#dietsoda → #nogood

Mary ET Boyle, Ph. D.
Department of Cognitive Science
UCSD
I don’t know.
Do artificial sweeteners have an effect on our metabolism?
a. Compare non-nutritive sweeteners (NNS) with sugars (glucose/fructose/sucrose)
Are artificial sweeteners using the same sensory pathways as sugar?
What is the purpose of the taste system?

dietary selection
Once taste system is activated → digestion 😊
An important, if unrecognized aspect of taste is that it serves functions in addition to guiding dietary selection. Stimulating taste buds initiates physiological reflexes that prepare the gut for absorption (releasing digestive enzymes, initiating peristalsis, increasing mesenteric flow) and other organs for metabolic adjustments (insulin release, sympathetic activation of brown adipose tissue, increased heart rate; Giduck et al., 1987; Mattes, 1997). Collectively, these reflexes that are triggered by the sensory (sight, smell, taste) recognition of food are termed cephalic phase responses.

cephalic phase response

The cell biology of taste

Nirupa Chaudhari, Stephen D. Roper

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Recall,

Aroma is what you smell
+ Taste is what you taste
= Flavour is what you Understand
How do we transduce taste?
Five recognized taste qualities – sweet, sour, bitter, salty, and umami—are detected by taste buds.
Type I cells degrade or absorb neurotransmitters. They also may clear extracellular K⁺ that accumulates after action potentials. K⁺ may be extruded through an apical K channel such as ROMK. Salty taste may be transduced by some Type I cells, but this remains uncertain.

Sweet, bitter, and umami taste compounds activate receptor cells, inducing them to release ATP through pannexin1 (Panx1) hemichannels. The extracellular ATP excites ATP receptors (P2X, P2Y) on sensory nerve fibers and on taste cells.

Presynaptic cells, in turn, release serotonin (5-HT), which inhibits receptor cells. Sour stimuli (and carbonation, not depicted) directly activate presynaptic cells. Only presynaptic cells form ultrastructurally identifiable synapses with nerves.
sweet or glutamate-rich foods activate T1R class of taste receptors. (Bitter activates T2R class)

TrpM5: transient receptor potential cation channel subfamily M member 5

IP₃: inositol 1,4,5-trisphosphate

Gustducin: a subunit

Ca²⁺: calcium ion

Na⁺: sodium ion

ATP: adenosine triphosphate

Purinergic receptors

Endoplasmic reticulum (ER)

IP₃ channel

TrpM5 channel

Pannexin channel
T1r2 + T1r3
- sweet taste receptor
- 1st mechanism to detect sweet compounds: sucrose, glucose, fructose
- non-nutritive sweeteners (saccharin, sucralose, etc)
But — when TIR2+TIR3 was disrupted — animals still responded to sugars — so, there is a secondary mechanism.
Taste cell-expressed α-glucosidase enzymes contribute to gustatory responses to disaccharides

Sunil K. Sukumarana,1, Karen K. Yeea,1, Shusuke Iwatab, Ramana Kotha, Roberto Quezada-Calvilloc,d, Buford L. Nichols, Sankar Mohane, B. Mario Pinto, Noriatsu Shigemura, Yozo Ninomiya, and Robert F. Margolskeea,2

aMonell Chemical Senses Center, Philadelphia, PA 19104; bSection of Oral Neuroscience, Graduate School of Dental Science, Kyushu University, Fukuoka 812-8582, Japan; cDepartment of Pediatrics, Baylor College of Medicine, Houston, TX 77030; dFacultad de Ciencias Químicas, Universidad Autónoma de San Luis Potosi, San Luis Potosi 78210, Mexico; and eDepartment of Chemistry, Simon Fraser University, Burnaby, BC, Canada V5A 1S6

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Dietary carbohydrates are mostly polysaccharides and disaccharides. Here we show that the disaccharide-digesting enzymes maltase-glucoamylase and sucrase-isomaltase are expressed selectively in sweet taste cells. Treating the tongue with inhibitors of disaccharidases specifically decreased gustatory nerve responses to disaccharides, but not to monosaccharides or noncaloric sweeteners, indicating that lingual disaccharidases are functional.

We hypothesize that these enzymes act in concert with salivary amylase to generate monosaccharide substrates for taste cell-expressed glucose transporters.

The transported monosaccharides can then be metabolized to ATP to close $K_{\text{ATP}}$ and activate the T1R-independent sweet taste pathway.

Sukumaran, S. et al. (2015) PNAS
Glucose transporters are expressed in taste receptor cells

Flavia Merigo, Donatella Benati, Mirko Cristofoletti, Francesco Osculati and Andrea Sbarbati

1Department of Neurological, Neuropsychological, Morphological and Movement Sciences, Human Anatomy and Histology Section, School of Medicine, University of Verona, Verona, Italy
2IRCCS, Messina, Italy

Abstract

In the intestine, changes of sugar concentration generated in the lumen during digestion induce adaptive responses of glucose transporters in the epithelium. A close matching between the intestinal expression of glucose transporters and the composition and amount of the diet has been provided by several experiments. Functional evidence has demonstrated that the regulation of glucose transporters into enterocytes is induced by the sensing of sugar of the enteroendocrine cells through activation of sweet taste receptors (T1R2 and T1R3) and their associated elements of G-protein-linked signaling pathways (e.g. α-gustducin, phospholipase C β type 2 and transient receptor potential channel M5), which are signaling molecules also involved in the perception of sweet substances in the taste receptor cells (TRCs) of the tongue. Considering this phenotypical similarity between the intestinal cells and TRCs, we evaluated whether the TRCs themselves possess proteins of the glucose transport mechanism. Therefore, we investigated the expression of the typical intestinal glucose transporters (i.e. GLUT2, GLUT5 and SGLT1) in rat circumvallate papillae, using immunohistochemistry, double-labeling immunofluorescence, immunoelectron microscopy and reverse transcriptase-polymerase chain reaction analysis. The results showed that GLUT2, GLUT5 and SGLT1 are expressed in TRCs; their immunoreactivity was also observed in cells that displayed staining for α-gustducin and T1R3 receptor. The immunoelectron microscopic results confirmed that GLUT2, GLUT5 and SGLT1 were predominantly expressed in cells with ultrastructural characteristics of chemoreceptor cells. The presence of glucose transporters in TRCs adds a further link between chemosensory information and cellular responses to sweet stimuli that may have important roles in glucose homeostasis, contributing to a better understanding of the pathways implicated in glucose metabolism.

Key words: circumvallate papilla; glucose transporter; immunohistochemistry; taste; ultrastructure.
The anticipation of eating initiates the cephalic phase of digestion.

Phase 1

Sensory cues: sight, aroma, bell

Recall Pavlov!
Do artificial sweeteners induce a cephalic phase response?
1. Stimuli

2. Higher brain centers

3. Dorsal vagal complex

4. Parasympathetic signaling via vagus nerve
STIMULI

Food

Higher Brain Centers

Dorsal Vagal Complex

Parasympathetic signaling via vagus nerve

Medulla oblongata

Preganglionic parasympathetic neuron in vagus nerve
Well, depends — there are 1,000s of articles and there are conflicting reports.
Effects of stevia, aspartame, and sucrose on food intake, satiety, and postprandial glucose and insulin levels

Stephen D. Anton a,b,d,e, Corby K. Martin f, Hongmei Han g, Sandra Coulon h, William T. Cefalu i, Paula Geiselman k,l, Donald A. Williamson m

a Pennington Biomedical Research Center, Baton Rouge, LA, United States
b Department of Neurology, Louisiana State University, United States
c Department of Psychology, Louisiana State University, United States
d Institute on Aging, University of Florida, 238 E. University Blvd, Gainesville, FL 32611, United States

A B S T R A C T

Consumption of sugar-sweetened beverages may be one of the dietary causes of metabolic disorders, such as obesity. Therefore, substituting sugar with low calorie sweeteners may be an efficacious weight management strategy. We tested the effect of preloads containing stevia, aspartame, or sucrose on food intake, satiety, and postprandial glucose and insulin levels. Design: 19 healthy lean (BMI = 20.0–24.9) and 12 obese (BMI = 30.0–39.9) individuals 18–50 years old completed three separate food test days during which they received preloads containing stevia (290 kcal), aspartame (290 kcal), or sucrose (493 kcal) before the lunch and dinner meal. The preload order was balanced, and food intake (kcal) was directly calculated. Hunger and satiety levels were reported before and after meals, and every hour throughout the afternoon. Participants provided blood samples immediately before and 20 min after the lunch preload. Despite the caloric difference in preloads (290 kcal vs. 493 kcal), participants did not compensate by eating more at their lunch and dinner meals when they consumed stevia and aspartame versus sucrose in preloads (mean differences in food intake over entire day between sucrose and stevia = 301 kcal, p < .01; aspartame = 330 kcal, p < .01). Self-reported hunger and satiety levels did not differ by condition. Stevia preloads significantly reduced postprandial glucose levels compared to sucrose preloads (p < .01), and postprandial insulin levels compared to both aspartame and sucrose preloads (p < .05). When consuming stevia and aspartame preloads, participants did not compensate by eating more at either their lunch or dinner meal and reported similar levels of satiety compared to when they consumed the higher calorie sucrose preload.

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Fig. 2. Changes in postprandial glucose levels for each condition. *Significant difference between stevia and sucrose conditions. †Significant difference between stevia and aspartame conditions.
Fig. 3. Changes in postprandial insulin levels for each condition. *Significant difference between stevia and sucrose conditions. †Significant difference between stevia and aspartame conditions. ‡Significant difference between aspartame and sucrose conditions.

?? why is the insulin level so high?
At 60 min post-lunch, there was a significant difference in the insulinogenic index, the ratio obtained by dividing increments of plasma insulin levels above fasting values by the relative net increase of plasma glucose levels (i.e., Δ insulin/Δ glucose at 30 min), between the aspartame and sucrose conditions ($p < .05$; see Fig. 4).
Compare the effects of NNS in solid vs beverages → cephalic phase response
The cephalic phase insulin response to nutritive and low-calorie sweeteners in solid and beverage form

Jaapna Dhillon, Janice Y. Lee, Richard D. Mattes*

Department of Nutrition Science, Purdue University, 226 Stone Hall, 700 W State Street, West Lafayette 47907, IN, USA

The purpose of the study was to examine the role of the cephalic phase insulin response (CPIR) following exposure to nutritive and low-calorie sweeteners in solid and beverage form in overweight and obese adults. In addition, the role of learning on the CPIR to nutritive and low-calorie sweetener exposure was tested.


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• Sucralose exposure elicited cephalic phase insulin response (CPIR) in responders.

• Both sucrose and sucralose elicited the same magnitude of CPIR in responders.

• The solid food form elicited a greater CPIR compared to the beverage form.
Is the taste receptor expressed in other areas of the body? [extragustatory areas?]
The sweet taste receptor is composed of two subunits, T1R2 and T1R3. The two subunits belong to the class C GPCRs. T1R2 and T1R3 possess a large aminoterminal domain (ATD) that includes a Venus flytrap domain (VFT) connected to a helical transmembrane domain (TMD) (characteristic of GPCRs) by a short cysteine-rich domain (CRD). The VFT is composed of two lobes separated by a large cleft, in which most sweeteners bind.

Functional roles of the sweet taste receptor in oral and extraoral tissues

Anni Laffitte, Fabrice Neiers, and Loïc Briand

Summary
The perception of sweet taste is mediated by the T1R2/T1R3 receptor, which is expressed in the oral cavity, wherein it provides input on the caloric and macronutrient contents of ingested food. This receptor recognizes all the chemically diverse compounds perceived as sweet by human beings, including natural sugars and sweeteners. Importantly, the expression of a functional sweet taste receptor has been reported in numerous extragustatory tissues, wherein it has been proposed to regulate metabolic processes. This newly recognized role of the sweet taste receptor makes this receptor a potential novel therapeutic target for the treatment of obesity and related metabolic dysfunctions, such as diabetes and hyperlipidemia.

Recent findings suggest that the sweet taste receptor T1R2/T1R3, which is expressed in many extraoral tissues, such as the intestine and pancreas, plays important roles in nutrient sensing and regulating metabolic processes that involve insulin secretion.

The sweet taste receptor is also found in tissues wherein its function appears less obvious, such as the brain, colon, bladder, lymphocytes, and heart. It would thus be interesting to study the physiological functions of the receptor in these tissues and to determine its impacts in human health and disease.

New information on polymorphisms in the human T1R2 and T1R3 genes and in α-gustducin has generated questions regarding whether these genetic variations play a role in individual differences in predisposition to metabolic diseases, such as type 2 diabetes and obesity. Further research will be necessary to clarify this issue.

Specialized endocrine cells of the small intestine, known as enteroendocrine cells, display T2R bitter receptors on their cell membranes. When bitter compounds bind to the T2R receptors, the cells release the peptide hormone cholecystokinin (CCK), which acts on CCK2 receptors located on enterocytes, or intestinal absorptive cells. This increases the expression of the transporter ABCB1, which pumps toxins or unwanted substances out of the cell and back into the intestinal lumen. CCK also binds to CCK1 receptors on sensory fibers of the vagus nerve, sending signals to the brain to cease food intake.
T1R-class receptors on enteroendocrine cells lining the small intestine detect sweet substances and respond by secreting the glucagon-like peptide GLP-1. GLP-1 then travels to the pancreas via the bloodstream, where it boosts the release of insulin from pancreatic β-cells, promoting the uptake of glucose by diverse tissues. Additionally, GLP-1 diffuses to neighboring enterocyte cells in the small intestine, driving the insertion of the glucose transporters SGLT-1 and GLUT2, which facilitates the uptake of glucose from the intestines.
In the colon, bitter ligands bind to T2R receptors on epithelial cells, where they induce the secretion of anions and water, which leads to fluid rushing into the intestine, resulting in diarrhea that flushes out the colon.
OH NO! Diet Coke has an insulin response!!

thank you for a great quarter!!
See you tomorrow & at the final!

our party 🎉 @ 11:30 Thurs.