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ORIGINAL ARTICLE

Saliva Production and Enjoyment of Real-Food Flavors in People with and Without Dysphagia and/or Xerostomia

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Abstract
Non-food gustatory stimulation has multiple potential therapeutic benefits for people with dysphagia and xerostomia. This study examined palatability and saliva flow associated with dissolvable flavored films. Taste strips with real-food flavors dissolved on the tongues of 21 persons with dysphagia and/or xerostomia and 21 healthy age- and sex-matched adults while sublingual gauze pads absorbed saliva over randomized 3-min trials. Participants rated taste enjoyment for each trial on a hedonic general labeled magnitude scale. Flavored strips elicited more saliva than baseline for both groups, and production was higher for controls than patients (M = 2.386 and 1.091 g, respectively; p = 0.036). Main effects of flavor were observed for saliva production (p = 0.002) and hedonics ($p < 0.001$). Hedonic ratings and saliva production were weakly correlated (r = 0.293, $p < 0.001$). Results support dissolvable taste strips as a tool for providing low-risk taste stimulation in dysphagia and for eliciting an increase in saliva flow that may provide temporary relief from dry mouth symptoms. The preferred flavors were, on average, also the ones that elicited greater saliva production. Taste strips have the potential to be beneficial for swallowing-related neural activity, timing, and safety in dysphagia. Further, they may ameliorate complications of xerostomia.

Keywords Deglutition · Deglutition disorders · Dysphagia · Xerostomia · Taste stimulation · Salivary flow

Introduction

Tasting a favorite food may be a simple pleasure, but it is a complex sensory experience. The tastant reacts with receptor cells on taste buds to initiate taste sensation; olfactory, chemesthetic, somatosensory, and proprioceptive inputs are transmitted to the brain; environmental factors are processed; the memories linked to various flavor profiles are retrieved and associated; and the body responds with saliva production [1], oral movements [1], and predigestive changes in the gastrointestinal (GI) tract [2]. These responses then generate further sensory input [1–3], creating a neurological cycle that reinforces patterns of sensorimotor integration for swallowing.

When dysphagia or xerostomia alters this cycle, there are implications for the affected individual's quality of life, oral health, and trajectory of rehabilitation. Though often overlooked in the face of serious medical concerns, the loss of the social, psychological, and emotional experiences of meals shared with family and friends is associated with reduced quality of life and a protracted recovery process [4, 5]. If severe dysphagia necessitates nil per os (NPO) status, the subsequent lack of taste sensation may further disrupt sensorimotor reintegration for dysphagia rehabilitation [6, 7]. Decreased or absent oral intake may also contribute to xerostomia [8, 9], or dry mouth. By definition, xerostomia is a subjective complaint that may or may not co-exist with hyposalivation, an objectively defined reduction in stimulated and unstimulated salivary flow [10]. A range of medical conditions and medications as

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well as overall medical complexity contribute to symptoms of dry mouth [11, 12]. Further, individuals with xerostomia often experience reduced dental health [13] and increased dysphagia symptoms such as globus sensation [14], which may further limit oral intake and stimulation for saliva flow.

In contrast to the complications associated with a lack of oral intake, gustatory stimulation is linked to a range of potential benefits for persons with dysphagia and xerostomia. First, the introduction of virtually any substance into the mouth is known to increase salivary flow [15–18]. For some patients with dysphagia who are unable to manage the increased secretions safely, a higher risk of aspiration and related complications could result. In contrast, an increase in salivation is desirable for patients with xerostomia. A second benefit relates to quality of life; recognition of familiar pleasant tastes is associated with increased activity in the brain's reward system [19] and can trigger nostalgic, positive emotional and psychological responses [20]. Third, certain types of gustatory stimulation have been shown to have immediate positive effects on the timing and safety of swallow function in some patients with neurogenic dysphagia or head/neck cancer [7, 21–25]. As such, it is conceivable that taste stimulation could help entrain advantageous swallowing biomechanics even in the absence of a bolus of food/liquid. Fourth, gustatory stimulation triggers a series of physiological responses in the gut that optimize digestion. It is possible that taste stimulation could facilitate GI processing of tube feedings, which by their nature would not elicit these beneficial GI changes independent of the gustatory stimulation [2]. Finally, enhanced neural activity in the cortical networks associated with swallowing during the provision of taste sensation [6, 26, 27] may support the use of taste stimulation to boost neuroplasticity.

Currently, gustatory stimulation presents a clinical conundrum since its potential benefits as a dysphagia treatment modality must be weighed against the safety considerations of oral intake for those with dysphagia and/or xerostomia. Dissolvable flavored films (taste strips) may offer a safer way to administer taste stimulation without the risk of aspirating food or liquid. However, responses to such taste products have not been systematically investigated in healthy individuals or in those with oropharyngeal dysphagia or xerostomia. Before taste strips can be utilized for quality-of-life purposes or management of such disorders, it is necessary to determine if (a) saliva flow increases to a degree that might be helpful for individuals with xerostomia but not detrimental for individuals with dysphagia who may have difficulty managing copious secretions and (b) individuals experiencing these disorders actually enjoy them.

Hypotheses

During trials of flavored taste strips, participants across groups were hypothesized to exhibit higher amounts of saliva production (H_1) and higher enjoyment ratings (H_2) compared to baseline (no taste strip) trials. Further, the healthy group was expected to have higher saliva flow amounts than the group of individuals with xerostomia and/or dysphagia (H_3). Finally, we anticipated that the strips with the strongest sour taste would elicit the greatest saliva flow (H_4), and the sweetest taste strip would receive the highest taste enjoyment scores (H_5).

Methods

Participants

Adult volunteers from two groups, (1) 21 individuals previously diagnosed with dysphagia requiring diet modification and/or with xerostomia and (2) 21 healthy sex- and age-matched (within 6:0 year:month) controls, were recruited from relevant clinics (rheumatology, speech-language pathology) and the community (staff, military health-care beneficiaries, and civilians). Two criteria were required to qualify as having xerostomia: (1) a diagnosis of xerostomia with associated ICD 9/10 code in the medical record and (2) documented complaints of dry mouth within the medical record from the rheumatology clinic. Three criteria were required to qualify as having dysphagia: (1) previous evaluation and treatment for dysphagia by a speech-language pathologist (SLP) at the medical center, (2) a diagnosis of dysphagia with associated ICD 9/10 code in the medical record, and (3) SLP recommendations for an altered diet texture/liquid consistency or NPO status at the time of study participation. Individuals with a history of radiation therapy to the region of the salivary glands were excluded, since the ability to produce saliva may have been impacted. Participants completed a brief questionnaire about their medical histories, current medications, and hydration/smoking status. For at least 1 h before testing, participants refrained from eating, drinking, chewing gum, or smoking. The Institutional Review Board at Walter Reed National Military Medical Center approved the project, and each participant provided written informed consent.

Stimuli

Paper-thin edible taste strips were approximately 25 mm × 30 mm, and were made from FDA generally recognized as safe ingredients (Tasteful Advances, LLC, no longer in business). They provided complex tastes with

primary characteristics of sweet (glazed donut, GD), sour (lemon-lime, LL), salty (buttered popcorn, BP), and chemesthetic (icy mint, IM). To account for changes in saliva production due to the saliva-collection methods themselves rather than a taste stimulus, baseline trials utilized identical procedures with no taste strip (NS).

Procedures

Prior to each trial, participants rinsed their mouths with distilled water. Next, the researcher placed a loosely rolled $2'' \times 2''$ gauze pad on the floor of the participant's mouth and a taste strip (or no strip in the case of the baseline condition) on the superior surface of the tongue to dissolve. After 1 min, the gauze pad was removed, set aside for weighing, and replaced with a dry pad [10]. The gauze pad was replaced with a new one after another minute for a total of 3 min of saliva collection per trial. Participants were instructed not to swallow during data collection and were asked to spit any residual saliva onto the weighing platform upon removal of the last gauze pad within each trial.

The gauze pads were weighed on a precision scale (APX-323, Denver Instrument) before and after each trial to calculate the saliva produced. After each trial, participants rated taste enjoyment (hedonics) using a computer with a customized MATLAB (v. 7.13) script displaying a mouse-controlled hedonic general labeled magnitude scale (H-gLMS; Fig. 1) [28–30].

Participants each completed seven trials in the following sequence: baseline trial with no taste strip (NS1), four taste trials in a randomized order that was counterbalanced across participants, another baseline trial (NS2), and a repeat presentation of the first taste trial for that participant. Participants were blinded to the specific tastant that was being administered.

Analysis

A fully factorial analysis of variance (ANOVA) was calculated to account for repeated-measures effects on outcome variables of saliva flow and palatability ratings. Independent variables included taste strip type/flavor and participant group. Post hoc pairwise comparisons were assessed via Sidak tests. A two-tailed Pearson Product Moment Correlation was calculated to assess the relationship between saliva production and hedonic ratings.

Results

Each group comprised 15 women and 6 men. Mean age was similar for the patient and control groups at 62.4 (SD 16.2, range 22:6–83:8) and 63.3 (SD 13.6, range 25:3–85:7) years, respectively ($p > 0.05$). The patient group included 5 persons with dysphagia, 13 with xerostomia, and 3 persons diagnosed with both dysphagia and xerostomia; sample size did not allow differentiation into subgroups for statistical analysis.

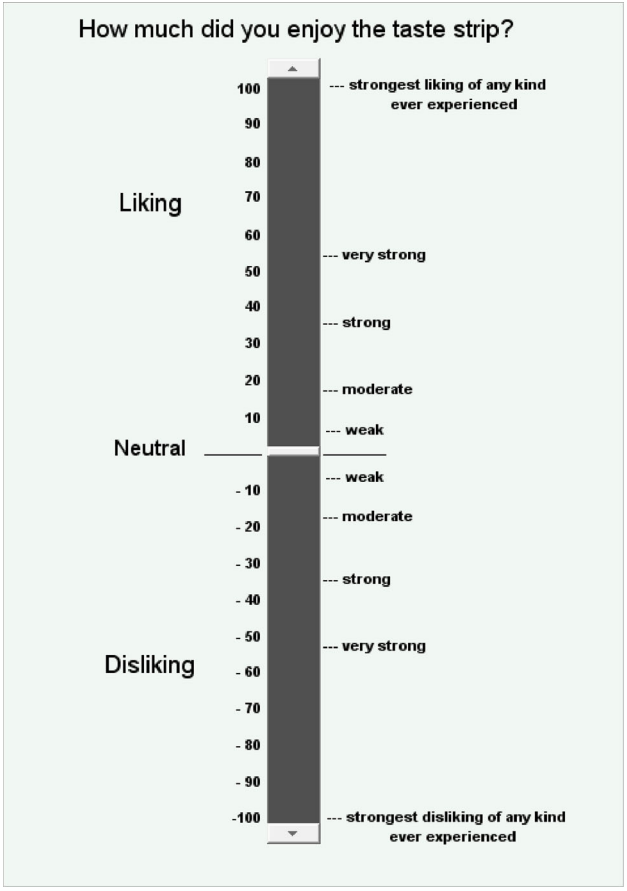

Fig. 1 Hedonic general labeled magnitude scale. Participants used a mouse to slide the marker (shown at neutral) to the desired rating. A customized MATLAB (v 7.13) script recorded the marked rating for each taste trial

Analysis of saliva production revealed significant interaction effects ($p = 0.036$) for group by flavor, which was driven by group similarities in the baseline NS condition compared to all trials (Fig. 2). Saliva production was greater with all taste profiles compared to the tasteless baseline condition (H_1) for both groups according to post hoc pairwise comparisons. The xerostomia/dysphagia patient group produced less saliva overall than did the control group (1.091 vs 2.386 g, respectively), resulting in a significant main effect of group on saliva production of $p = 0.002$ (H_3). Within the main effect of flavor, pairwise comparisons indicated that the NS trials elicited significantly less saliva than did the BP, whereas GD, IM, and LL triggered similarly high productions (H_4).

Regarding hedonic ratings, a significant main effect was noted for flavor ($p < 0.001$), with NS and BP eliciting

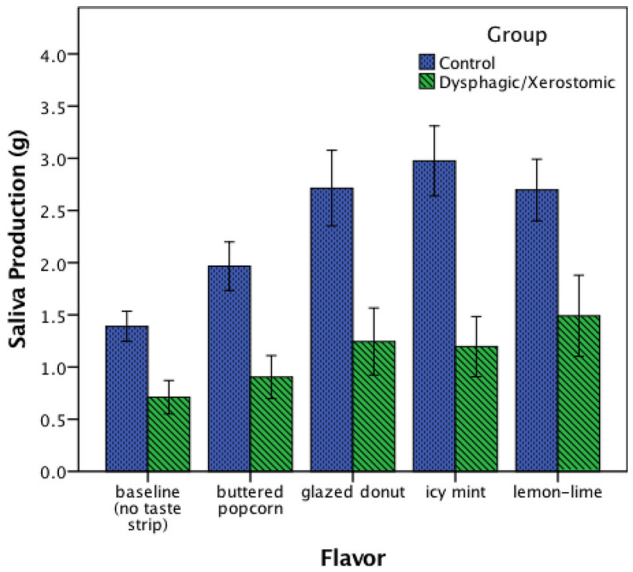

Fig. 2 Mean saliva production. Mean saliva production over 3-min trials for the dysphagia/xerostomia and control groups for the baseline (no taste strip) and taste strip trials. Error bars = ± 1 SE

similarly low ratings (H_2), IM and LL receiving similar moderately preferred ratings, and GD receiving the highest ratings across groups (H_5, Fig. 3). The interaction effect for group by flavor did not reach statistical significance ($p = 0.069$), but two areas of difference were evident; BP was strongly disliked by the patient group, whereas the controls were neutral, and IM was liked by both groups but more so by the controls than the patient group, some of whom reported a "burning" sensation with IM trials. Main effect for group was not statistically significant ($p = 0.202$). There was a weak positive correlation between hedonic ratings and saliva production ($r = 0.293$, $p < 0.001$), with more preferred flavors eliciting greater saliva production.

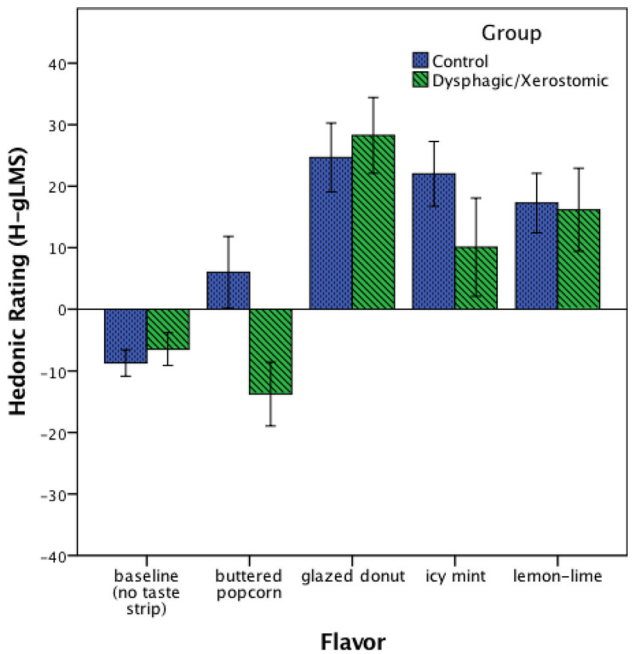

Fig. 3 Mean hedonic rating. Mean rating on the hedonic general labeled magnitude scale for the dysphagia/xerostomia and control groups for the baseline (no taste strip) and taste strip trials. Error bars = ± 1 SE

Analysis of differences across repeated trials (NS for all participants, plus the first flavor within each randomized sequence) revealed interaction effects for flavor by trial for saliva production ($p < 0.001$), with BP and LL eliciting less saliva on the second trials, whereas the second NS, GD, and IM trials were associated with higher saliva production than first trials for each. Likewise for hedonic ratings, the interaction between flavor and repeat presentation was the only significant result ($p < 0.001$), with the NS and GD trials receiving higher ratings on the second trials, whereas the other three flavors were liked less on the repeated trials.

Discussion

The goal of the present study was to characterize the effects of dissolvable flavor films on salivary flow and taste enjoyment in persons with dysphagia or xerostomia. The five study hypotheses were largely supported, and can be consolidated into three main findings.

First, flavored strips elicited increased saliva production compared to the baseline trials for all participants, supporting H_1 and suggesting that taste strips may be a useful tool for managing dry mouth symptoms. As expected based on diagnostic characteristics, participants with xerostomia and/or dysphagia produced less saliva overall compared to their healthy counterparts (H_3). Consistent with previous literature, stimulation type influenced the amount of saliva produced [15], as did group status. More specifically, the NS and BP conditions elicited the least saliva production in both groups, whereas saliva production for the other three tastants differed by group (LL < GD < IM for the healthy group, and IM < GD < LL for the patient group). These results partially support H_4 and suggest that individuals with dysphagia/xerostomia may benefit most from a palatably sour stimulus in contrast to the mint flavors associated with most of the typically recommended mouth rinses, candies, and gums.

Second, participants in both groups generally found the taste strips to be enjoyable. Hedonic ratings were higher for all flavored trials compared to the NS baselines (H_2), though some taste profiles were clearly preferred to others. Collapsing across participant groups, BP was the least preferred of the taste strips, whereas GD was the most popular (supporting H_5). Although the group by flavor

interaction did not reach statistical significance because of high variability in hedonic ratings ($p = 0.069$), large cross-group disparities were noted for BP and IM, both of which were disliked more by the patient group than the healthy participants. This result could reflect differences in taste sensation as a function of underlying oral moisture and salivary content [31]. It might also be related to heightened sensitivity of the mucous membranes as evidenced by subjective statements offered by some participants with dysphagia/xerostomia, such as "that minty one kind of burns." From a therapeutic perspective, it may be possible to accommodate certain patient preferences among the taste profiles provided that they elicited similar increases in saliva flow.

Third, several ancillary analyses of these data underscore the clinical potential of taste strips in xerostomia and dysphagia management. The more preferred flavors were, on average, also the ones that elicited greater saliva production. This is good news for clinical application of the taste strips for xerostomia symptom relief and dysphagia therapy, in that patients are more likely to comply with treatments that they enjoy. Furthermore, saliva production for taste trials remained higher than NS trials over the course of each participant's data collection (albeit to a lesser extent for repeated trials of BP). This indicates that, even for persons with xerostomia/dysphagia, the increases in oral hydration were sustainable for at least 30 min with repeated taste stimulation. Also of note, total saliva production over each 3-min collection period exceeded 4 g (roughly equivalent to 4 ml) in less than 10% of trials, representing two participants with dysphagia over nine trials and seven healthy participants over 20 trials. The level of saliva production observed was enough to relieve dry mouth symptoms per participant report, but not so much as to induce evidence of difficulty managing secretions (such as drooling or clinical signs of aspiration) for any participant during any trial. Though it is not possible to rule out silent aspiration, these results indicate that the taste strips did not elicit an overwhelming amount of saliva that would jeopardize the health and safety of the patients with dysphagia during taste stimulation trials.

Interpretation of these preliminary findings is tempered by several considerations. First, participants with xerostomia did not undergo objective testing to confirm whether or not they also had hyposalivation. Since persons with dry mouth often seek symptom relief regardless of the medical diagnosis associated with their complaints, the taste strips may offer benefit regardless of the diagnostic category. Second, the method used for saliva collection does not capture all residual saliva in the oral cavity. Thus, it is possible that some residual secretions were missed; this residue can be expected to be similar for all samples collected from that person. Third, the limited sample size in this preliminary study did not allow for statistical comparison between xerostomic and dysphagic conditions. Though these conditions often co-exist, differentiation of the responses within these subgroups should be considered in future work involving taste stimulation. Finally, assumptions about homogeneity and normal distribution were not met for every group/flavor/outcome combination. Repeated-measures ANOVA is relatively robust to violations of these assumptions, but larger sample sizes in future work will help to overcome these limitations.

Based on these results, it appears that dissolvable taste strips effectively increase saliva flow in healthy adults and persons with dysphagia and/or xerostomia, and are enjoyable as a potential means of stimulating saliva flow and taste sensation for immediate relief of dry mouth symptoms. Next steps may include assessing the long-term effects of taste strips on saliva production, oral health, perceptions of mouth dryness, and quality of life compared to other taste stimulation and dry mouth relief products. Beyond this immediate clinical relevance, future work will characterize the effects of taste stimulation on neural activity, including the potential of gustatory input to influence neuroprotection and adaptation in a manner similar to somatosensory input via trigeminal channels [32]. The present findings open the door to evaluating the efficacy of non-food taste stimuli as a management strategy for xerostomia and dysphagia.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflicts of interest. Tasteful Advances/First Flavor, LLC, provided the taste strips according to a Cooperative Research and Development Agreement (CRADA #382400-12).

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