Chemical Senses, 2018 Vol 43, 645–653
doi:10.1093/chemse/bjy055
Original Article
Advance Access publication 27 August 2018

OXFORD

Original Article

Regional Differences in Taste Responsiveness: Effect of Stimulus and Tasting Mode

Julie L. Colvin, Alexa J. Pullicin and Juyun Lim

Department of Food Science and Technology, Oregon State University, 100 Wiegand Hall, Corvallis, OR 97331, USA

Correspondence to be sent to: Juyun Lim, Department of Food Science and Technology, Oregon State University, 100 Wiegand Hall, Corvallis, OR 97331, USA. e-mail: juyun.lim@oregonstate.edu

Editorial Decision 20 August 2018.

Abstract

Previous studies have shown that there are differences in taste responses between various regions of the tongue. Most of those studies used a controlled "passive" tasting mode due to the nature of investigation. However, food is rarely tasted in a passive manner. In addition, recent studies have suggested that humans can taste maltooligosaccharides (MOS) and that the gustatory detection of MOS is independent of the known sweet receptor. It is unknown whether regional differences in responsiveness to MOS exist. This study was set up to revisit previous work by investigating the effects of tasting mode ("passive" vs. "active") on regional differences in taste responsiveness to sucrose, monopotassium glutamate (MPG), and quinine, while also investigating potential regional differences in responsiveness to MOS. The stimuli were applied to 1 of 4 target areas, the left and right sides of the front and back of the tongue, using cotton-tipped swabs. In the passive tasting condition, the front of the tongue was found to be more responsive to both sucrose and MOS, but no regional differences were seen for quinine and MPG. In contrast, in the active tasting condition, the back of the tongue was found to be more responsive to quinine and MPG, but no differences were found for sucrose or MOS. These findings indicate that there are regional differences in taste responsiveness between the front and back of the tongue and that regional responsiveness is dependent on stimulus and tasting mode.

Key words: carbohydrate, regional differences, taste, tasting mode, umami

Introduction

Since the classic study by Hänig (1901), it has been widely acknowledged that responses to tastes vary across the human tongue and other parts of the mouth (e.g., soft palate). However, there are only a limited number of studies (Collings 1974; Nilsson 1979; Hänig 1901; Sato et al. 2002; see Table 1) supporting this notion, and further, there is no clear agreement about which regions are most sensitive to the 4 prototypical taste qualities (i.e., sweet, sour, salty, and bitter). Notably, all of these early investigations measured regional differences in taste responses in terms of thresholds, which cannot necessarily be generalized to taste responsiveness at suprathreshold levels (Bartoshuk 1978; Keast and Roper 2007; Webb et al. 2015).

Studies of regional differences at suprathreshold levels have also been rare (see Table 1). An early example of one such study was conducted by Collings (1974), who reported that psychophysical functions for sour, salty, and bitter tastes differ between loci (i.e., front fungiform, side fungiform, foliate, vallate, and soft palate). More recently, Feeney and Hayes (2014) compared taste responsiveness on the anterior and posterior parts of the tongue for 5 taste qualities. They reported no regional differences for sweet, sour, and salty tastes, but significant differences for umami and bitter tastes; both were perceived as more intense on the posterior tongue than on the anterior tongue. Others have also measured responses to some or all of these taste qualities across various gustatory regions (Green and Schullery 2003; Green and George 2004; Green and Nachtigal 2012; Doty et al. 2016), although the primary concern of these studies was

Table 1. Summary of studies on regional differences in taste responses to threshold- and suprathreshold-level stimuli

Reference	Regions	Stimuli	Concentration	Stimuli delivery	Tasting mode
Threshold level					
Hänig (1901)	Ventral tip of tongue Middle of tongue Soft palate Hard palate Uvula Tonsils	Sucrose Quinine NaCl Citric acid	Concentration tested unclear	Brush	Mode not specified
Collings (1974)	Fungiform front Fungiform side Foliate Vallate Soft palate	Sucrose Quinine HCl Urea NaCl Citric acid	2.5–6.3 mM[a] 1.6–10 µM 1.6–100 mM 1.6–100 mM 15.8 µM–1.0 mM	Filter paper, 4.0 mm ⌀	Passive
Nilsson (1979)	Fungiform Foliate Vallate Soft palate Hard palate	Sucrose Quinine HCl NaCl Citric acid	7.8 mM–1.0 M[b] 2.0 µM–32 mM 3.9 mM–1.0 M 500 µM–500 mM	Wire loop, 4 mm ⌀	Passive
Sato et al. (2002)	Fungiform center Foliate Soft palate	Sucrose Quinine HCl NaCl Tartaric acid	600 µM–2.3 M[b,c] 14 µM–111 mM 1.7 mM–3.4 M 267 µM–533 mM	Filter paper, 8.0 mm ⌀	Passive
Suprathreshold level					
Collings (1974)	Fungiform front Fungiform side Foliate Vallate Soft palate	Sucrose Quinine HCl Urea NaCl Citric acid	88 mM–2.2 M[a] 64 µM–10 mM 330 mM–8.2 M 160 mM–5.0 M 3.2 mM–1.3 M	Filter paper, 4.0 mm ⌀	Passive
Green and Schullery (2003)	Fungiform Foliate Circumvallate	Sucrose Quinine HCl NaCl Citric acid Capsaicin l-Menthol	500 mM 1.0 mM 500 mM 25 mM 100 or 320 µM 100 or 320 mM	Cotton swab	Mode not specified
Green and George (2004)	Fungiform Circumvallate	Sucrose Quinine sulfate PROP MSG Citric acid NaCl	180 mM 180 µM 56 µM 29 mM 18 mM 100 mM	Cotton swab	Mode not specified
Green and Nachtigal (2012)	Fungiform Circumvallate Soft palate Hard palate	Sucrose MSG NaCl	320 mM 180 mM 320 mM	Cotton swab	Passive and active
Feeney and Hayes (2014)	Fungiform circumvallate	Sucrose Quinine HCl MSG/IMP NaCl Citric acid	2.0 M 2.0 mM 200/100 mM 1.12 M 112 mM	Cotton swab	Mode not specified
Doty et al. (2016)	16 Loci between circumvallate and tip	Sucrose NaCl Caffeine	12% v/v 1.25% v/v 0.7% v/v	Filter paper, 6 mm ⌀	Passive

IMP, inosine monophosphate; MSG, monosodium glutamate; PROP, propylthiouracil.

[a]Threshold values not provided; threshold range calculated from figures in Collings (1974).

[b]Stimuli concentrations were presented in the study. Threshold values were not clearly presented.

[c]Stimuli concentrations converted to molarity from reported w/v%.

not investigating regional differences in tastes responsiveness per se. Nevertheless, the findings of these studies seem to generally agree with those of Feeney and Hayes (2014) with a few exceptions. For instance, some studies (Green and Schullery 2003; Green and George 2004) found no significant difference in taste responsiveness to quinine between fungiform and circumvallate regions.

Interestingly, there are a wide range of methodological variations across these studies (see Table 1), which may contribute to differences in study findings. First, studies have used various stimulus delivery techniques including filter paper disks (Collings 1974; Sato et al. 2002; Doty et al. 2016) and cotton-tipped swabs (Green and Schullery 2003; Green and George 2004; Green and Nachtigal 2012; Feeney and Hayes

2014). Second, the instructions given to subjects on mouth movement while evaluating stimuli (i.e., "tasting mode") range from passively keeping the mouth open (Nilsson 1979; Sato et al. 2002; Doty et al. 2016) to actively pressing the tongue against the roof of the mouth and subsequently swallowing (Green and Nachtigal 2012). Others do not describe the tasting mode used (Green and Schullery 2003; Green and George 2004; Feeney and Hayes 2014). Importantly, an active tasting mode can spread a stimulus to other locations within the oral cavity and increase perceived intensity (Green and Nachtigal 2012; Running and Hayes 2017). Third, the areas of the tongue where taste stimuli are delivered vary between studies. For example, Doty et al. (2016) applied taste stimuli on each side of posterior tongue, whereas others delivered stimuli onto the circumvallate papillae (e.g., Green and Schullery 2003; Feeney and Hayes 2014). Finally, the concentrations tested vary widely from threshold to suprathreshold levels and from low to high within suprathreshold levels. Relative differences between regions may be concentration dependent as evidenced by the finding that slopes of psychophysical functions vary between loci (Collings 1974).

The taste of fat (Running et al. 2015) has been suggested as potential novel taste categories. Accordingly, regional differences in fat taste have been investigated to better understand peripheral transduction mechanisms underlying the gustatory detection of free fatty acids (Mattes 2009); study findings showed no regional differences in detection threshold for any of the free fatty acids tested. However, the average intensity ratings for all free fatty acids tested were highest at the fungiform papillae followed by the circumvallate papillae and then the foliate papillae. Recent studies in our laboratory and others have shown evidence that humans can taste maltooligosaccharides (MOS) (Lapis et al. 2014, 2016; Low et al. 2017; Pullicin et al. 2017) and that the gustatory detection of MOS is independent of the known sweet receptor (Lapis et al. 2014, 2016; Pullicin et al. 2017). Accordingly, human subjects described the taste of MOS as "starchy," whereas they described sucrose and sucralose as "sweet" (Lapis et al. 2016). Regional differences in taste responsiveness to MOS have not yet been investigated in humans. An interesting study conducted by Vigorito et al. (1987) on rats reported that bilateral transection of the glossopharyngeal nerve, which innervates the posterior third of the tongue, reduced the consumption of Polycose (i.e., a glucose oligomer and polymer mixture), but not sucrose, whereas bilateral transection of the chorda tympani nerve, which innervates the anterior two thirds of the tongue, produced comparable reduction. Based on these findings, the authors suggested that although the detection of both classes of carbohydrates is mediated by multiple gustatory nerves, some of these nerves may have specialized functions.

The intent of this study was to revisit previous work on regional differences in taste responsiveness to prototypical tastants, while investigating those to glucose oligomers, that is, MOS. Sucrose was included to compare the regional differences of taste responsiveness between 2 classes of carbohydrate. As a comparison to sweet taste, bitter and umami tastants also known to be transduced by G protein-coupled receptors (Hoon et al. 1999) were included. For bitter taste, one of the most common bitter compounds, quinine hydrochloride, was used. Monopotassium glutamate (MPG) was included to represent umami taste instead of the more commonly used monosodium glutamate (MSG); this decision was made because unlike MSG, MPG does not elicit significant salty taste (Maruyama et al. 2006; Chen et al. 2009; Green et al. 2016). Given that the mode of tasting has been shown to modulate perceived intensities of tastes, in particular umami taste (Green and Nachtigal 2012), a key aspect of this study was to measure regional differences in taste responsiveness to the target stimuli using "passive" and "active" tasting modes in 2 separate experiments. In Experiment 1, a "passive" tasting mode was used to minimize the spread of the stimulus to other regions of the tongue. After stimulus delivery, subjects were told not to allow their tongue to touch any part of their mouth by keeping their mouth open while rating. In Experiment 2, an "active" tasting mode was used to mimic the motions that a subject might make during a normal eating condition.

Materials and methods

Subjects

Initially, a total of 31 subjects (17 females, 14 males) between the ages of 18 and 53 years of age (median: 26 years old) were recruited from Oregon State University and surrounding areas and participated in the study. Data from 2 subjects were excluded due to localized taste insensitivity. One subject rated all stimuli below "barely detectable" on one side of the tongue indicating potential damage to cranial nerves or some other condition (Tomita et al. 1986; Bartoshuk et al. 2012). Another subject had a thick white film covering the back of the tongue, resulting in no perception on the region. Hence, data from 29 subjects (16 females, 13 males; median: 26 years old) were used for data analyses. A total of 26 subjects (14 females, 12 males) who participated in Experiment 1 returned for the Experiment 2. Of those who participated, one subject could not follow the protocol (see Experimental procedure, Experiment 2) due to difficulty simulating an active tasting motion. Therefore, data from 25 of the returning subjects (14 females, 11 males; median: 26 years old) were included in data analysis. All subjects confirmed that they were healthy, nonsmokers, not pregnant, and not taking prescription pain medication or insulin; had no history of taste or smell loss, or other oral disorders; had no oral lesions, canker sores, or oral piercings; and did not have a history of food allergies. Subjects were further asked to comply with the following restrictions prior to their testing session: 1) no consumption of food or beverage except water within 1 h; 2) no use of any menthol-containing products within 1 h, 3) no physically demanding activity within 1 h, and 4) no consumption of spicy food on the day of testing. All subjects gave written consent and were compensated for their time. The experimental protocol was approved by the Oregon State University Institutional Review Board and registered under the Clinical Trial Registry (NCT02589353).

Stimuli

Five test stimuli were included in this study, prepared as aqueous solutions: 56 mM sucrose (Spectrum Chemical MFG Corp.), 0.1 mM quinine hydrochloride (Sigma–Aldrich), 320 mM MPG (Ajinomoto), 224 mM MOS (average degree of polymerization of 14; prepared in Balto et al. 2016), and a deionized water blank. The 4 taste stimuli were chosen to represent sweet, bitter, savory/umami, and "starchy" tastes (Lapis et al. 2016), respectively. The water blank was included as a negative control. Stimuli concentrations were selected based on pilot studies to ensure that they were 1) approximately equi-intense when applied on the front of the tongue and 2) high enough to avoid quality confusion between stimuli. To prevent oral enzymatic hydrolysis of MOS, this stimulus was prepared using an aqueous solution of 5 mM acarbose, a salivary α-amylase, and α-glucosidase inhibitor (Clissold and Edwards 1988; Balfour and McTavish 1993; Martin and Montgomery 1996). At this concentration, acarbose does not have a detectable taste, but is effective to prevent oral hydrolysis of MOS (Lapis et al. 2016). Test stimuli were applied to the targeted locations using cotton-tipped swabs (see Experimental procedure). The length of the cotton tip was on average ~1.3 cm, and saturated swabs contained approximately 0.20 mL of stimulus. All stimuli were stored at 4–6 °C and used within 1 week of preparation. Stimuli were served to subjects at room temperature (20–22 °C).

Experimental procedure

Experiment 1

Over 2 separate sessions, subjects were presented with a total of 20 trials composed of the 5 test stimuli (4 taste stimuli and water control) applied in 4 targeted locations: the front and back of the left and right sides of the tongue (Figure 1). Fungiform and circumvallate papillae were targeted for the front and back of the tongue, respectively. During each session, subjects received a total of 10 trials, which included all 5 stimuli applied on both the front and back of one side (left or right) of the tongue; the order of sides was counter-balanced across subjects. The presentation order of the 10 trials within each session was randomized across subjects. In addition, stimuli were presented on the front and back of the tongue in alternating order so that the same location would not be stimulated twice in a row. The location (front or back) of the first sample given was also alternated between sessions to ensure all subjects received both possible location presentation orders (i.e., back-front-back vs. front-back-front).

At the beginning of the first session, subjects were verbally instructed on the use of the general version of the labeled magnitude scale (gLMS; Green et al. 1993, 1996; Bartoshuk et al. 2003). Subjects were asked to rate 15 remembered or imagined taste sensations (e.g., the sweetness of milk, the burning sensation of eating a whole hot pepper) to familiarize themselves with making ratings over a broad context of sensations. Following training on scale usage, a diagram of the 4 targeted tongue locations (see Figure 1) was shown to subjects. Subjects were asked to visually locate the target locations on their own tongue using a mirror and to touch 2 of the targeted locations (i.e., front and back on one side) using a cotton swab saturated with water. This was done to minimize potential anxiety, discomfort, or gagging during swabbing, especially at the back of the tongue. To familiarize the subjects with the testing procedure, 2 practice trials were given using a water blank. During this practice trial, the experimenter swabbed one of the targeted regions of the tongue (e.g., front left) by rolling the saturated cotton swab across the target area 3 times (see Figure 2); this practice trial was repeated on the opposite region (e.g., back left).

During each test trial, one of the 5 stimuli was applied by the experimenter to a targeted location following the swabbing procedure described earlier. Once a stimulus was applied to the tongue, subjects were asked to rate the peak taste intensity of the stimulus on the gLMS. Importantly, subjects were instructed not to touch other areas of the mouth by keeping mouth slightly open while making ratings; this was done to minimize the spread of the stimulus to other regions of the tongue or mouth. Between each trial, subjects rinsed their mouth at least 3 times with deionized water and then chewed on a 2-inch piece of plastic straw for 30 s to encourage saliva production. Subjects were instructed to chew the straw at the same rate that they naturally chew food. This procedure was found to effectively reduce carry over tastes between stimuli and also to counter dryness in the mouth after repeated rinsing. Subjects were given an additional 30-s break between trials and a 3-min break after half of the trials were presented.

Experiment 2

Experimental design was consistent with that described in the previous experiment except subjects were told to taste samples using their natural "active" tasting motion. This motion was described as being similar to how they may taste a new food or beverage for the first time; for example, it may be a smacking motion. The subjects were asked to practice active tasting by mimicking their natural tasting motion 3 times. Importantly, subjects were instructed not to swallow while tasting or rating samples, as swallowing has been shown to increase the perceived intensity of bitter taste (Running and Hayes 2017). In addition, subjects were asked to open their mouth immediately after completing 3 tasting motions and to keep their mouth open while rating the peak taste intensity of the stimulus on the gLMS; this was done to prevent continued contact between the tongue and the rest of the mouth while rating. To familiarize subjects with the test procedure, subjects performed 2 practice trials using the water control as described in Experiment 1, but with the inclusion of the active tasting motion.

Data analysis

All data collected were log transformed before any statistical analysis, as gLMS responses tend to be log-normally distributed (Green et al. 1993, 1996). Repeated-measures analysis of variance (ANOVA) was first

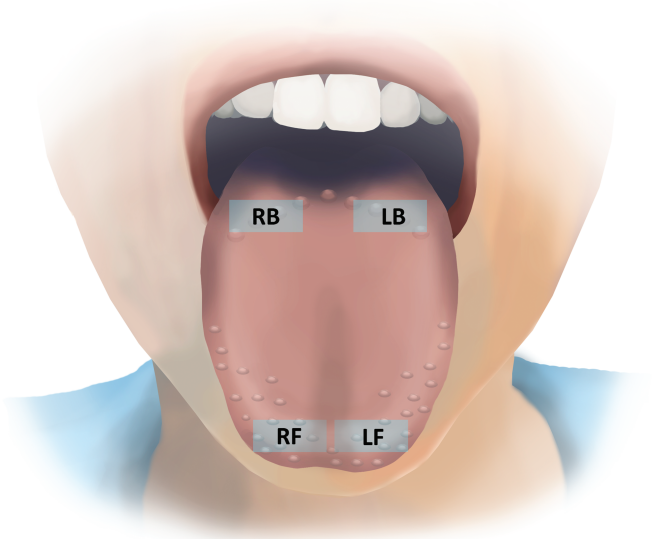

Figure 1. Diagram of the 4 target locations on a tongue.

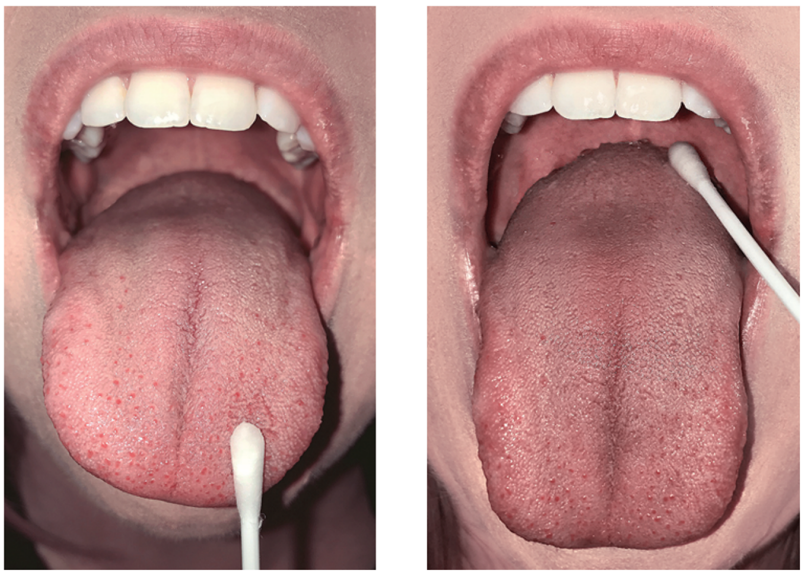

Figure 2. Picture of the front (left) and back (right) of the tongue being swabbed by the experimenter. The fungiform and circumvallate papillae were targeted using cotton-tipped swabs. The length of the cotton tip was about 1.3 cm.

performed on taste ratings using stimulus, region (front vs. back), and side (left vs. right) as factors. Sex was also included as a predictor in the model. Although stimulus and region were found to be significant, side and sex alone were not found to be significant ($P > 0.05$). Therefore, data obtained from each side were treated as replicates and ratings were averaged across replicates. To further analyze the effects of stimulus and tongue region on the perceived intensities, a repeated-measures ANOVA was conducted again using averaged data. Paired *t*-tests were then used to specifically test regional differences (i.e., front vs. back) within each stimulus. To avoid the increased Type I error, the Bonferroni correction was made, and thus an adjusted α of 0.05 was used ($P < 0.01$). In addition, regional differences in taste responsiveness were compared between active and passive tasting modes for subjects that completed both experiments. To determine how tasting mode affects the regional differences in taste responsiveness of the stimuli, a repeated-measures ANOVA was conducted on averaged data (left and right replicates) using tasting mode, region, and stimulus as factors. Statisica 8 (Stat Soft, Inc.) was used for all statistical analysis.

Results

Experiment 1: passive tasting

Figure 3 displays the log mean ratings of all 5 stimuli on 2 different tongue regions: front (gray bars) and back (black bars). Mean perceived intensities for the 4 taste stimuli were rated around "weak," whereas the water control was rated around "barely detectable." When considering individual responses, all subjects rated sucrose, MOS, and MPG above "barely detectable" on the front of the tongue; in contrast, 5 subjects rated quinine below "barely detectable" on this site. On the back of the tongue, there were 3–5 responses per stimulus that fell below "barely detectable," which suggests some subjects were less sensitive on the back of the tongue to the 4 target stimuli at the concentrations tested. Repeated-measures ANOVA revealed that stimulus ($F(4,112) = 25.90$, $P < 0.0001$), region ($F(1,28) = 9.77$, $P < 0.005$), and the interaction between region and stimulus ($F(4,112) = 5.99$, $P < 0.0005$) had significant effects. To further investigate regional differences in taste responsiveness, paired *t*-tests were performed for each stimulus. As expected, there was no regional difference in perceived intensity for the water control (*t* value = –0.11, $P > 0.05$). Surprisingly, regional differences in perceived intensity for quinine and MPG were not found to be significant (*t* values: –1.02 and 1.33, with $P > 0.05$, respectively). However, both sucrose and MOS were perceived as significantly stronger on the front of the tongue (*t* values: 3.77 and 4.69, $P < 0.001$ and $P < 0.0001$, respectively).

Experiment 2: active tasting

Figure 4 displays the log mean ratings of all 5 stimuli on 2 different tongue regions: front (gray bars) and back (black bars). Repeated-measures ANOVA revealed that stimulus ($F(4,96) = 35.09$, $P < 0.0001$) and region ($F(1,24) = 6.26$, $P < 0.05$) had significant effects. The interaction effect between region and stimulus ($F(4,96) = 3.49$, $P < 0.05$) was also found to be significant. Post hoc paired *t*-tests were performed to further investigate regional differences for each stimulus. The water control was found to be perceived as stronger on the back of the tongue, but this difference fell short of significance (*t* value = –1.96, $P = 0.06$). Unlike Experiment 1, no significant regional differences were found for sucrose and MOS (*t* values: –0.27 and 0.61, with $P > 0.05$). However, quinine and MPG were found to be perceived as significantly stronger on the back of the tongue (*t* values: –2.92 and –3.88, $P < 0.01$ and $P < 0.001$, respectively).

Impact of tasting mode on regional differences in taste responsiveness across stimuli

To directly compare the impact of tasting mode on the regional differences observed across the stimuli tested, repeated-measures ANOVA was conducted with tasting mode, region, and stimulus as factors. The analysis revealed that tasting mode and region were not significant factors alone ($P > 0.05$), but stimulus was significant ($F(4,96) = 37.17$, $P < 0.0001$), though the latter can be attributed to the inclusion of the blank stimulus. The interaction effects between mode and region ($F(1,24) = 21.87$, $P < 0.0001$), mode and stimulus ($F(4,96) = 2.78$, $P < 0.05$), and region and stimulus ($F(4,96) = 7.52$, $P < 0.0001$) were significant. These results suggest that the mode of tasting and region did not vary in a systematic matter, but that the impact of tasting mode differed across the regions.

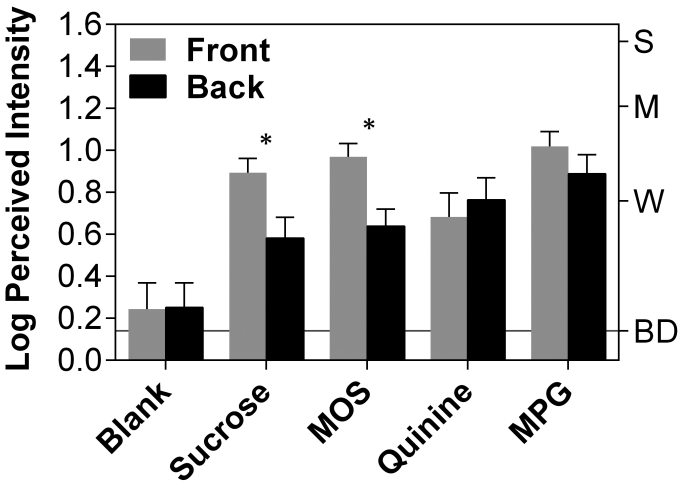

Figure 3. The mean log perceived intensities of stimuli sampled on the front and back using a passive tasting mode are displayed. Bars represent standard error. Left *y* axis represents log perceived taste intensity. The right *y* axis represents the semantic labels of the gLMS: BD, barely detectable, W, weak, M, moderate, and S, strong. *Significant differences between mean perceived intensity ratings performed by paired *t*-tests.

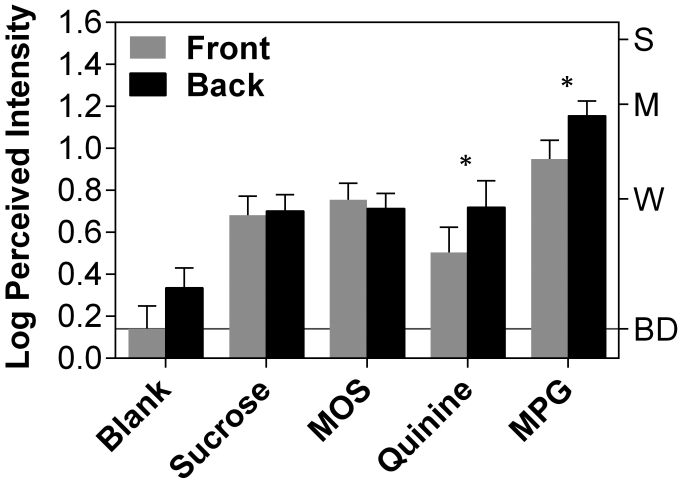

Figure 4. The mean log perceived intensities of stimuli sampled on the front and back using an active tasting mode are displayed. Bars represent standard error. Left *y* axis represents log perceived taste intensity. The right *y* axis represents the semantic labels of the gLMS: BD, barely detectable, W, weak, M, moderate, and S, strong. *Significant differences between mean perceived intensity ratings performed by paired *t*-tests.

Discussion

The results from the present study generally support the notion that responsiveness to taste varies across gustatory regions. More notably, our results indicate that regional differences depend on stimulus and tasting mode. Although the "tongue map" is the most widely known example of regional differences in taste perception, it has become clear that the premise was probably based on a misinterpretation of Hänig's (1901) classic study (Bartoshuk and Beauchamp 1994). The major critique of the "tongue map" is that it implies localized regions of the tongue are solely responsible for eliciting each taste quality (Breslin 2001). However, Hänig's original findings indicate that taste sensitivity varies across the tongue in a stimulus-dependent manner; for example, the front of the tongue was found to be slightly more sensitive to sweet compound than the rest of the tongue.

Regional differences in taste responsiveness: stimulus

In the present study, both carbohydrate stimuli, sucrose and MOS, were perceived as more intense on the front of the tongue than the back of the tongue when a passive tasting mode was used (see Figure 3). This result is in contrast with the recent findings (Green and Schullery 2003; Green and George 2004; Green and Nachtigal 2012; Feeney and Hayes 2014), which found no regional difference in the perceived intensity of sweetness. One noticeable difference between those studies and the present study is stimulus concentration; although those studies used 180 mM to 2 M (6.2%–68.5%) sucrose, the present study used 56 mM (1.9%) sucrose. Recall that Collings (1974) found psychophysical functions vary between loci. Importantly, studies using a similar concentration range have reported that the front of the tongue is more sensitive to sucrose than the back of the tongue in terms of taste detection threshold (Hänig 1901) or quality recognition threshold (i.e., subjects correctly identify sucrose as "sweet"; Collings 1974; Nilsson 1979). Combined together, it appears that at relatively lower concentrations, the front of the tongue is more responsive than the back of the tongue to the 2 carbohydrate stimuli tested, and this difference may subside as concentration increases.

Previous studies have reported a marked degree of regional differences in responsiveness to MSG or a mixture of MSG and inosine

monophosphate, with responses being considerably stronger on the back of the tongue (Yamaguchi and Ninomiya 2000; Green and Nachtigal 2012; Feeney and Hayes 2014). In contrast, the present study showed the front and back of the tongue were equally responsive to MPG, with a slight trend of the front being more responsive, when a passive tasting mode was used (see Figure 3). Notably, the concentrations tested were fairly comparable between the present (320 mM) and previous studies (80–250 mM). One possible explanation could be the differences in the stimuli tested. Although MSG is commonly used as a prototypical umami substance, it has a significant "salt-dependent" gustatory component (Maruyama et al. 2006; Chen et al. 2009; Green et al. 2016). Accordingly, the qualitative similarity between MSG and NaCl at the abovementioned concentrations has been noted previously (Yoshida and Saito 1969), along with a possible confusion between saltiness and umami (Green et al. 2016). More interestingly, Ninomiya and Funakoshi (1989) demonstrated using a mouse model that the afferent input from the glossopharyngeal nerve, which innervates the posterior tongue, plays a more significant role for behavioral discrimination between MSG and NaCl than that from the chorda tympani nerve, which innervates the anterior tongue; the authors speculated that the glossopharyngeal nerve conveys relatively more information of the anion (glutamic acid) than the cation (sodium) component of MSG, whereas the reverse is true for the chorda tympani nerve. Potential differences in the detection mechanism for MSG and MPG are further supported by more recent studies. It has been shown that lactisole (i.e., a sweet taste blocker), which binds to the transmembrane region of T1R3 (Jiang et al. 2005), can also significantly suppress the umami taste of MSG (Galindo-Cuspinera and Breslin 2006), but not MPG (Green et al. 2016). These study findings together suggest that transduction mechanisms may differ between MSG and MPG, which can explain the disagreement in the reported regional differences for the 2 umami substances. The concept that stimuli representative of the same taste quality (e.g., aspartame and sucrose) exhibit different spatial profiles has been acknowledged previously (Breslin 2001).

The present study found the front and back of the tongue to be similarly responsive to quinine with a nonsignificant trend for elevated responsiveness on the back of the tongue when a passive tasting mode was used (see Figure 3). Previous studies have also found similar results and trends for the responsiveness to quinine (Green and Schullery 2003; Green and George 2004), although one study reported the back of the tongue being significantly more responsive (Feeney and Hayes 2014). It should be noted that the latter study used a higher concentration (2 mM) of quinine than any other studies (0.18–1 mM) including the present study (0.1 mM), which suggests regional differences in responsiveness to quinine may also be affected by stimulus concentration. This possibility gains support from the study of Collings (1974), which showed bitter taste imparted by quinine and urea intensified more quickly on the back of the tongue as a function of concentration. Therefore, although the back of the tongue is generally more responsive to these bitter tastants, variation in concentration may have affected the degree of differences shown between the regions.

Regional differences in taste responsiveness: tasting mode

The pattern of regional differences in taste responsiveness differed depending on the tasting mode. When a passive tasting mode was used, the front of the tongue was more responsive to sucrose and MOS than the back of the tongue, whereas the 2 tongue regions were equally responsive to quinine and MPG (see Figure 3). In contrast, when an active tasting mode was used, both regions were equally responsive to sucrose and MOS, whereas the back of the tongue was more responsive to quinine and MPG (see Figure 4). The comparison of these findings demonstrates that regional differences in taste responsiveness depend not only on stimulus, but also on tasting mode.

A careful inspection suggests that using an active tasting mode decreased the perceived intensities of all stimuli on the front of the tongue, but increased the perceived intensities of all stimuli, except quinine, on the back of the tongue. This finding is illustrated in Figure 5. When the passive tasting mode was used, subjects were instructed to keep their tongue from touching other parts of the mouth by keeping the mouth slightly open. During the active

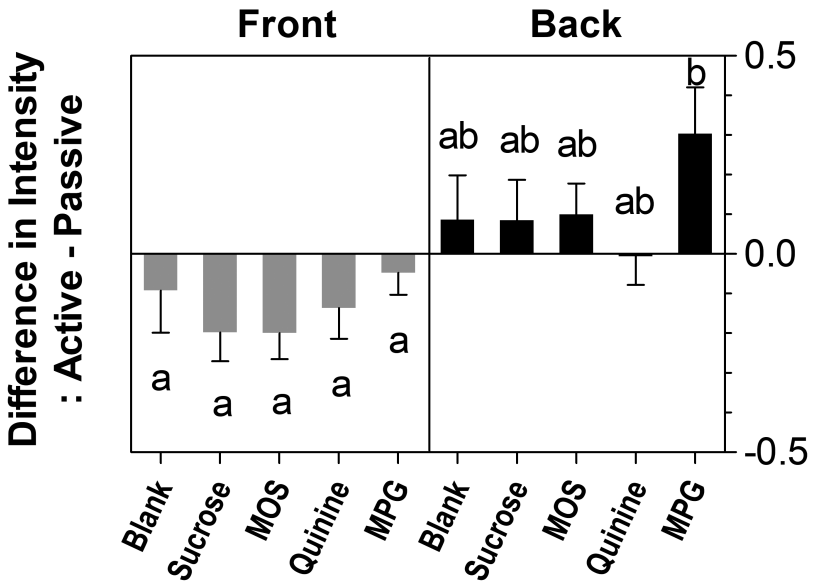

Figure 5. The mean differences in log perceived intensities between passive and active tasting modes are displayed. Differences between modes were calculated by subtracting the log perceived intensities of each stimulus obtained under the passive tasting mode from those under the active tasting mode. The means of those differences were calculated for all stimuli on each region. Right *y* axis represents differences (active – passive) in log perceived taste intensities between the 2 tasting modes. Different letters (a,b) indicate significant differences in values (Tukey's Honestly Significant Difference test, $P < 0.05$).

tasting trial, subjects were asked to mimic their own natural tasting motion, which was described as "the motion you would naturally make when tasting a new food or beverage; for example, a smacking motion." Subjects were also asked not to swallow after making the active tasting motion. Given the natural variation in the extent and pattern of tongue and mouth movements made during this active tasting motion, the impact on taste responsiveness could have differed slightly across subjects. However, considering the steps of typical oral processing of food (de Wijk et al. 2003), subjects probably pressed the tongue against the palate and used a tongue movement of some kind. Accordingly, when a motion like this is made, a stimulus applied on the front of the tongue is likely to be spread to relatively insensitive regions such as the hard palate (Nilsson 1979; Green and Nachtigal 2012) and medial tongue (Doty et al. 2016), which would result in a decrease in responsiveness. In contrast, when a stimulus is applied to the back of the tongue, the tongue and mouth movement can spread the stimulus to the soft palate, a sensitive gustatory region (Collings 1974; Nilsson 1979; Sato et al. 2002). We speculate that the spread of a stimulus from the tongue to the soft palate would increase the area of gustatory stimulation, and consequently, increases perceived intensity due to spatial summation (Smith 1971; Delwiche et al. 2001). Notably, the perceived intensity of MPG was increased by active tasting on the back of the tongue more than other taste stimuli, although it did not reach a statistical significance (see Figure 5). A similar trend was noted in previous work on the effects of tongue and mouth movement on the responsiveness to MSG; in this case, however, active tasting produced significant increases in the responsiveness to MSG not only in the back but also front of the mouth (Green and Nachtigal 2012). This observation suggests that a mechanism other than spatial summation may also play a role in the advantage of active tasting for MSG.

Regional taste responsiveness to carbohydrate stimuli

Recent studies in our laboratory have shown that humans can taste MOS and that their gustatory detection is independent of the hT1R2/hT1R3 sweet receptor (Lapis et al. 2016; Pullicin et al. 2017). The present study investigated the regional differences in taste responsiveness to MOS in human subjects for the first time. Our results suggest that the front of the tongue is more responsive to MOS than the back of the tongue under the passive tasting mode, but that both areas are equally responsive when the active tasting mode is used (see Figures 3 and 4). These findings are not necessarily in good agreement with one available study; Vigorito et al. (1987) reported that bilateral transection of the glossopharyngeal nerve in rats reduced the consumption of Polycose, but not sucrose, whereas bilateral transection of the chorda tympani nerve produced comparable reduction. Note that Polycose is a mixture of MOS and maltopolysaccharides (MOS and MPS). Based on these findings, the authors hypothesized that stimulating the posterior tongue with MOS/MPS would produce a stronger response than stimulating the same region with sucrose. However, we found no differences between the responses to MOS and sucrose on either the front or the back of the tongue, which implies a spatial distribution of the presumed MOS receptor may be similar to that of hT1R2/hT1R3. It is difficult to explain these conflicting results at this time, although we speculate that differences between species along with experimental procedures (e.g., chemical specificity of stimuli, the control of salivary amylase) may have caused the discrepancy. Further investigation is warranted to determine the sensory mechanisms underlying the gustatory detection of glucose oligomers in humans.

Summary

The current findings suggest that regional differences in taste responsiveness depend on stimulus and further that tasting mode modulates responsiveness in a region-specific manner. It has been suggested that the regional differences in taste responses could have a functional purpose; although the primary function of the anterior tongue may be stimulus discrimination, the role of the posterior tongue may be to promote acceptance versus rejection of the stimulus (Breslin 2001). Although the present study did not intend to investigate functional differences between gustatory regions, we speculate that some of the regional differences we observed may fit in this notion. For example, relatively heightened responsiveness to quinine and MPG on the back of the tongue may serve us to promote rejection and acceptance of its consumption, respectively. The fact that responsiveness to MPG was increased the most by active tasting is also intriguing given that savory foods, such as cooked meat (Breslin 2013), require chewing. Taken together, the regional differences demonstrated in the current study may be built in to serve the gustatory functions of selecting and subsequently accepting/rejecting potential foods that are complex in nature.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or non-for-profit sectors.

Conflict of interest

The authors declare no competing financial interests.

References

Balfour JA, McTavish D 1993. Acarbose. An update of its pharmacology and therapeutic use in diabetes mellitus. *Drugs*. 46:1025–1054.

Balto AS, Lapis TJ, Silver RK, Ferreira AJ, Beaudry CM, Lim J, Penner MH. 2016. On the use of differential solubility in aqueous ethanol solutions to narrow the DP range of food-grade starch hydrolysis products. *Food Chem*. 197:872–880.

Bartoshuk LM. 1978. The psychophysics of taste. *Am J Clin Nutr*. 31:1068–1077.

Bartoshuk LM, Beauchamp GK. 1994. Chemical senses. *Annu Rev Psychol*. 45:419–449.

Bartoshuk LM, Catalanotto F, Hoffman H, Logan H, Snyder DJ. 2012. Taste damage (otitis media, tonsillectomy and head and neck cancer), oral sensations and BMI. *Physiol Behav*. 107:516–526.

Bartoshuk LM, Duffy VB, Fast K, Green BG, Prutkin J, Snyder DJ. 2003. Labeled scales (e.g., category, Likert, VAS) and invalid across-group comparisons: what we have learned from genetic variation in taste. *Food Qual Prefer*. 14:125–138.

Breslin PAS. 2001. Human gustation and flavour. *Flavour Fragr J*. 16:439–456.

Breslin PAS. 2013. An evolutionary perspective on food and human taste. *Curr Biol*. 23:R409–R418.

Chen QY, Alarcon S, Tharp A, Ahmed OM, Estrella NL, Greene TA, Rucker J, Breslin PA. 2009. Perceptual variation in umami taste and polymorphisms in TAS1R taste receptor genes. *Am J Clin Nutr*. 90:770S–779S.

Clissold SP, Edwards C 1988. Acarbose. A preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential. *Drugs*. 35:214–243.

Collings VB. 1974. Human taste response as a function of locus of stimulation on the tongue and soft palate. *Percept Psychophys*. 16:169–174.

Delwiche JF, Buletic Z, Breslin PA. 2001. Relationship of papillae number to bitter intensity of quinine and PROP within and between individuals. *Physiol Behav*. 74:329–337.

Doty RL, Heidt JM, MacGillivray MR, Dsouza M, Tracey EH, Mirza N, Bigelow D. 2016. Influences of age, tongue region, and chorda tympani

nerve sectioning on signal detection measures of lingual taste sensitivity. *Physiol Behav*. 155:202–207.

Feeney EL, Hayes JE. 2014. Regional differences in suprathreshold intensity for bitter and umami stimuli. *Chemosens Percept*. 7:147–157.

Galindo-Cuspinera V, Breslin PA. 2006. The liaison of sweet and savory. *Chem Senses*. 31:221–225.

Green BG, Alvarado C, Andrew K, Nachtigal D. 2016. The effect of temperature on umami taste. *Chem Senses*. 41:537–545.

Green BG, Dalton P, Cowart B, Shaffer G, Rankin K, Higgins J. 1996. Evaluating the 'Labeled Magnitude Scale' for measuring sensations of taste and smell. *Chem Senses*. 21:323–334.

Green BG, George P. 2004. 'Thermal taste' predicts higher responsiveness to chemical taste and flavor. *Chem Senses*. 29:617–628.

Green BG, Nachtigal D. 2012. Somatosensory factors in taste perception: effects of active tasting and solution temperature. *Physiol Behav*. 107:488–495.

Green BG, Schullery MT. 2003. Stimulation of bitterness by capsaicin and menthol: differences between lingual areas innervated by the glossopharyngeal and chorda tympani nerves. *Chem Senses*. 28:45–55.

Green BG, Shaffer GS, and Gilmore MM. 1993. Derivation and evaluation of a semantic scale of oral sensation magnitude with apparent ratio properties. *Chem Senses*. 18:683–702.

Hänig DP. 1901. Zur psychophysik des geschmackssinnes. *Philosophische Studien*. 17:576–623.

Hoon MA, Adler E, Lindemeier J, Battey JF, Ryba NJ, Zuker CS. 1999. Putative mammalian taste receptors: a class of taste-specific GPCRs with distinct topographic selectivity. *Cell*. 96:541–551.

Jiang P, Cui M, Zhao B, Liu Z, Snyder LA, Benard LM, Osman R, Margolskee RF, Max M. 2005. Lactisole interacts with the transmembrane domains of human T1R3 to inhibit sweet taste. *J Biol Chem*. 280:15238–15246.

Keast RS, Roper J. 2007. A complex relationship among chemical concentration, detection threshold, and suprathreshold intensity of bitter compounds. *Chem Senses*. 32:245–253.

Lapis TJ, Penner MH, Lim J. 2014. Evidence that humans can taste glucose polymers. *Chem Senses*. 39:737–747.

Lapis TJ, Penner MH, Lim J. 2016. Humans can taste glucose oligomers independent of the hT1R2/hT1R3 sweet taste receptor. *Chem Senses*. 41:755–762.

Low JYQ, Lacy KE, McBride RL, Keast RSJ. 2017. Evidence supporting oral sensitivity to complex carbohydrates independent of sweet taste sensitivity in humans. *PLoS One*. 12:e0188784.

Martin AE, Montgomery PA. 1996. Acarbose: an alpha-glucosidase inhibitor. *Am J Health Syst Pharm*. 53:2277–2290.

Maruyama Y, Pereira E, Margolskee RF, Chaudhari N, Roper SD. 2006. Umami responses in mouse taste cells indicate more than one receptor. *J Neurosci*. 26:2227–2234.

Mattes RD. 2009. Oral thresholds and suprathreshold intensity ratings for free fatty acids on 3 tongue sites in humans: implications for transduction mechanisms. *Chem Senses*. 34:415–423.

Nilsson B. 1979. Taste acuity of the human palate. III. Studies with taste solutions on subjects in different age groups. *Acta Odontol Scand*. 37:235–252.

Ninomiya Y, Funakoshi M. 1989. Behavioral discrimination between glutamate and the four basic taste substances in mice. *Comp Biochem Physiol A Comp Physiol*. 92:365–370.

Pullicin AJ, Penner MH, Lim J. 2017. Human taste detection of glucose oligomers with low degree of polymerization. *PLoS One*. 12:e0183008.

Running CA, Craig BA, Mattes RD. 2015. Oleogustus: the unique taste of fat. *Chem Senses*. 40:507–516.

Running CA, Hayes JE. 2017. Sip and spit or sip and swallow: choice of method differentially alters taste intensity estimates across stimuli. *Physiol Behav*. 181:95–99.

Sato K, Endo S, Tomita H. 2002. Sensitivity of three loci on the tongue and soft palate to four basic tastes in smokers and non-smokers. *Acta Otolaryngol (Stockh)*. 122:74–82.

Smith DV. 1971. Taste intensity as a function of area and concentration: differentiation between compounds. *J Exp Psychol*. 87:163–171.

Tomita H, Ikeda M, Okuda Y. 1986. Basis and practice of clinical taste examinations. *Auris Nasus Larynx*. 13(Suppl 1):S1–S15.

Vigorito M, Sclafani A, Jacquin MF. 1987. Effects of gustatory deafferentation on Polycose and sucrose appetite in the rat. *Neurosci Biobehav Rev*. 11:201–209.

Webb J, Bolhuis DP, Cicerale S, Hayes JE, Keast R. 2015. The relationships between common measurements of taste function. *Chemosens Percept*. 8:11–18.

de Wijk RA, Engelen L, Prinz JF. 2003. The role of intra-oral manipulation in the perception of sensory attributes. *Appetite*. 40:1–7.

Yamaguchi S, Ninomiya K. 2000. Umami and food palatability. *J Nutr*. 130:921S–926S.

Yoshida M, Saito S. 1969. Multidimensional scaling of the taste of amino acids. *Jpn Psychol Res*. 11:149–166.