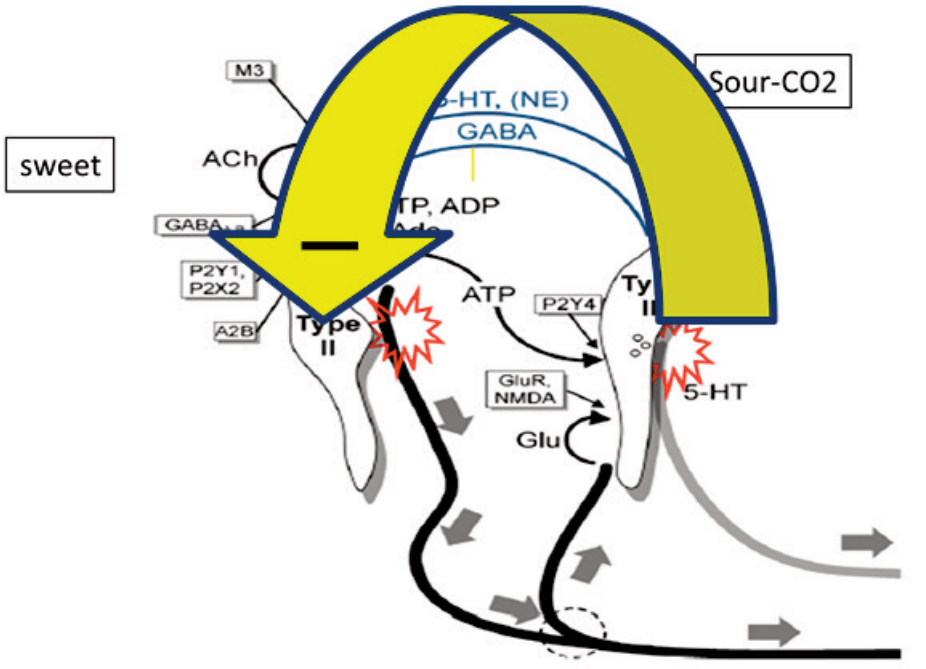

Figure 1. Presynaptic (type III) cells respond directly to acid (sour) taste stimuli and indirectly, via ATP, to sweet, umami, and bitter stimuli. Presynaptic taste cells secrete serotonin (5-HT), norepinephrine (NE) and GABA. 5-HT and GABA are inhibitory paracrine transmitters, acting on postsynaptic 5-HT1A and receptors on type II cells, as shown. 5-HT is also believed to be the neurotransmitter at the synapses type III cells form with axon terminals (solid gray line). The full identification of these putative serotonergic axon terminals remains to be established (Roper 2013).

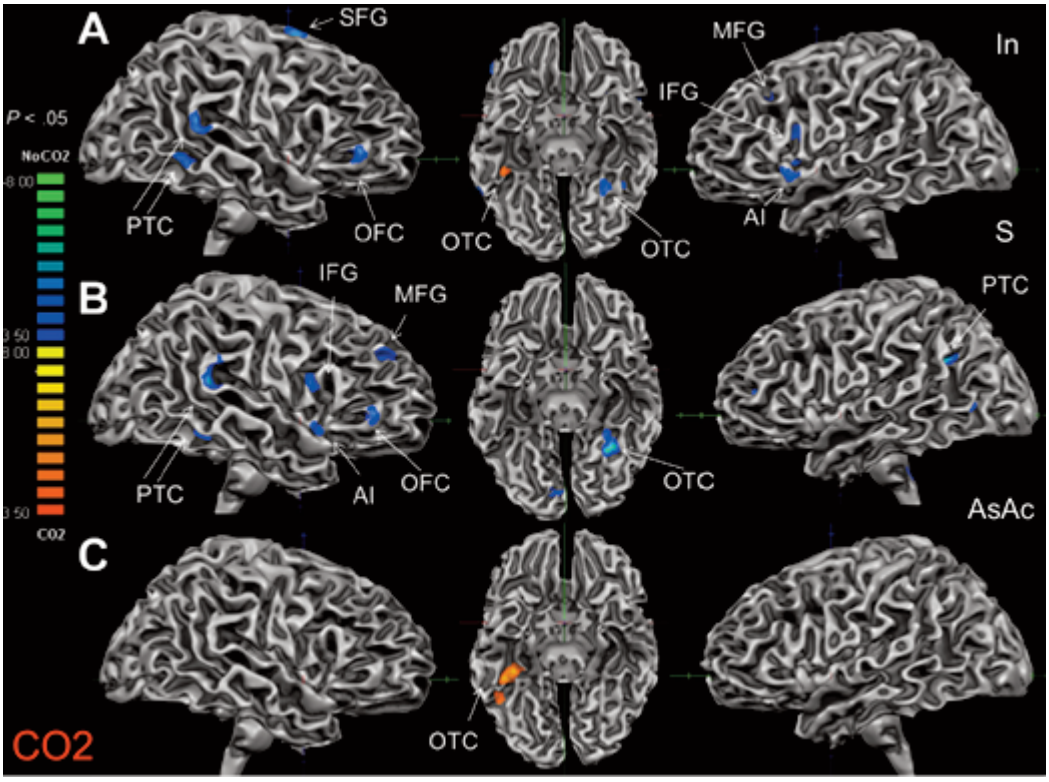

Figure 2. Effect of Carbonation on neural activity: the presence of carbonation independently of the sweetening agent (A) reduced (blue-green color) activity in AI, and other cortical areas. (Di Salle 2013).

Conclusions

These findings provide insightful information on the central architecture of taste processing with the application of fMRI technique, elucidating, from a behavioral point of view, some peripheral molecular mechanisms.

Our data suggested that CO_2 modulates sweetness perception, reducing the perception of sweetness with a stronger reduction of sucrose processing.

Furthermore, the gustatory system seems responsive to CO_2, both at peripheral and central levels.

Conflict of Interests

The Authors declare that they have no conflict of interests.

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