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Effects of Sweet Flavorings and Nicotine on the Appeal and Sensory Properties of e-Cigarettes Among Young Adult Vapers: Application of a Novel Methodology*

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Abstract

Introduction—Product characteristics that impact e-cigarette appeal by altering the sensory experience of vaping need to be identified to formulate evidence-based regulatory policies. While products that contain sweet flavorings and produce a "throat hit" (i.e., desirable airway irritation putatively caused by nicotine) are anecdotally cited as desirable reasons for vaping among young adults, experimental evidence of their impact on user appeal is lacking. This experiment applied a novel laboratory protocol to assess whether: (1) sweet flavorings and nicotine affect e-cigarette appeal; (2) sweet flavorings increase perceived sweetness; (3) nicotine increases throat hit; and (4) perceived sweetness and throat hit are associated with appeal.

Methods—Young adult vapers (N=20; age 19–34) self-administered 20 standardized doses of aerosolized e-cigarette solutions varied according to a 3 flavor (sweet [e.g., cotton candy] vs. non-sweet [e.g., tobacco-flavored] vs. flavorless) × 2 nicotine (6 mg/mL nicotine vs. 0 mg/mL [placebo]) double-blind, cross-over design. Participants rated appeal (liking, willingness to use again and perceived monetary value), perceived sweetness and throat hit strength after each administration.

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Contributors

All authors contributed to the manuscript and have approved the final article.

Dr. Leventhal, Dr. Kirkpatrick and Mr. Goldenson conceptualized and designed the study, drafted the initial manuscript, and approved the final manuscript as submitted.

Dr. Samet, Dr. Pentz, Dr. Pang, Dr. Barrington-Trimis and Ms. McBeth reviewed the manuscript, and approved the final manuscript as submitted.

Conflict of Interest

No conflict declared (Conflicts of interest: none).

Results—Sweet-flavored (vs. non-sweet and flavorless) solutions produced greater appeal and perceived sweetness ratings. Nicotine produced greater throat hit ratings than placebo, but did not significantly increase appeal nor interact with flavor effects on appeal. Controlling for flavor and nicotine, perceived sweetness was positively associated with appeal ratings; throat hit was not positively associated with appeal.

Conclusions—Further identification of compounds in e-cigarette solutions that enhance sensory perceptions of sweetness, appeal, and utilization of e-cigarettes are warranted to inform evidence-based regulatory policies.

Keywords

e-cigarette; tobacco regulatory science; flavoring; nicotine; appeal

1. INTRODUCTION

E-cigarette use (vaping) is highly popular among young adult smokers and nonsmokers (McMillen et al., 2015). While evidence about the possible harms and benefits of e-cigarettes continues to mount, there are little empirical data regarding popular e-cigarette product features that enhance the appeal of vaping, particularly flavorings and other product characteristics that alter vaping's sensory effects (Miech et al., 2016). The U.S. Food and Drug Administration has requested research on product characteristics that impact e-cigarette appeal in order to formulate evidence-based regulatory policies (Backinger et al., 2016). Data assessing the role of flavorings and nicotine in e-cigarette appeal amongst young vapers could inform regulatory policies that affect the persistence of vaping in this population.

The combustible cigarette literature demonstrates that the direct psychoactive effects of nicotine on the central nervous system account for only part of the reinforcing value of smoking (Rose, 2006). Pleasurable sensations associated with the tobacco self-administration procedure (e.g., taste, smells, airway stimulation) play an important role in smoking reinforcement (Przulj et al., 2012). Thus, e-cigarette product features that alter the sensory experience of vaping could impact user appeal.

Anecdotal reports indicate that sensory perceptions of sweetness and nicotine-induced sensations of "throat hit," a reportedly desirable organoleptic sensation presumed to result from the stimulation of nicotinic cholinergic receptors lining the oropharynx and lungs, are important reasons for vaping (Pokhrel et al., 2015). The presence of flavorings and nicotine in e-cigarette solutions could impact appeal via their *sensory-altering* effects. Apart from the sensory experience of vaping, numerous exogenous factors (e.g., marketing strategies, cultural trends, pre-existing expectations about product effects, and social influences) could also influence the perceived appeal of certain e-cigarette products (Chu et al., 2015; Vasiljevic et al., 2016). Human laboratory paradigms provide a platform for testing the effects of specific product characteristics on e-cigarette appeal under double-blind conditions capable of controlling for such exogenous factors (Henningfield et al., 2011).

In this laboratory experiment involving young adult vapers, we applied and integrated methods from consumer product testing and drug abuse liability evaluation to assess: (1) the effects of sweet flavorings and nicotine on e-cigarette product appeal; (2) whether sweet flavorings increase perceived sweetness; (3) whether nicotine increases throat hit; and (4) the extent to which perceived sweetness and throat hit are associated with product appeal. A secondary aim of the study was to evaluate the utility of a novel paradigm for rapidly screening the effects of specific e-cigarette product characteristics on user appeal and sensory effects.

2. METHODS

2.1 Participants

Vapers (N=20; 19–34 years old) were recruited via online advertisements. Eligibility criteria were: 1) e-cigarette use ≥1 day/week for ≥1 month; 2) smoking ≤15 conventional cigarettes/day; 3) no use of smoking cessation medication; and 4) not pregnant or breastfeeding. All participants provided written informed consent for this IRB-approved protocol.

2.2 Design and Procedure

Following eligibility confirmation, participants attended a 2-hour laboratory session. The test procedure involved self-administration of 20 different e-cigarette solutions (10 flavors × 2 nicotine concentrations) that were separated into two counterbalanced blocks (nicotine and placebo). Within each block, 10 different e-cigarette solutions (6 sweet, 3 non-sweet and 1 flavorless) were presented in random order—constituting a Flavor (sweet vs. non-sweet vs. flavorless) × Nicotine (nicotine vs. placebo) within-participant full factorial design. In the 30 minutes separating the 2 blocks, participants completed demographic and tobacco product use surveys.

During each administration, a video display cued participants to inhale and exhale from the e-cigarette device following a standardized puff sequence of a 10-s preparation, 4-s inhalation, 1-s hold, and 2-s exhale—approximating typical vaping topography (Yip and Talbot, 2013). The puff sequence was repeated twice for each solution (i.e., 2 puffs). Each two-puff sequence was separated by a one-minute period during which participants were provided with water.

2.3 Materials

Solutions were loaded into Joyetech “Delta 23 Atomizer” tanks that were connected to a Joyetech “eVic Supreme” battery (a recent-generation device). The 20 e-cigarette solutions (Dekang Biotechnology Co., Ltd.) were composed of 50/50 propylene glycol/vegetable glycerin with either 6 mg/mL or 0 mg/mL nicotine concentrations. The 6 mg/mL concentration was selected based on evidence that recent-generation devices efficiently deliver nicotine to the bloodstream (Farsalinos et al., 2014) and pre-study pilot testing indicating that doses greater than 6 mg/mL produced aversive effects. The 10 flavors included 6 sweet-flavored (peach, watermelon, blackberry, cotton candy, cola and sweet lemon tea), 3 non-sweet-flavored (mint, tobacco and menthol) and a single flavorless solution.

2.4 Measures

2.4.1 Outcomes—After each 2-puff cycle, participants were asked to rate three dimensions of appeal, to rate two sensory qualities, and to guess the flavor administered (to determine whether participants remained blind to flavor), by answering the following questions: (1) “How much did you like it?” (100 mm Visual analog scale [VAS], 0–100 with “Not at all” to “Extremely” as anchors); (2) “Would you use it again?” (VAS, “Not at all” to “Definitely”); (3) “How much would you pay for a day’s worth of it?” (open-ended, U.S. dollars); (4) “How sweet was it” (VAS, “Not at all” to “Extremely”); (5) “How strong was the throat hit?” (VAS, “Very Weak” to “Very Strong”); and (6) “What flavor is it?” (forced choice of one of 14 flavors, 10 of which were used in the study).

2.4.2 Participant Characteristics—In addition to a survey assessing vaping and smoking characteristics, all participants were administered the Penn State Electronic Cigarette Dependence Index (PSECD; Foulds et al., 2015) and past 30-day smokers (N=16) completed the agerstr m est of igarette Dependence (FTCD; Heatherton et al., 1991).

2.5 Data Analyses

Each outcome provided 400 data points (20 observations × 20 participants) analyzed in five separate multilevel linear models (one model each for the 3 appeal and 2 sensory quality ratings) that included an independent, fixed flavor main effect, nicotine main effect and flavor × drug interaction. Post hoc pairwise comparisons followed-up significant omnibus flavor effects. Associations between each sensory rating (sweetness or throat hit) and the appeal outcomes were tested using separate multilevel linear models controlling for flavor and nicotine condition, with the respective sensory quality rating treated as a time-varying regressor.

3. RESULTS

3.1 Preliminary Analyses

Participants (N=20; 55% male; age $M \pm SD$=26.3±4.6 years-old; 45% White, 35% African American, 20% Other race/ethnicity) reported, on average, low to medium e-cigarette dependence on the PSECD (M=8.4[95% CI: 6.4–10.4]) and vaping for 3 years (SD=1.5). Past-30 day smokers in the sample (N=16; 80%) reported, on average, medium levels of cigarette dependence on the FTCD (M=6.3[95% CI: 5.8–6.8]). In response to the question, “What flavor do you typically vape?,” 11 participants reported regularly using a sweet flavor and 9 reported a non-sweet flavor.

The average accuracy rate in identifying the flavor administered across cycles was 9.7% and did not differ by Flavor condition (p=0.82; Figure S1[1]), suggesting that participants remained blind to the characterizing flavor they received.

[1]*Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:…

3.2 Effects of Flavor and Nicotine Conditions on Appeal and Sensory Quality

As illustrated in Figure 1 panels A–C, there was a significant main effect of Flavor on each appeal outcome (*p*s<0.0001). Pairwise comparisons revealed that sweet-flavored solutions produced higher appeal ratings than non-sweet and flavorless solutions (*p*s<0.0001), which did not significantly differ from one another (*p*s=0.06–0.12). For all appeal outcomes, there were no significant main effects of Nicotine (*p*s=0.25–0.59; Figure 1, E–G) or Flavor × Nicotine interaction effects (*p*s=0.76–0.99).

There was a significant main effect of Flavor on sweetness (*p*<0.0001), with three significant pairwise contrasts showing a graded effect on sweetness across flavorless, non-sweet, and sweet conditions (*p*s<0.0001; Figure 1, D). A main effect of Nicotine on throat hit was observed (*p*<0.0001); with a stronger throat hit in nicotine versus placebo solutions (Figure 1, H).

3.3. Associations of Sensory Quality Ratings with Appeal Ratings

Regardless of the flavor administered, ratings of sweetness were positively associated with each appeal outcome (*p*s<0.0001; Figure 2, A–C). Each one point increase in sweetness rating (0–100) was associated with an estimated 0.51 increase in “liking,” a 0.51 increase in “willingness to use again,” and a $0.04 increase in “amount willing to pay for a day’s worth of the solution.” Throat hit ratings were not associated with willingness to use again and subjective value (*p*s=0.23–0.61), respectively, and were *inversely* associated with liking (*p*=0.01; Figure 2, D–F).

3.4 Re-Analysis Among Vapers Who Did Not Regularly Use Sweet Flavors

Given the potential impact of pre-existing flavor preference, we re-analyzed the data among participants who reported regularly using non-sweet flavors (N=9). As in the overall sample, all appeal outcomes were positively associated with sweetness ratings (*p*s<0.0001); willingness to use again and subjective value were not associated with throat hit (*p*s=0.35–0.41), and liking was *inversely* associated with throat hit (*p*=0.02; see Table S1[2]).

The direction of the Flavor condition effects paralleled the findings in the entire sample (i.e., higher mean appeal ratings for sweet than non-sweet and flavorless solutions; Figure S2, A–C[3]). However, for each appeal rating, the Flavor main effects (*p*s=0.09–0.17) and pairwise contrasts of sweet-flavored to non-sweet or flavorless solutions (*p*s=0.06–0.23) did not reach statistical significance.

4. DISCUSSION

This double-blind experiment held exogenous determinants of appeal constant, allowing participants’ to base their subjective judgments of appeal primarily on sensory experience. Under such conditions, e-cigarette solutions producing greater perceptions of sweetness increased the subjective appeal of vaping in the overall sample. Supplemental analyses provided suggestive evidence of the appealing properties of sweet flavorings amongst vapers

[2]Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:…
[3]*Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:…

who did not typically use sweet flavors. An implication of this finding is that e-cigarette solutions that stimulate orosensory perceptions of sweetness (in and of themselves) may be primary drivers of appeal, and should be considered in the development of evidence-based policies targeting young adults who vape.

Solutions containing nicotine significantly increased user reports of “throat hit,” but did not enhance appeal. Correlational analyses revealed that solutions producing a stronger throat hit clearly were *not* more appealing. Some sensory stimuli associated with the tobacco self-administration process are reinforcing in conjunction with nicotine’s psychoactive effects (Chaudhri et al., 2006). It is possible that the study solutions or devices stimulated peripheral nicotine receptors enough to produce throat hit sensation, but did not deliver sufficient levels of nicotine into the blood stream to activate central nervous system and make such sensations desirable.

This study integrates the very limited experimental evidence on whether and how e-cigarette flavorings impact user appeal. A recent study found that e-cigarette solutions with (vs. without) menthol increased sensations of coolness, reduced perceived airway irritation and harshness and increased subjective appeal independently of nicotine concentration (Rosbrook and Green, 2016). Another experiment found that fruit and dessert-flavored (vs. unflavored) e-cigarette solutions with constant nicotine concentrations increased the rewarding and reinforcing value of vaping in young adults; but perceived sweetness was not examined (Audrain-McGovern et al., 2016). In conjunction with the current results, the emerging evidence suggests that flavorings in e-cigarette solutions that alter the sensory experience of vaping, independent of nicotine, directly affect e-cigarette product appeal.

This study also provides initial support for a novel methodology for rapidly testing the effects e-cigarette product characteristics on sensory qualities and user appeal. In addition to the tight experimental control, a key strength of the design is the multivariate outcome data structure that can be analyzed with multilevel modeling, substantially increasing the number of data points and statistical power to detect effects and estimate them with precision (e.g., 20 participants × 20 ratings produced 400 data points in this study). Extension of this experimental platform to study more diverse outcomes (e.g., physiological responses, vaping choice behavior), additional forms of product diversity (e.g., device type and voltage), other contexts (e.g., participants deprived from nicotine) and across user populations (e.g., prior experience with e-cigarette vs. new users) could increase the external validity of these results.

In this initial application of a novel human laboratory e-cigarette product appeal testing methodology, flavorings in e-cigarette solutions that produced sensory perceptions of sweetness during vaping increased appeal among young adult vapers. These results suggest that this new methodology may be useful in identifying specific chemical compounds in e-cigarette solutions and other product components that alter the sensory experience, appeal and utilization of e-cigarettes to inform evidence-based regulatory policies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

- Sweet flavorings in e-cigarettes enhanced user perceptions of product appeal.
- Nicotine in e-cigarettes increased throat hit but did not affect product appeal.
- Provides initial validation of a novel methodology for evaluating e-cigarettes.

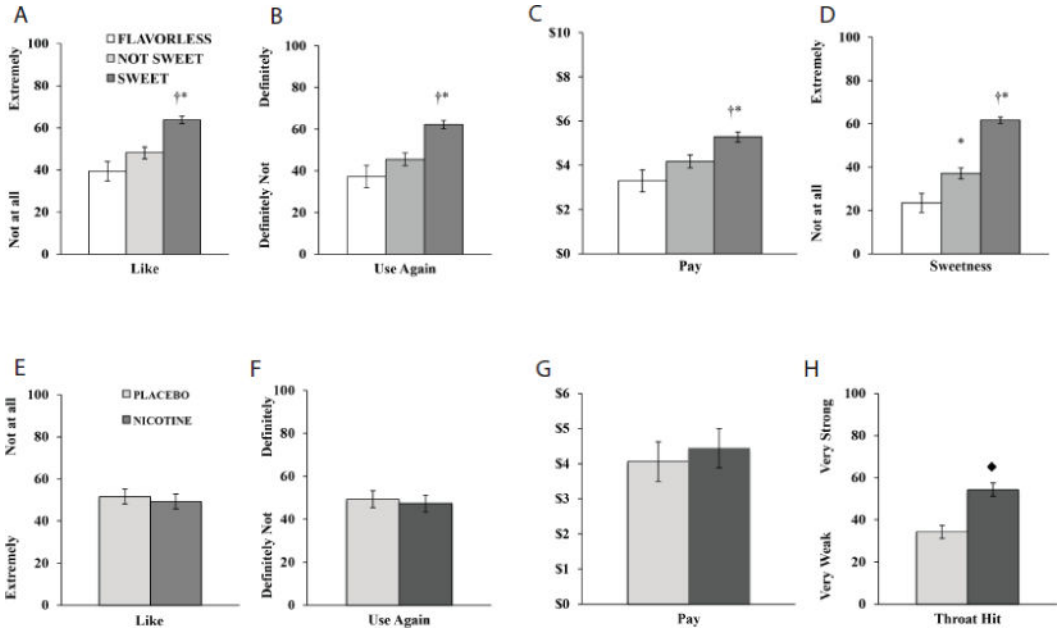
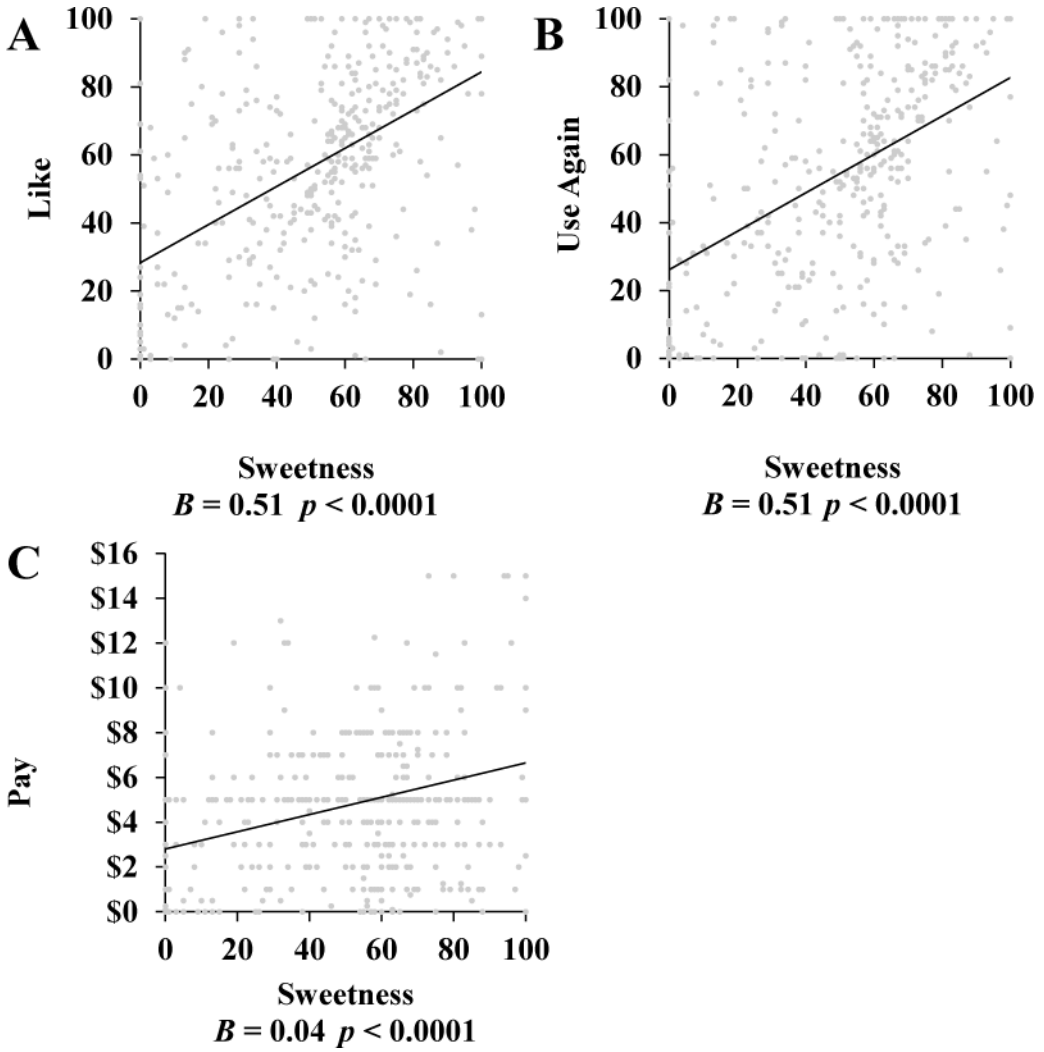


Figure 1.

Appeal, Sweetness and Throat Hit Ratings by Flavor Type and Nicotine (*Mean ±SE*). †Significantly greater than "Not Sweet" in pairwise contrast ($p<0.0001$). *Significantly greater than " lavorless" in pairwise contrast ($p<0.0001$). ◆Significantly greater than "Placebo" in pairwise contrast ($p<0.0001$). Like = "How much did you like it?"; Use Again = "Would you use the it again?"; Pay = "How much would you pay for a day's worth of it?"; Sweetness = "How sweet was it?"; hroat Hit = "How strong was the throat hit?"



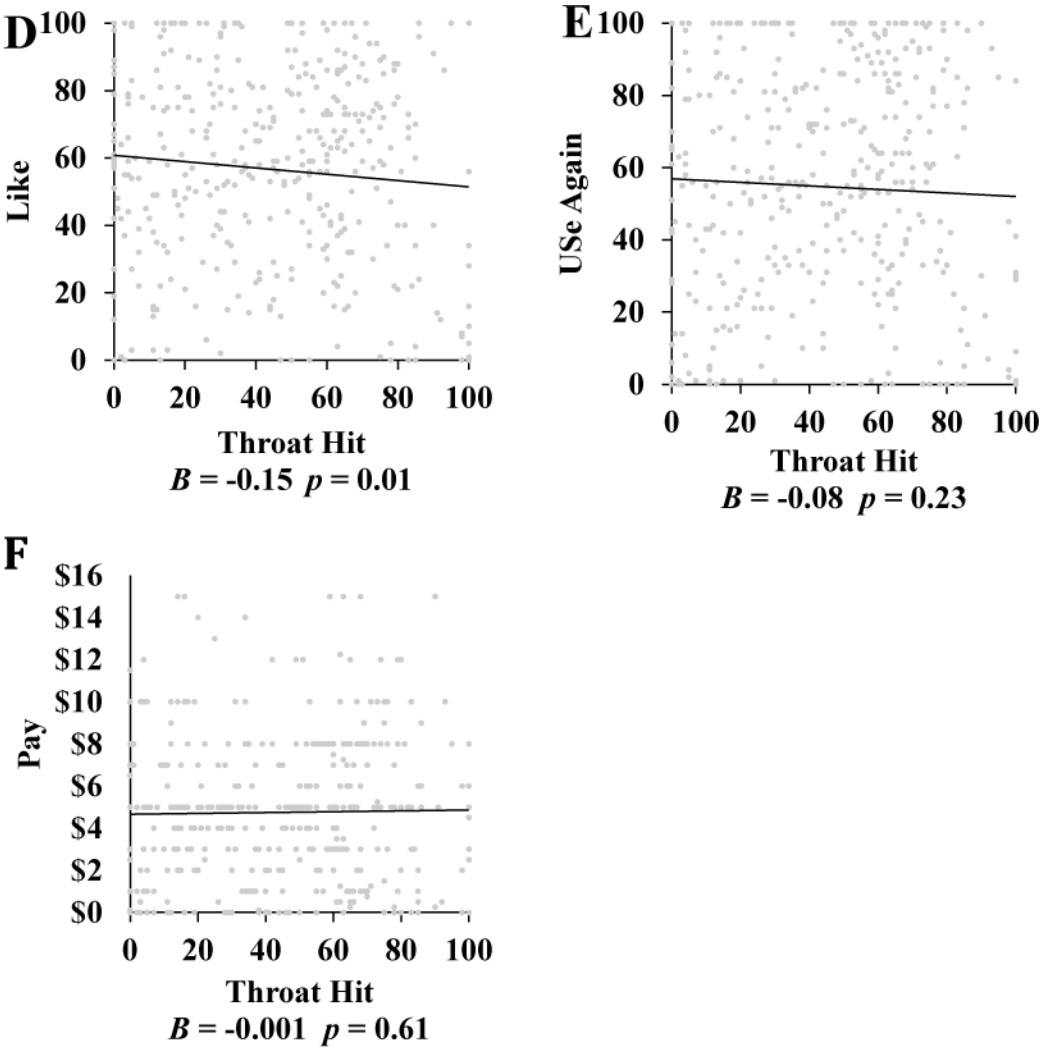


Figure 2.

Scatter Plots with Linear Trend Line of Appeal Ratings by Sweetness and Throat Hit Rating. *B*'s and *p*-values were obtained from multilevel linear models that treated sweetness and throat hit rating as a time-varying regressor variable. All ratings besides "Pay" were made on Visual Analog Scales (0–100). Like = "How much did you like it?"; Use Again = "Would you use the it again?"; Pay = "How much would you pay for a day's worth of it?"; Sweetness = "How sweet was it?"; hroat Hit = "How strong was the throat hit?".