

Original Article

# Psychophysical Evaluation of Sweetness Functions Across Multiple Sweeteners

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## Abstract

Sweetness is one of the 5 prototypical tastes and is activated by sugars and non-nutritive sweeteners (NNS). The aim of this study was to investigate measures of sweet taste function [detection threshold (DT), recognition threshold (RT), and suprathreshold intensity ratings] across multiple sweeteners. Sixty participants, 18–52 years of age (mean age in years = 26, SD = ±7.8), were recruited to participate in the study. DT and RT were collected for caloric sweeteners (glucose, fructose, sucrose, erythritol) and NNS (sucralose, rebaudioside A). Sweetness intensity for all sweeteners was measured using a general Labeled Magnitude Scale. There were strong correlations between DT and RT of all 4 caloric sweeteners across people ( $r = 0.62–0.90$ ,  $P < 0.001$ ), and moderate correlations between DT and RT for both of the NNS ( $r = 0.39–0.48$ ,  $P < 0.05$ ); however, weaker correlations were observed between the DT or RT of the caloric sweeteners and NNS ( $r = 0.26–0.48$ ,  $P < 0.05$ ). The DT and RT of glucose and fructose were not correlated with DT or RT of sucralose ( $P > 0.05$ ). In contrast, there were strong correlations between the sweetness intensity ratings of all sweeteners ( $r = 0.70–0.96$ ,  $P < 0.001$ ). This suggests those caloric sweeteners and NNS access at least partially independent mechanisms with respect to DT and RT measures. At suprathreshold level, however, the strong correlation between caloric sweeteners and NNS through weak, moderate, and strong intensity indicates a commonality in sweet taste mechanism for the perceived intensity range.

**Key words:** detection thresholds, recognition thresholds, suprathresholds, sweet taste, sweet taste intensity, sweetener

## Introduction

A range of sweetness intensities can be experienced when sweet-tasting compounds activate sweet taste receptor cells in areas of the tongue, soft palate, and oropharyngeal region of the oral cavity (Breslin and Spector 2008). For instance, when 1 mM sucrose is dissolved in water, an individual may find it challenging to differentiate the sucrose-containing solution from plain water. However, as the concentration of sucrose is increased, differentiation becomes

possible (Bartoshuk 1978; Keast and Roper 2007; Webb et al. 2015). The lowest concentration level at which a difference can be detected is termed the sucrose detection threshold (DT). At this concentration level, the individual cannot accurately identify the sucrose solution as sweet, and only when the concentration of sucrose is further increased does the sweet taste quality become apparent (Amerine et al. 1965). The lowest concentration at which this occurs is termed the sucrose recognition threshold (RT) (Amerine et al. 1965; Snyder

et al. 2006; Keast and Roper 2007). As sucrose is progressively added beyond this point, the perceived sweetness will range from just perceivable to strong, until it reaches the individual's terminal threshold for sucrose, beyond which any increase in concentration no longer causes consequential increase in perceived sweetness intensity (Paulus and Reisch 1980; Bartoshuk et al. 2006; Keast and Roper 2007). Perceived sweetness above the RT is defined as the suprathreshold intensity perception range (Bartoshuk 1978; Bartoshuk et al. 2006).

Theoretically, it seems reasonable to expect that an individual's sweetness DT, RT, and suprathreshold intensity perception might be interrelated (Bartoshuk 1978, 2000; Bartoshuk et al. 2006; Keast and Roper 2007; Wise and Breslin 2013). An example of this hypothetical model was observed from a bitter compound, 6-*n*-Propylthiouracil (PROP). For example, an individual who is able to detect and/or recognize bitterness from PROP at a lower concentration level may, when tasting a concentrated PROP solution, be more likely to experience greater bitterness intensity than another individual with a higher bitterness DT for PROP (i.e., strong negative correlation between DT and suprathreshold intensity for PROP) (Keast and Roper 2007; Hayes et al. 2008). This, however, has not been confirmed for sweet compounds (Faurion 1987; Webb et al. 2015).

Previous human psychophysical studies have consistently found large individual variation in the capability to perceive sweet taste from sucrose (Fontvieille et al. 1989; Faurion 1993; Kennedy et al. 1997; Hayes and Duffy 2007; Lim et al. 2008; Yoshiko and Roswith 2012; Cicerale et al. 2012; Webb et al. 2015) and/or a range of sweeteners (Eylamb and Kennedy 1998; Schiffman et al. 1981; Schiffman et al. 1995). Such individual variation may be due to differences in human physiology [e.g., variation in the human TAS1R2 gene (Kim et al. 2006)] or cognitive functioning when perceiving a sweet stimulus (Webb et al. 2015). Most human psychophysical studies investigating sweet taste, however, have employed only one measure of taste function to measure sweet taste. As each measure of sweet taste function represents a different dimension of the sense of taste, there is currently no single method to measure taste function in totality (Webb et al. 2015). Although the transduction mechanisms of sweet taste (Liman et al. 2014) and the perceptual relationships between caloric and non-nutritive sweeteners (NNS) (Antenucci and Hayes 2015) have been reported, collecting a range of psychophysical measures across multiple sweeteners within a single group of individual allows direct comparison that cannot be made across prior studies. In this study, therefore, the aim was to investigate the 3 main measures of sweet taste function—DT, RT, and suprathreshold intensity—across a range of caloric and NNS.

## Materials and methods

### Study design

This study comprised 3 measures of taste perception routinely used in chemosensory research: 1) DT, 2) RT, and 3) suprathreshold intensity. These measures were determined for all participants for each of 6 sweeteners and prototypical stimuli for salty, sour, bitter, and umami during a total of 16 sessions (2 sessions per day separated by a minimum of 1 h for 8 non-consecutive days). All measurements were collected in duplicate. If there were more than 3 concentration steps between the duplicate measures, participants attended another session to complete the assessment. DT, RT, and suprathreshold intensity tasks were conducted in computerized, partitioned sensory booths in the Centre for Advanced Sensory Science using Compusense Five Software Version 5.2 (Compusense Inc., Ontario, Canada). Filtered deionized water was used as an oral rinsing agent.

Participants were instructed to rinse their mouths with filtered deionized water for 5 s before beginning each task and between each sample set. To eliminate any visual and olfactory input, all testing sessions were conducted under red lighting, and participants were asked to wear nose clips during testing. All solutions were served at room temperature, with a 3-digit code allocated to each sample.

### Participants

Sixty participants (28 males), 18–52 years of age (mean age in years = 26, SD =  $\pm 7.8$ ), were recruited from locations adjacent to the Deakin University, Melbourne campus, Australia. Potential participants were excluded if they: 1) smoked; 2) were pregnant or lactating; 3) were taking any prescription medication that may interfere with their ability to taste; or 4) had a history of food allergies that may interfere with the study. Participants were asked to refrain from eating, drinking (except room temperature water), brushing their teeth, and chewing gum for 1 h prior to testing. All participants gave written informed consent and were compensated for their participation. This study was approved by the institutional review board regulations of Deakin University (DUREC 2013–156). The experimental protocol was also registered under the Australian New Zealand Clinical Trials Registry (ACTRN12613000701729), [www.anzctr.org.au](http://www.anzctr.org.au). This study also complies with the Declaration of Helsinki for Medical Research involving Human Subjects.

### Participant training

Prior to using the general Labeled Magnitude Scale (gLMS) to rate taste intensity, participants were trained using the standard protocol outlined by Green et al. (1993, 1996) except the top of the scale was described as the strongest imaginable sensation of any kind (Bartoshuk 2000). The 100-point scale comprised the following adjectives: “no sensation” = 0, “barely detectable” = 1.5, “weak” = 6, “moderate” = 17, “strong” = 35, “very strong” = 52, and “strongest imaginable” = 100 (Bartoshuk 2000). Only scales with adjectives were presented to participants (no equivalent numbers, although numerical data were extracted from the scale for data analysis) (Webb et al. 2015). During the training session, participants were asked to rate the intensity of the perceived sensation relative to a remembered or imagined sensation. Participants were required to rate a list of 7 remembered or imagined sensations, such as the warmth of lukewarm water, the pain from biting of the tongue, and the sweetness of fairy floss (known as cotton candy in the United States, or candy floss in the United Kingdom).

### Stimuli

Prototypical stimuli (sucrose, sodium chloride, citric acid, caffeine, and monosodium glutamate) were used to investigate taste function for the 5 basic tastes (for details of stimuli see Table 1). Both caloric (glucose, fructose, sucrose, erythritol) and NNS (sucralose, rebaudioside A) were used to investigate sweet taste (for details of stimuli see Table 2). On the morning of testing, solutions were prepared with filtered deionized water (Cuno Filter Systems F5117S) and stored in glass beakers at room temperature ( $20 \pm 1^\circ\text{C}$ ).

### Detection and RT determination for the 5 primary tastes

DT and RT were determined using the procedure outlined in the International Standards Organization (ISO) Method of Investigating Sensitivity of Taste (ISO3972 1991). Table 1 gives the 9 concentrations used for each taste quality (the ninth concentration being presented only when participants were unable to recognize the taste

**Table 1.** Stimulus concentrations used for prototypical threshold testing

Taste quality	Stimulus	Concentrations (mM)								
		1	2	3	4	5	6	7	8	9
Sweet	Sucrose	1.0	1.6	2.7	4.5	7.5	12.6	21.0	35.0	70.0
Salty	Sodium chloride	2.7	4.1	5.8	8.2	11.8	16.8	24.0	34.2	68.0
Sour	Citric acid	0.7	0.8	1.0	1.3	1.6	2.0	2.5	3.1	6.2
Bitter	Caffeine	0.3	0.4	0.5	0.6	0.7	0.9	1.1	1.4	2.8
Umami	Monosodium glutamate	0.5	0.7	1.0	1.4	2.0	2.9	4.1	5.9	12.0

The concentration series were adapted from ISO3972 (1991). Reference chemical details: sucrose (CSR); sodium chloride (Saxa, Premier Foods Inc); caffeine (Sigma Aldrich); citric acid (Ward McKenzie Private Limited); and monosodium glutamate (Ajinomoto Cooperation).

**Table 2.** Sweetener concentrations used for determination of detection and recognition thresholds

Sweetener	Concentration (mM)											
	1	2	3	4	5	6	7	8	9	10	11	12
Glucose monohydrate	1.0	1.6	2.7	4.5	7.4	12.1	20.0	33.0	54.5	89.9	148.3	244.7
Fructose	0.6	1.0	1.6	2.6	4.4	7.2	11.8	19.6	32.3	53.4	88.1	145.4
Sucrose	0.4	0.6	1.0	1.6	2.7	4.5	7.5	12.6	21.0	35.0	57.8	95.4
Sucralose	0.0005	0.0008	0.0014	0.0023	0.0038	0.0063	0.010	0.017	0.03	0.05	0.08	0.13
Rebaudioside A	0.001	0.002	0.003	0.004	0.007	0.012	0.02	0.03	0.05	0.09	0.15	0.25
Erythritol	1.5	2.4	4.0	6.6	10.9	18.0	29.6	48.9	80.7	133.0	220.0	363.0

The concentration series for sucrose was adapted from ISO3972 (1991). The concentration series for glucose monohydrate, fructose, sucralose, rebaudioside A, and erythritol were prepared in successive 0.25 log dilution steps. Reference chemical details: glucose monohydrate (The Melbourne Food Depot); fructose (The Melbourne Food Depot); sucrose (CSR); sucralose (The Melbourne Food Depot); rebaudioside A (AuSweet); and erythritol (AuSweet).

quality in the previous 8) (ISO3972 1991). The 8 samples from each taste quality were served in ascending concentration (15 mL per sample, in accordance with the standard ISO method), and each taste quality was presented to participants independently. Participants were unaware of the presentation order but were informed of the possible taste qualities. Participants were instructed to taste each sample for 5 s then expectorate and record whether: there was an absence of taste (water-like); a taste was identified but not recognized; or a taste quality was perceived (ISO3972 1991). DT was defined as the concentration at which the participants selected the “taste identified, but unknown taste quality” response (ISO3972 1991). RT was defined as the concentration at which they were able to recognize the correct taste quality twice consecutively (Webb et al. 2015).

### Detection and RT determination for sweet taste

Detailed in Table 2 are the concentration ranges used to assess DT and RT for sweet taste. The concentration series for sucrose was adapted from ISO3972 (1991); concentrations for the remaining sweeteners were prepared with successive 0.25 log dilution steps. Initial starting concentrations were determined through informal bench-top testing, based on modified findings of matching sweetness intensity ratios published by Keast et al. (2004). DTs for each of the sweeteners were determined using ascending series 3-Alternate Forced Choice methodology (Meilgaard et al. 2006; Stewart et al. 2010), in which the participants were provided with three 25 mL samples, 2 of which were controls (filtered deionized water) and one containing sweetener, in ascending order from the lowest to the highest concentration. DT was defined as the concentration of sweetener required for a participant to correctly identify the sweetened sample as the odd 1 out in 3 consecutive sample sets at one concentration level (Meilgaard et al. 2006). The RTs for each of the sweeteners

were measured using a whole-mouth, sip-and-spit procedure (Wise and Breslin 2013). Each participant received a single 15 mL sample, presented in a medicine cup, in ascending order starting from his or her DT concentration level. Participants were asked to identify the quality of the taste after holding the sample in their mouth for at least 5 s. Response options included “sweet”, “sour”, “bitter”, “salty”, “umami”, or “unknown taste”. Participants tasted each sample once, in ascending concentration order, until they identified the target taste quality “sweet” for all of the sweeteners (Wise and Breslin 2013). RT was defined as the concentration at which they were able to recognize the correct taste quality 3 times consecutively. To prevent participants from learning the purpose of the task, they were told that the purpose of this experiment was to investigate if they were able to detect any other potential taste qualities before the final “sweet” perception. They were also given examples of how some people were able to detect other taste qualities such as bitterness when tasting NNS. We found that this strategy encouraged participants to attempt recognition (not only sweet) prior to concentrations associated with probabilistic recognition (i.e., the concentrations at which participants were able to recognize quality imperfectly at above chance level) (Wise and Breslin 2013). At the end of the final visit, participants were debriefed about the experiment, and none was aware that the purpose of this task was a sham.

### Suprathreshold intensity ratings for the 5 prototypical tastes and sweeteners

Three concentrations (weak, medium, and strong) were prepared to determine perceived suprathreshold intensity for each prototypical tastant (Table 3) and sweetener (Table 4). These concentrations were derived through informal bench-top testing (ascending taste intensity) and were similar to the concentrations outlined by Webb et al. (2015). The concentrations for each prototypical stimulus ranged

**Table 3.** Concentrations of prototypical tastants used for determination of suprathreshold taste intensity

Taste quality	Stimulus	Concentration (mM)		
		Weak	Medium	Strong
Sweet	Sucrose	100	200	400
Salty	Sodium chloride	100	200	400
Sour	Citric acid	1.0	3.0	7.0
Bitter	Caffeine	1.0	2.0	4.0
Umami	Monosodium glutamate	3.0	6.0	12.0

The concentration series were adapted from Webb *et al.* (2015).

**Table 4.** Concentrations of sweeteners used for determination of suprathreshold taste intensity

Sweetener	Concentration (mM)		
	Weak	Medium	Strong
Glucose monohydrate	240	480	960
Fructose	140	280	560
Sucrose	100	200	400
Sucralose	0.14	0.28	0.56
Rebaudioside A	0.27	0.54	1.08
Erythritol	400	800	1600

from “weak” to “strong” on the gLMS. These samples were presented to participants in randomized order.

### Standardization of gLMS usage with weight ratings

To standardize gLMS usage within participants, a modified version of Delwiche *et al.* (2001) was adapted for this study. To control for idiosyncratic scale usage, participants were asked to rate the heaviness of 6, visually identical weights (opaque bottles filled with sand and stone and completely wrapped in aluminium foil; weights of 53, 251, 499, 724, 897, and 1127 g). Participants were asked to hold out their non-dominant hand palm up, whereas the experimenter placed the weighted bottle on the palm of the hand. Participants were instructed to rate the heaviness of each weight using the gLMS.

There was a significant correlation between the overall mean prototypical ratings and overall mean heaviness ratings ( $r = 0.28$ ,  $P < 0.05$ ). Assuming that the intensity ratings of prototypical tastants and the heaviness of the bottles were unrelated, the significant correlation indicates that the gLMS ratings were subject to differences in individual scale-use and thus require standardization across participants (Delwiche *et al.* 2001; Keast and Roper 2007; Webb *et al.* 2015). To determine a personal standardization factor, the grand mean for heaviness across weight levels and participants was divided by each participant's average intensity for heaviness (Keast and Roper 2007). Each individual's prototypical taste intensity and sweetness intensity ratings were multiplied by his or her personal standardization factor for scale-use bias (Delwiche *et al.* 2001; Keast and Roper 2007).

### Statistical analysis

Statistical analysis was performed using IBM SPSS statistical software version 23.0 (SPSS). Data are presented as means with standard errors of mean (SEM). For suprathreshold intensity ratings, the geometric mean score of the 3 ratings (weak, moderate, and strong) was calculated. Spearman's rank correlation coefficient was calculated between distinct measures of taste function.

As noted earlier, if the measures of taste function are interrelated, then participants who are less sensitive to the sweet compounds tested should have higher detection and RTs and lower sweetness intensity ratings than the more sensitive participants (who should have lower detection and RTs and higher sweetness intensity ratings). That is, the correlation between the threshold measures (DT and RT) and suprathreshold intensity should be negative. In order to simplify the data presentation, negative  $r$ -values were converted to positive and vice versa. The criterion for statistical significance was set at  $P < 0.05$ .

## Results

### Detection and RTs of sweeteners

Mean ( $\pm$ SEM) DT and RT values for the sweeteners are presented in Table 5. There was large individual variation among the participants; for example, DT for glucose ranged from 1.0 to 89.9 mM, whereas the RT for glucose ranged from 2.7 to 148.3 mM (Figure 1a).

The DTs of caloric sweeteners (glucose, fructose, sucrose, and erythritol) were strongly correlated with one another ( $r = 0.82$ – $0.90$ ,  $P < 0.001$ ; Figure 2). However, there were only moderate correlations between the DT of the caloric sweeteners and NNS ( $r = 0.34$ – $0.48$ ,  $P < 0.001$ ), except between the DT of 2 of the caloric sweeteners (glucose, fructose) and NNS (sucralose) where no correlations were observed ( $P > 0.05$ ).

Similarly, there were strong correlations between participants' RTs for all caloric sweeteners ( $r = 0.62$ – $0.84$ ,  $P < 0.001$ ; Figure 3). The RT for sucralose was moderately correlated with sucrose ( $r = 0.32$ ,  $P < 0.05$ ), but not with other caloric sweeteners (all  $P > 0.05$ ). RT for rebaudioside A was moderately correlated with glucose, fructose, and sucrose ( $r = 0.26$ – $0.30$ ,  $P < 0.05$ ), but not with erythritol ( $P > 0.05$ ). Moreover, the RTs for the NNS, sucralose, and rebaudioside A, were moderately correlated with each other ( $r = 0.39$ ,  $P < 0.01$ ).

### Suprathreshold intensities for sweeteners

Figure 4 shows the psychophysical functions for all sweeteners. As expected there were monotonic increases in perceived intensity as the concentration of the stimuli was increased. Spearman's rank correlation revealed a significant relationship between the sweetness ratings on a sweetener's psychophysical function: (glucose  $r = 0.79$ – $0.93$ ,  $P < 0.001$ ; fructose  $r = 0.67$ – $0.89$ ,  $P < 0.001$ ; sucrose  $r = 0.73$ – $0.94$ ,  $P < 0.001$ ; erythritol;  $r = 0.81$ – $0.91$ ,  $P < 0.001$ ; rebaudioside A;  $r = 0.55$ – $0.83$ ,  $P < 0.001$ ; sucralose;  $r = 0.64$ – $0.90$ ,  $P < 0.001$ ). Analysis of variance revealed significant differences between all incremental steps on the psychophysical functions ( $P < 0.05$ ). This indicates that when a participant is given increasing concentration of a sweetener (above the RT), there is an ordinal increase in sweetness intensity relative to intensity ratings across all participants. For each participant, there were strong correlations between the sweetness intensity of all sweeteners ( $r = 0.70$ – $0.95$ ,  $P < 0.001$ ; Figure 5).

### Relationships between sweet taste measures

Strong correlations between DT and RT were observed for all sweeteners ( $r = 0.58$ – $0.68$ ,  $P < 0.001$ ). However, no significant correlation was observed between sweetness intensity ratings and DT or RT for any of the sweeteners tested (all  $P$  values  $> 0.05$ ).

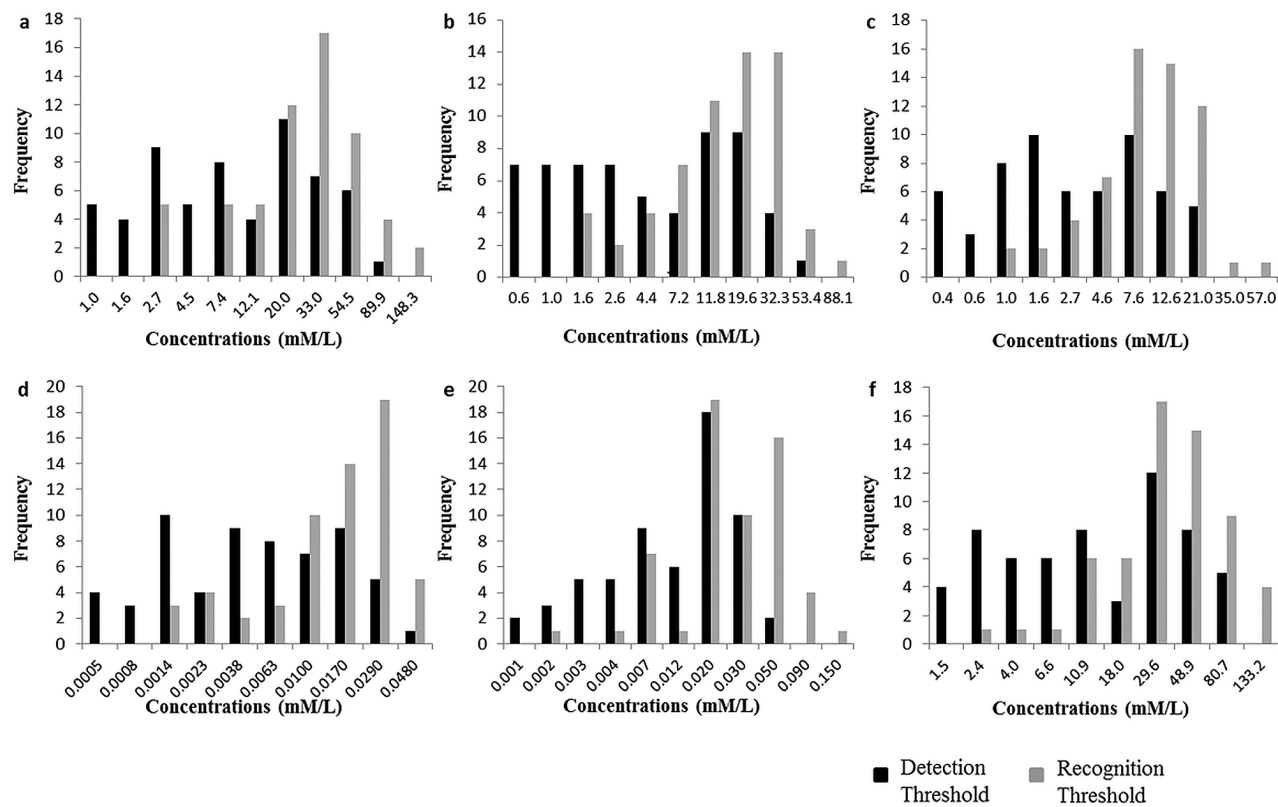
### Detection and RTs of prototypical tastants

DT and RT of the 5 prototypical tastes are presented in Table 6. DT of sweet, salty, and umami were strongly correlated with each other ( $r = 0.56$ – $0.89$ , all  $P$  values  $< 0.001$ ). However, DT of sour



**Table 5.** Detection and recognition thresholds for sweeteners (mM), including mean, standard error (SEM), and range

	Detection threshold		Recognition threshold	
	Mean ± SEM	Range	Mean ± SEM	Range
Glucose	17.2 ± 2.5	1.0–89.9	35.2 ± 4.0	2.7–148.3
Fructose	9.3 ± 1.4	0.6–53.4	19.7 ± 2.1	1.6–88.1
Sucrose	5.5 ± 0.8	0.4–21.0	11.7 ± 1.2	1.0–57.0
Sucralose	0.013 ± 0.002	0.0005–0.09	0.02 ± 0.002	0.0014–0.0048
Rebaudioside A	0.02 ± 0.002	0.001–0.05	0.03 ± 0.003	0.002–0.09
Erythritol	23.0 ± 3.0	1.5–80.7	44.7 ± 4.2	2.4–133.2



**Figure 1.** Frequency distributions of detection and recognition thresholds for: (a) glucose, (b) fructose, (c) sucrose, (d) sucralose, (e) Rebaudioside A, and (f) erythritol.

and bitter were not correlated with the other taste qualities ( $P$  values  $> 0.05$ ). RT of sour, sweet, umami, and salty were positively correlated with each other ( $r = 0.34$ – $0.79$ ,  $P < 0.05$ ). There were also strong correlations between sucrose DT and RT as obtained by the 3-Alternate Forced Choice method and the ISO method ( $r = 0.64$ – $0.66$ ,  $P < 0.001$ ).

**Suprathreshold intensities of prototypical tastants and relationship with detection and RTs**

As expected, there were monotonic increases in perceived intensity as the concentrations of stimuli were increased (Table 7). No correlations were observed between suprathreshold intensities and DT of sweet, salty, sour, and umami (all  $P > 0.05$ ). A correlation was observed for bitter ( $r = 0.52$ ,  $P < 0.01$ ). Similarly, no correlations were observed between suprathreshold intensities and RT of sweet, sour, and umami (all  $P > 0.05$ ). Correlations were observed for bitter and salty ( $r = 0.31$ – $0.48$ ,  $P < 0.05$ ).

**Relationships between sweet taste function and prototypical taste function**

Participants were stratified into tertile groups according to the sweeteners tested and all sweet taste measures. We observed that those who were able to detect sucrose in water at lower concentrations (lower tertile;  $n = 8$ ) were also more sensitive to all of the sweeteners tested. Interestingly, we also observed that 6 participants were more sensitive only towards caloric sweeteners but not to NNS (lower tertile). Similarly for RT, those who were able to recognize sweetness from sucrose at a lower concentration (lower tertile;  $n = 4$ ) were also able to recognize sweetness from all 6 sweeteners tested at lower concentration levels. When separated according to caloric sweeteners and NNS, 4 participants were more sensitive (lower tertile) to caloric sweeteners but not to NNS. In contrast, 3 participants were more sensitive (lower tertile) to NNS but not to caloric sweeteners. For sweetness intensity ratings, we observed that some participants experienced higher intensity (higher tertile;  $n = 9$ ).

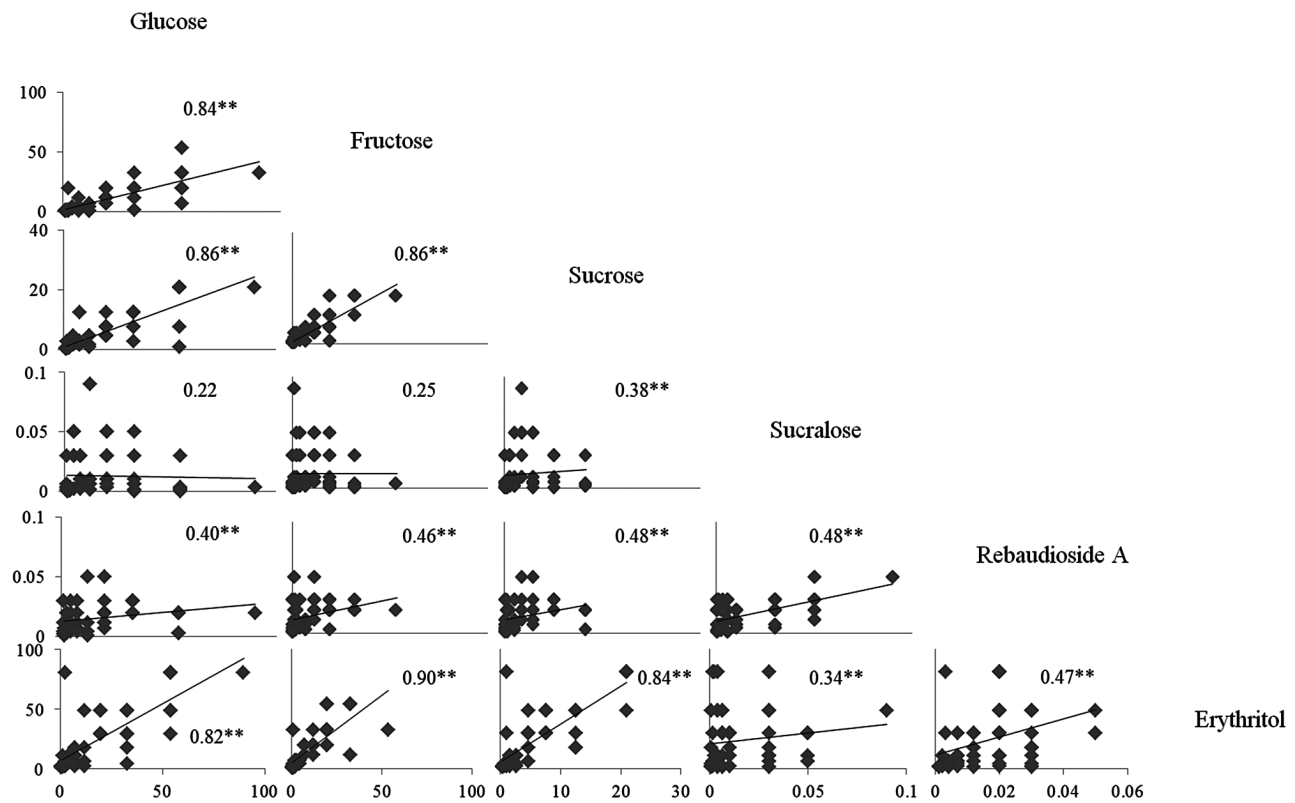


Figure 2. Scatter plot matrix and spearman rank correlations of DTs for sweeteners evaluated. \*\* $P < 0.01$ .

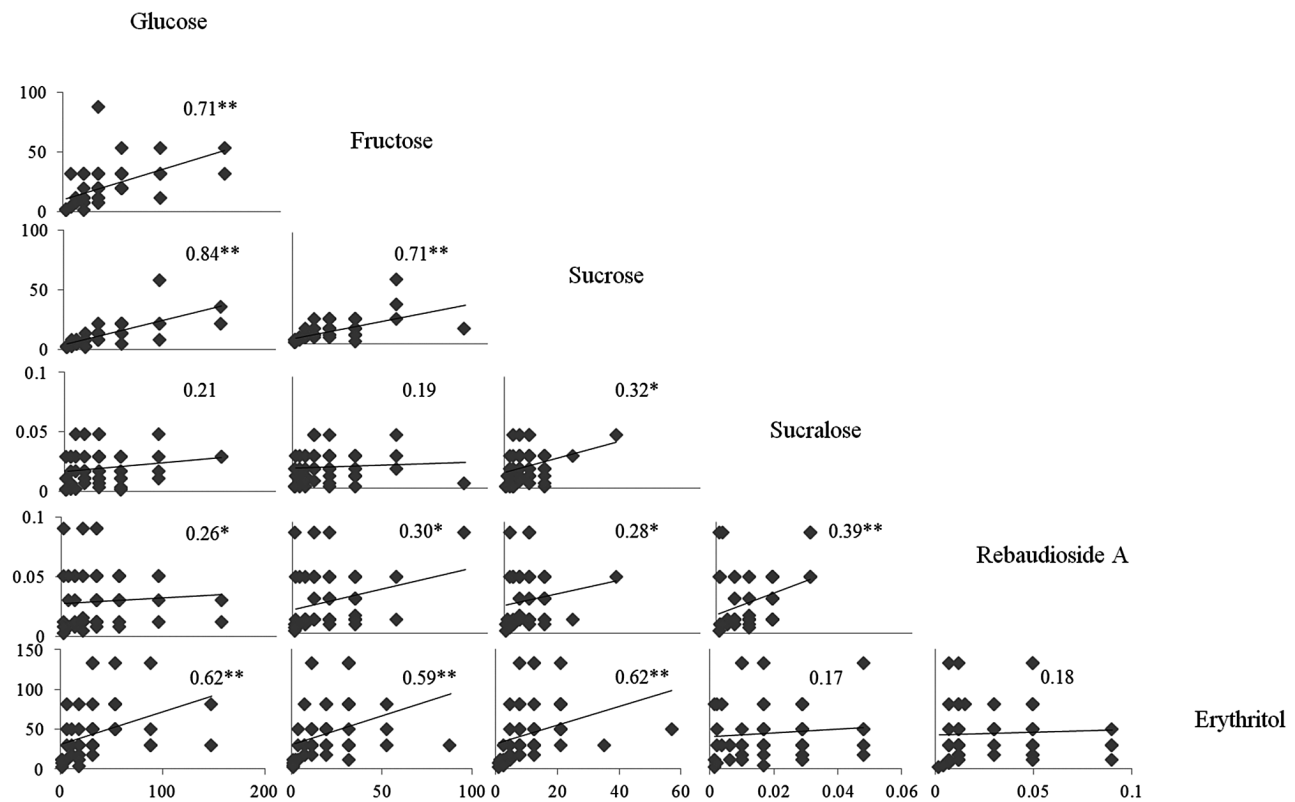
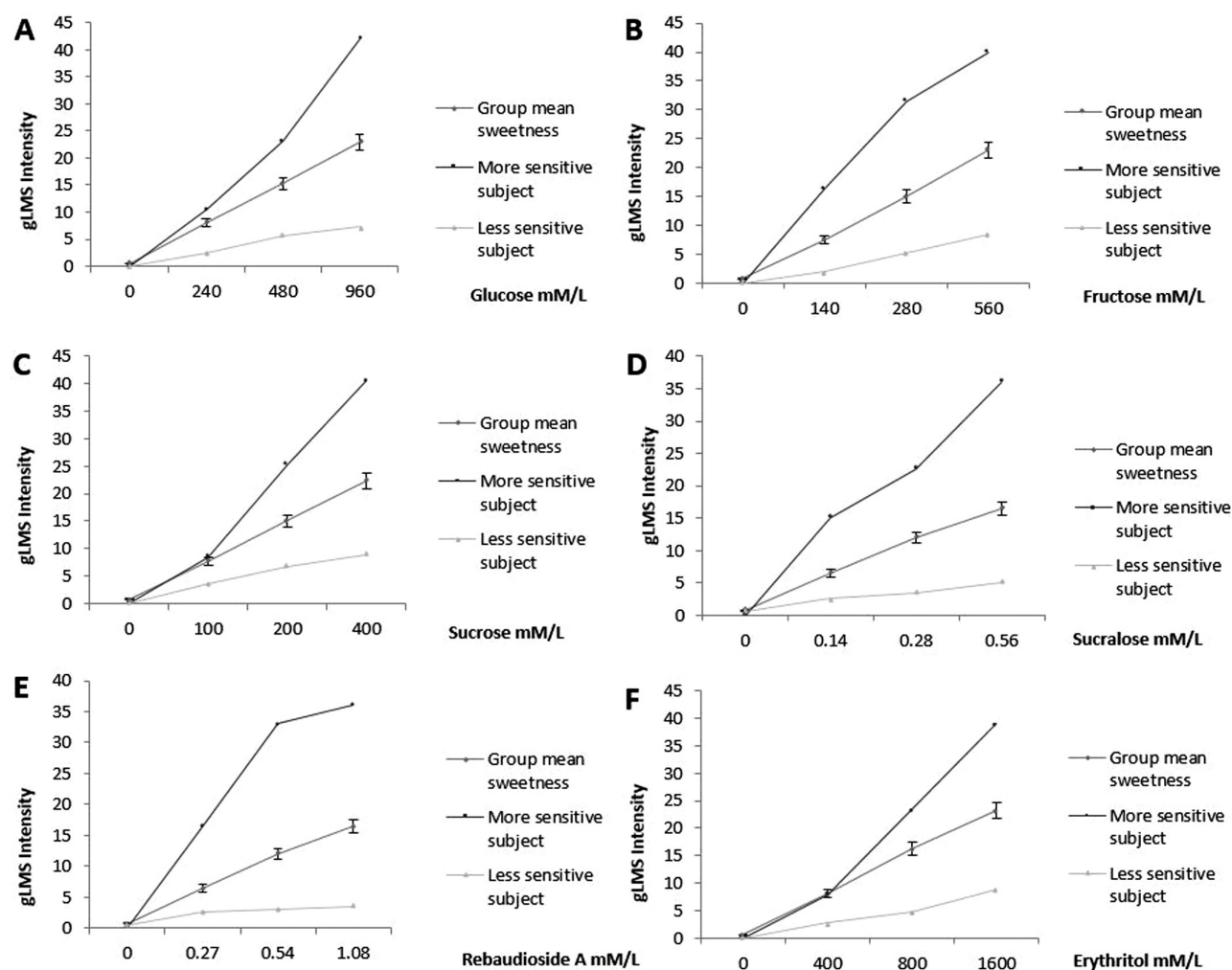


Figure 3. Scatter plot matrix and spearman rank correlations of recognition thresholds for sweeteners evaluated. \*  $P < 0.05$ , \*\*  $P < 0.01$ .



**Figure 4.** Mean psychophysical functions for suprathreshold taste intensity together with examples of more and less sensitive participants: (a) glucose, (b) fructose, (c) sucrose, (d) sucralose, (e) Rebaudioside A, and (f) erythritol.

or lower intensity (lower tertile;  $n = 14$ ) for all sweeteners measured. One participant was more sensitive to all sweeteners and across all sweet taste measures.

When participants were further stratified into tertile groups according to the prototypical tastes and all taste function measures, we observed that some were more sensitive or less sensitive towards all 5 prototypical tastes within a single taste measure [DTs either low (more sensitive;  $n = 4$ ) or high (less sensitive;  $n = 1$ ); RTs either low (more sensitive;  $n = 5$ ) or high (less sensitive;  $n = 4$ ); sweetness intensities either low (less sensitive;  $n = 5$ ) or high (more sensitive;  $n = 4$ )]. These findings refute the notion of generalized hypergeusia (Hayes and Keast 2011; Webb et al. 2015), and suggest there is a great deal of inter-individual variation both across and within measures of a quality. Of particular note, no participant was more sensitive or less sensitive to all taste qualities across all taste measures.

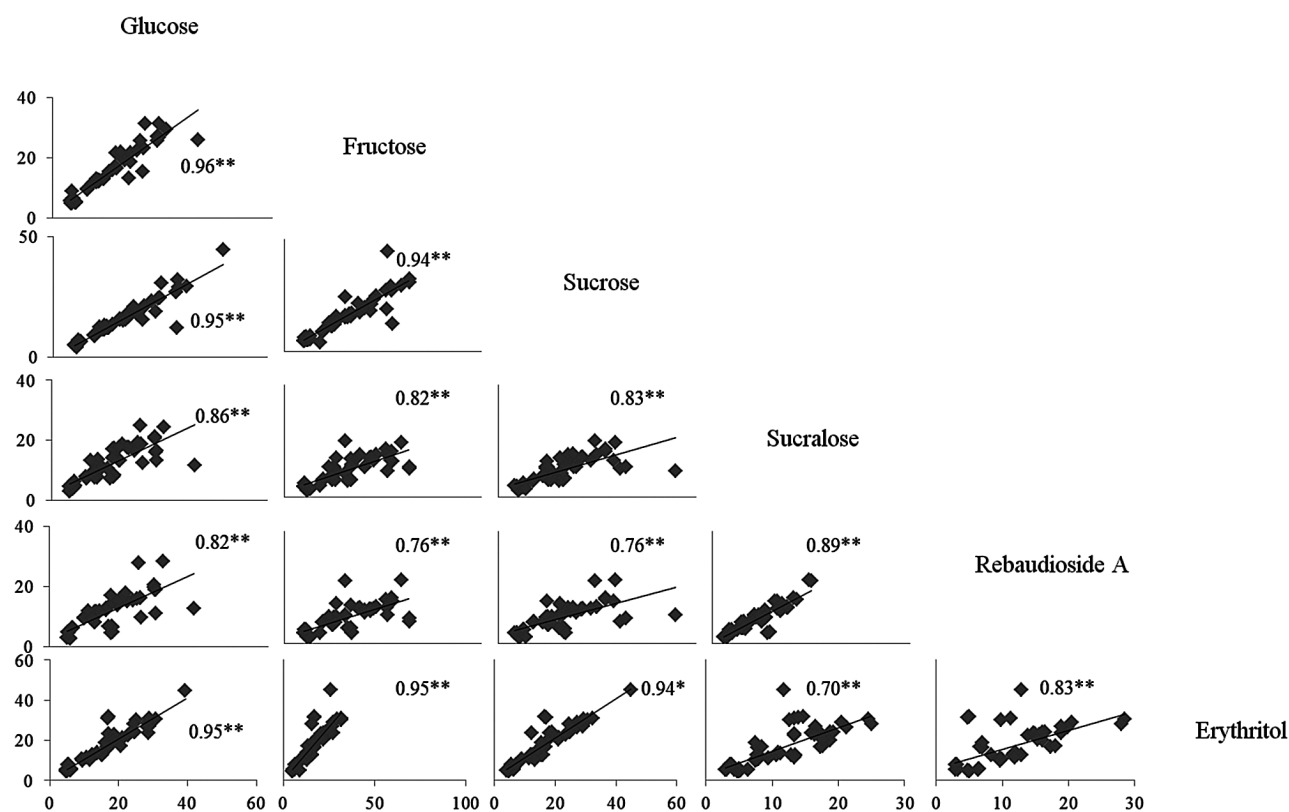
## Discussion

Our data suggest that threshold sensitivity (both DT and RT) to the sweetness of caloric sweeteners (glucose, fructose, and sucrose) does not necessarily imply threshold sensitivity to NNS (sucralose and rebaudioside A). On the contrary, the present data are more supportive of the hypothesis that caloric sweeteners and NNS access at least

partially independent peripheral physiology responsible for DT and RT measures (Liman et al. 2014).

The prevailing understanding at present is that humans have one primary sweet taste receptor (i.e., heterodimer of 2 G-protein coupled receptors, the T1R2-T1R3) (Zhang et al. 2003; Zhao et al. 2003). Both the T1R2 and T1R3 dimers entail a large extracellular area (i.e., Venus fly trap domain), which is connected to the transmembrane via a cysteine-rich domain (Liman et al. 2014). It has been suggested that the Venus flytrap domain of T1R2 targets a large variety of sweet substances (natural sweeteners and most of the NNS); the Venus flytrap domain of T1R3 targets other NNS, such as cyclamate and the sweet receptor blocker, lactisole; and the cysteine-rich domains activate sweet proteins (Cui et al. 2006; Liman et al. 2014). In the present study there were strong correlations between DT and RT of all caloric sweeteners (sucrose, glucose, fructose, erythritol), and also between DT and RT of the NNS (sucralose, rebaudioside A). However, the DT and RT of caloric sweeteners and NNS were weakly correlated suggesting at least some independence between the 2 groups at lower concentrations. This may be due to differences in downstream signaling pathways, or even differences in receptor kinetics as a result of binding to different sites of the sweet taste receptor (Hayes 2008; Liman et al. 2014).

The lack of correlation between detection and RTs of caloric sweeteners and NNS may also be partly explained from the available



**Figure 5.** Scatter plot matrix and spearman rank correlations of sweetness intensity ratings for sweeteners evaluated. \* $P < 0.05$ , \*\* $P < 0.01$ .

**Table 6.** Detection and recognition thresholds (mM) for prototypical tastants, including mean, standard error (SEM), and range

Taste quality		DT		Recognition threshold	
		Mean $\pm$ SEM	Range	Mean $\pm$ SEM	Range
Sweet	Sucrose	4.3 $\pm$ 0.7	1.0–21.0	15.0 $\pm$ 2.6	1.0–70.0
Salty	Sodium chloride	5.2 $\pm$ 0.4	1.0–12.0	33.4 $\pm$ 2.5	5.8–68.0
Sour	Citric acid	0.8 $\pm$ 0.1	0.7–1.0	1.8 $\pm$ 0.2	0.8–6.2
Bitter	Caffeine	0.4 $\pm$ 0.02	0.3–0.8	0.8 $\pm$ 0.09	0.3–2.8
Umami	Monosodium glutamate	3.3 $\pm$ 0.4	0.5–12.0	5.8 $\pm$ 0.4	1.0–12.0

data comparing NNS and caloric sweeteners in brain studies (Frank et al. 2008; Smeets et al. 2011; Green and Murphy 2012). These data suggest that there is only one primary sweet taste receptor involved in sensing sweetness, but that some individuals may not be able to sense sweetness from NNS as effectively as from caloric sweeteners, due to impairment in their brain's sweet reward system. In the past decade, studies using functional magnetic resonance imaging (fMRI) data have revealed that the human brain responds differently to caloric sweeteners and NNS, particularly in the area involved in the reward pathway (Frank et al. 2008; Smeets et al. 2011). It has also been found that, compared to non-habitual consumers of NNS, habitual consumers were found to have greater overall activation in the brain reward pathways to both caloric sweeteners and NNS, further suggesting that NNS may impair and adapt the brain's capability to detect or sense nutrients (Small 2006; Green and Murphy 2012).

In contrast, there were strong correlations between the sweetness intensity ratings of caloric sweeteners and NNS, supporting commonality of sweet mechanism throughout the perceptual range. This result does support current knowledge of the sweet taste transduction mechanism, in which there is only one primary sweet taste

receptor (T1R2-T1R3 heterodimer) responsible for sensing different types of chemical sweeteners at suprathreshold levels.

The finding that, for each sweetener, detection, and RTs were correlated with one another, but not with suprathreshold intensity ratings, suggests added complexity within the sweet taste system. These findings are consistent with previous studies investigating the associations between sucrose taste function, where DTs for sucrose were found to correlate poorly with sucrose suprathreshold intensity ratings (Faurion 1987; Webb et al. 2015). This suggests that there are distinct perceptual stages for sweet threshold and suprathreshold intensities, with each measure of sweet taste characterizing a different component of taste function (Webb et al. 2015). There is, therefore, no single measure capable of being a definitive marker of sweet taste function (Keast and Roper 2007; Webb et al. 2015).

In this study, we measured sucrose DT and RT using both the ISO standard method of limits and the more intensive ascending concentration 3-Alternate Forced Choice technique. This study found significant correlations between sucrose DT and RT using both methods. Thus the results confirm the ISO standard method of limits as a reliable method for the rapid estimation of detection and RTs for sweet taste (sucrose).



**Table 7.** Suprathreshold intensity ratings for prototypical tastants on gLMS, given by mean and standard error (SEM)

Taste quality		Concentration (mM)	Mean $\pm$ SEM
Sweet	Sucrose	100	10.1 $\pm$ 1.0
		200	20.2 $\pm$ 1.8
		400	25.4 $\pm$ 1.6
Salty	Sodium chloride	100	17.6 $\pm$ 1.5
		200	20.2 $\pm$ 1.3
		400	27.3 $\pm$ 1.9
Sour	Citric acid	1.0	11.2 $\pm$ 1.4
		3.0	19.6 $\pm$ 1.9
		7.0	26.7 $\pm$ 1.9
Bitter	Caffeine	1.0	9.2 $\pm$ 1.0
		2.0	19.1 $\pm$ 1.5
		4.0	25.5 $\pm$ 1.7
Umami	Monosodium glutamate	3.0	12.8 $\pm$ 1.4
		6.0	14.0 $\pm$ 1.3
		12.0	16.3 $\pm$ 1.5

There was large inter-individual variation in sweetness perception. The concentration required to reach DT or RT for a sweetener varied approximately 150-fold across the sample population. There was also large individual difference in perceived sweetness intensity; for example, sucrose (400 mM) was rated 8.8 gLMS by 1 participant and 40.5 gLMS by another. Inter-individual differences or variability in sweet taste function has been previously observed for sucrose (Fontvieille et al. 1989; Faurion 1993; Kennedy et al. 1997; Hayes and Duffy 2007; Lim et al. 2008; Yoshiko and Roswith 2012; Cicerali et al. 2012; Webb et al. 2015) and a range of sweeteners (Schiffman et al. 1981; Schiffman et al. 1995; Eylamb and Kennedy 1998).

The hypothesis that those who were able to detect and/or recognize low concentrations of sweeteners would also experience higher sweetness intensities was not supported. This relationship was only weakly observed between the DT and suprathreshold intensity measures of erythritol, glucose, and fructose (i.e.,  $r = 0.26$ – $0.29$ ), but not for the other sweeteners. These findings are consistent with previous studies investigating the relationships between taste functions in other taste qualities (Bartoshuk 1978; Pangborn and Pecore 1982; Mojet et al. 2005; Keast and Roper 2007; Wise and Breslin 2013; Webb et al. 2015).

## Conclusion

This is the first study to explore the interrelations of DT, RT, and suprathreshold perception of sweet taste, in caloric sweeteners and NNS, both within and between individuals. The present data highlight the complexity of human sweetness perception: no single measure of sweet taste function was able to characterize sensitivity, and no one sweet compound was representative of other sweet compounds. The findings are consistent with the proposition of 1 primary sweet taste receptor for both non-nutritive and caloric sweeteners, with different domains in the receptor.

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## Conflicts of Interest

The authors declare no conflict of interest.

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