Oral Digestion Contributes to the Hedonic Appeal of Sugar in Mice

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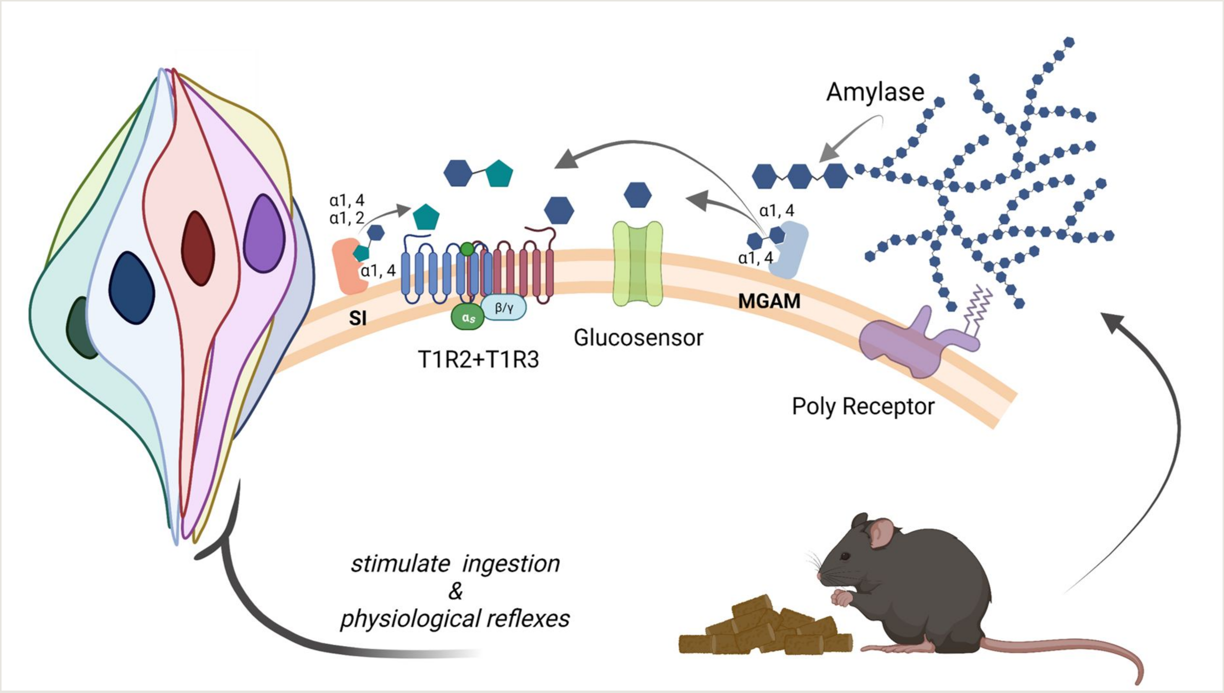
Introduction

- Previous research from our lab showed that sugar-experienced mice lacking a key channel for "sweet" taste transduction (TRPM5-) and their wild type counterparts (TRPM5+) lick more avidly for glucose and maltose than naïve C57BL6/J (B6) mice.[1]
- In sweet sensitive B6 mice, the acquired preference for glucose taste is abolished after glucokinase (GCK) has been virogenetically knockdown (KD).[2] However, whether this same mechanism contributes to the preference of maltose in mice is unknown.
- In the taste cells, α-glucosidases (enzyme which cleave complex sugars to monosaccharides) are expressed.[3] Therefore, we hypothesized that the digestive enzyme, maltase glucoamylase (MGAM) rapidly cleaves maltose to free glucose, which effectively generate more ligands nearby glucosensors.



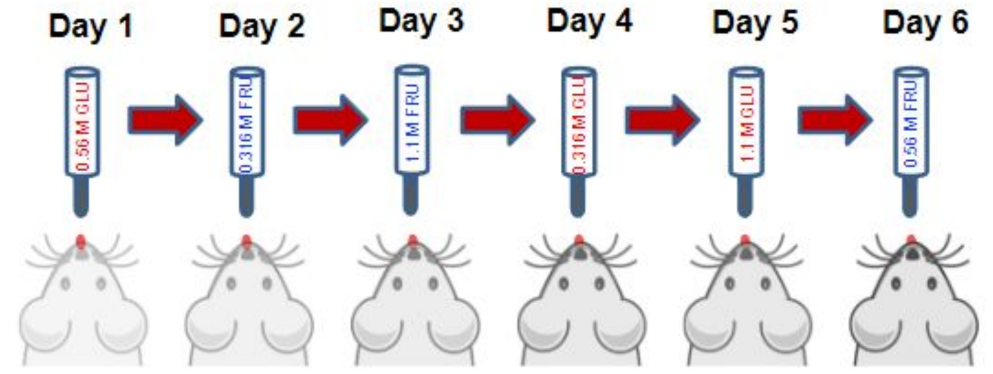
In this experiment, we aim to investigate whether two enzymes involved in glucose assimilation, glucokinase (GCK) and maltase-glucoamylase (MGAM), which are also localized in taste cells, are required to express a preference for the taste of maltose.

Methods

1. Do sweet sensitive and subsensitive mice express different levels of GCK and MGAM in the taste papillae?

Experimental Subjects and Procedures

Mouse♦	Sample size and Sex	Sugar Exposure Groups	
Subjects			
B6	16 Male	8 Sugar Naive	8 Sugar Exposed
TRPM5+	5 Male 5 Female	5 Sugar Naive	5 Sugar Exposed
TRPM5-	7 Male 6 Female	4 Sugar Naïve	9 Sugar Exposed
Procedures: Sugar exposure (vs naïve), Brief Access Test, Tissue Harvest, and **RT-qPCR●**			



Single Access Sugar Exposure

- 24-hour access sessions
- 1 solution/day for 18 days
- Randomized order
- Only source of fluid
- Food restricted to 85% body mass

Naïve mice were food restricted to 85% body mass and had water as their fluid source.

2. Does reduced GCK in the taste fields reduce the appeal of maltose compared to sucrose?

Experimental Subjects and Procedures

Mouse♦	Sample size and Sex	Sugar Exposure	Condition
Subjects			
TRPM5+	4 Males 7 Females	Sugar Exposed	shRNA Scramble
TRPM5+	7 Males 5 Females	Sugar Exposed	shRNA GCK KD
Procedures: Sugar Exposure, Glucose versus Fructose Brief Access Test, GCK (vs scramble) KD, **Maltose vs Sucrose Brief Access test,** Tissue Harvest, RT-qPCR.			

Post-KD Test	Stimuli	Parameters
Maltose versus Sucrose Brief Access Test°	0.316 M, 0.56 M, 1.1. M maltose 0.316 M, 0.56 M, 1.1 M sucrose, dH_2O	20-minute test Serial 10-s trials Stimulus order randomized Food restricted to 85%

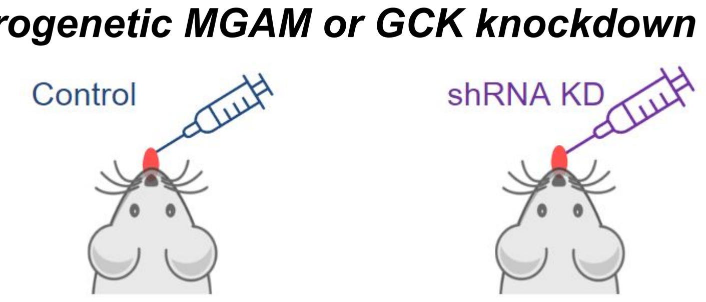
3. Does reduced MGAM in the taste fields reduce the appeal of maltose compared to sucrose?

Experimental Subjects and Procedures

Mouse♦	Sample Size and Sex	Sugar Exposure	Condition
Subjects			
TRPM5+	5 Males 5 Females	Sugar Exposed	shRNA Scramble
TRPM5+	5 Males 5 Females	Sugar Exposed	shRNA MGAM KD
Procedures: Sugar Exposure, Glucose versus Fructose Brief Access Test, MGAM (vs scramble) KD, **Maltose vs Sucrose Brief Access test,** Tissue Harvest, RT-qPCR			

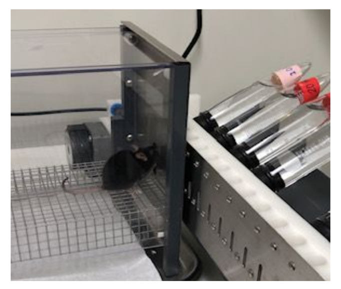
Test	Stimuli	Parameters
Maltose versus Sucrose Brief Access Test°	0.316 M, 0.56 M, 1.1. M maltose 0.316 M, 0.56 M, 1.1 M sucrose, dH_2O	20-minute test Serial 10-s trials Stimulus order randomized Food restricted to 85% body mass

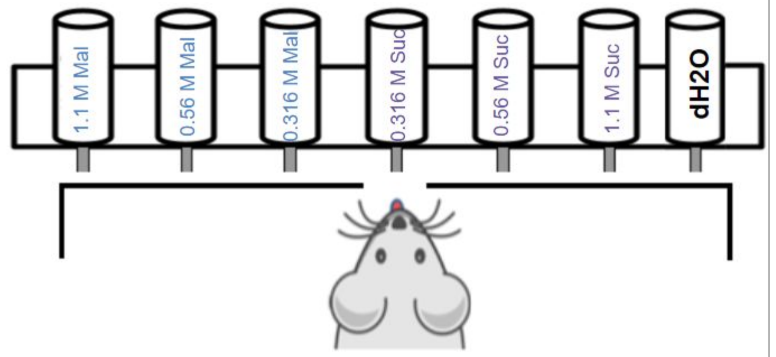
Virogenetic MGAM or GCK knockdown (KD)



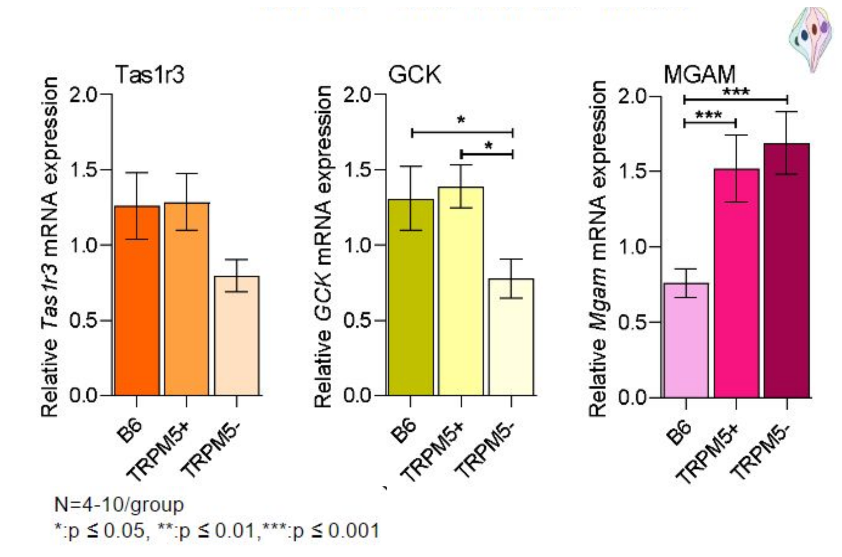
2 µl of vector was infused onto the fungiform and circumvallate taste papillae

Post-exposure Brief Access Taste Test

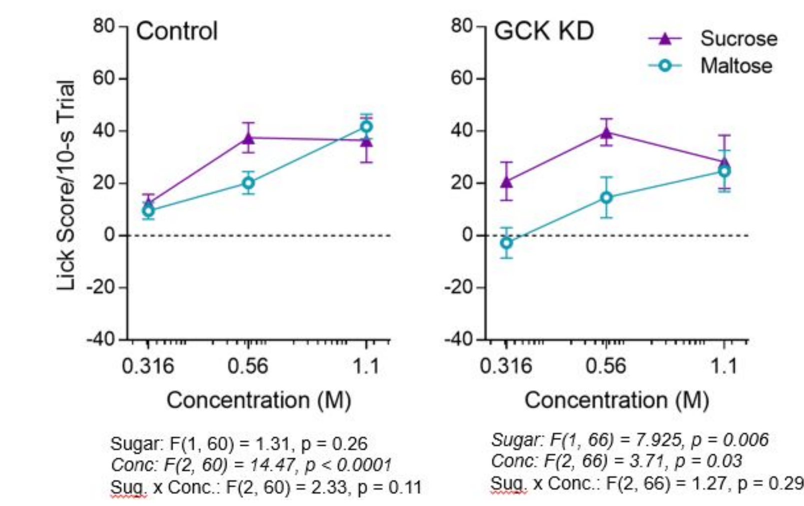




Results



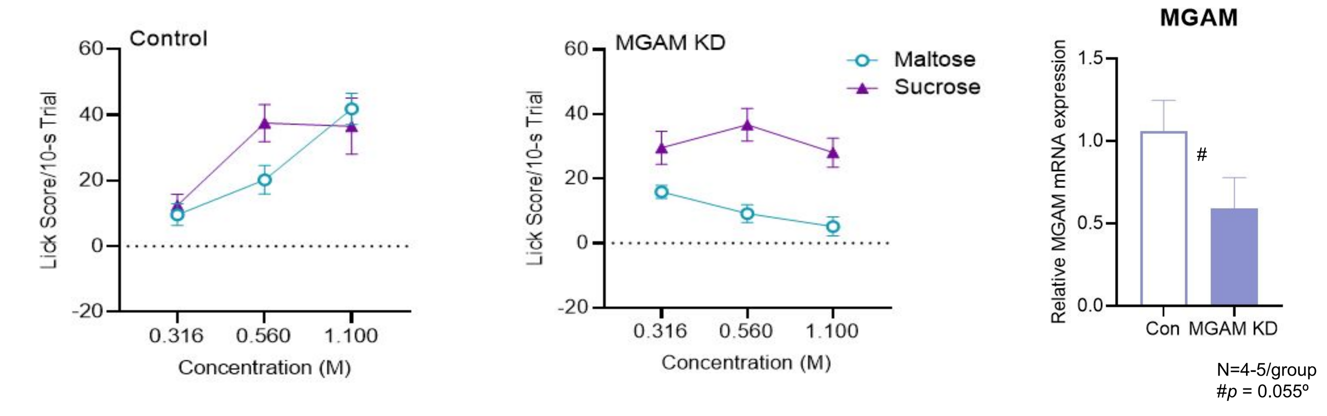
Sweet-sensitive (B6 and TRPM5+) mice have more GCK in the taste buds than do the sweet-subsensitive (TRPM5-) mice. Yet, B6 mice have less MGAM in the taste buds than TRPM5+ and TRPM5- mice.



Sweet-sensitive (TRPM5+) mice with deficient lingual GCK lick significantly less for maltose than sucrose in a brief access taste test.

Expected Results

Sweet-sensitive (TRPM5+) mice with deficient lingual MGAM will lick less for maltose than sucrose in a brief access taste test.



Hypothetical Data

°one-sample, one-tailed t-test

Discussion

- Sweet-subsensitive mice (TRPM5-deficient) have diminished sweet receptor gene expression (Tas1r3) or GCK in the taste papillae coupled with greater expression of a gene that encodes for the main enzyme involved in maltose digestion (Mgam). Sweet-sensitive B6 mice, on the other hand, express less peri-taste Mgam.
- Knockdown of GCK in the major taste fields decreases the hedonic appeal of maltose in sugar-exposed sweet-sensitive mice.
- These findings raise the interesting possibility that sweet-subsensitive mice have an increased capacity to rapidly digest complex saccharides, effectively generating more ligands to engage diffuse sweet receptors and/or glucosensors at the level of the taste bud.
- Knockdown of MGAM in the major taste fields *is predicted* to reduce licking avidity for maltose in sugar exposed TRPM5+ sweet-sensitive mice.
- The results will provide the first evidence that two key metabolic enzymes (glucokinase and maltase-glucoamylase) act within the taste buds to bolster signals that drive complex sugar ingestion.

References & Acknowledgement

1.Gutierrez V, *Nutritional Neuroscience*, 2022.
2.Chometton S et al. Molecular Metabolism, 2022.
3.Sukumaran et al, *Proc Natl Acad Sci,* 113, 6035-40, 2016.

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