Harsh and sweet sensations predict acute liking of electronic cigarettes, but flavor does not affect acute nicotine intake: a pilot laboratory study in men

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Abstract

Introduction: Electronic cigarette (eCig) use is increasing in popularity, and thousands of flavors are available. Adolescent vaping rates in the United States have nearly doubled in the past year. Unlike combustible tobacco, added flavors are not currently regulated for electronic cigarette products. Here, we investigated the role of flavor in eCig liking and acute intake. *Methods:* Men (n=39) aged 18-45 vaped in a controlled laboratory setting after being randomized to one of four e-liquids: 6mg nicotine/ml Cherry, 18mg/ml Cherry, 6mg/ml Chocolate, or 18mg/ml Chocolate. They completed several questionnaires, and vaped ad libitum for 10 minutes. After the first puff, participants rated sensations (sweetness, bitterness, coolness, harshness/irritation) on general labeled magnitude scales (gLMS) and rated overall liking on a generalized hedonic scale. Once the 10-minute session ended, participants made another set of ratings. *Results:* Liking was generally stable across the vaping session and liking varied substantially across the 4 conditions. Across all conditions, sensory ratings predicted liking: harshness/irritation was negatively associated with first puff liking while perceived sweetness was positively associated with first puff liking. First puff liking associated with increased amount of e-liquid vaped, but not total nicotine intake. Participants appeared to titrate their nicotine intake regardless of assigned condition. *Conclusion:* Flavored eLiquids affect acute rated liking, but not acute nicotine intake. *Implications:* These data suggest individuals who regularly vape may titrate their nicotine intake, regardless of flavor, and contrary to expectations, acute liking did not predict total intake. However, more-liked flavors may potentially make higher nicotine levels more tolerable by adding pleasant sensations directly, rather than by perceptual masking that reduce aversive sensations.

Introduction

Electronic cigarette (eCig) use is increasing in popularity. New data indicate the prevalence of high school seniors in the United States (US) who had vaped in the last 30 days nearly doubled from 11% in 2017 to 30.9 in 2018 ¹. Although US federal regulations prevent combustible tobacco cigarettes from containing flavorings other than menthol, these rules do not currently apply to eCigs. Thus, manufacturers of eCig liquid are not constrained in the flavors they can use — varieties such as fruits, desserts, cocktails, menthols, tobacco, and others are widely available, with thousands of options that appeal to diverse preferences. While vaping is less risky for those who already smoke combustible cigarettes ², vaping also presents a substantial risk for nicotine dependence in its appeal to individuals who do not already use nicotine products ³. Thus, it is important to inform the evidence base to guide potential regulations on allowed flavors in eCigs.

It is clear that taste and flavor are a key factor in the appeal of eCigs. According to the 2016 National Youth Tobacco survey, “availability of flavors such as mint, candy, fruit, or chocolate” was among the most commonly reported reasons for eCig use ¹. Likewise, Kim and colleagues assessed liking and disliking of several e-liquids, all with the same nicotine concentration, and found that sweet flavors were rated as more liked ⁴. In 2015, Berg investigated preferred eCig flavors among never, current, and former eCig users and cigarette smokers ⁵. She found sweet flavors were attractive to both current eCig users and smokers who did not use eCigs. Also, tobacco flavored e-liquids were unappealing to never smokers, and current combustible tobacco users (cigarette smokers) were more likely to select tobacco flavored e-liquids. Litt, Duffy, and Oncken

examined the influence of flavor on smoking and vaping behavior and found that rates of eCig vaping were significantly influenced by flavor ⁶. Over 6 weeks, individuals assigned to either tobacco or cherry flavors had the highest vaping rates, whereas those assigned to chocolate flavored eCigs had the lowest rates. More recently, Pullicin and colleagues reported that increasing nicotine concentration increased perceived harshness from eCig vapor, and that perceived sweetness increased liking ⁷. Collectively, these studies indicate that flavor plays a central role in eCig use. However, while recent work has explored liked flavors across different populations of eCig users, interactions between the sensations evoked by nicotine and added flavors, and their influence on liking and acute intake remain understudied. The present study logically extends the work of Pullicin and colleagues ⁷ by explicitly measuring acute intake in a laboratory setting, which was not assessed in their study on liking. Elsewhere, Litt, Duffy, and Oncken measured intake over 6 weeks, but they measured it as eCig episodes per day rather than amount of e-liquid vaped ⁶. In the eating behavior literature, it is widely accepted that liking is a central driver of intake ⁸; however, such data is currently lacking for eCigs, so we addressed this knowledge gap here.

The public health implications of eCigs are complex and nuanced. On one hand, eCigs are less risky than combustible tobacco and might play an important role in harm reduction by helping smokers transition away from combustible cigarettes (e.g., ⁹). Conversely, eCigs also represent a substantial public health threat for development of nicotine dependence in never smokers, particularly for adolescents and young adults who find the diverse flavor options of eCigs highly attractive ¹⁰. Among high school seniors in the United States, rates of self-reported vaping in the last 30 days nearly

doubled from 2017 to 2018, from 11% to 20.9% ¹. It is possible that non-tobacco flavored e-liquids may reduce barriers to initiation and use among adolescents by reducing aversive sensations that are typically experienced when inhaling nicotine ⁴. **Still**, established smokers or eCig users may seek to lower the amount of nicotine they consume, which is feasible with the range of nicotine concentrations found in commercially available e-liquids. Thus, the availability of diverse eCig flavors may be beneficial for individuals trying to taper their use of combustible tobacco while also increasing the risk of nicotine dependence in individuals who would not consider smoking. Additional empirical data on the role of flavor in eCig use is needed to support evidence-based regulation of eCig products.

The original objective of this study was to investigate if there is an interaction between flavor and nicotine reinforcement: we wished to determine if participants might be more accepting of a lower nicotine concentration when paired with a well-liked flavor – that is, could well liked flavors facilitate tapering nicotine dose in smoking cessation trials? If so, eCig users might be able to reduce nicotine consumption by selecting a different flavor that is more liked. Prior data suggests that cherry e-liquids are better liked than chocolate e-liquids ⁵, so they were studied here. Alternatively however, higher nicotine levels are also more irritating (e.g., ⁷), so well-liked flavors might also facilitate use of higher nicotine levels that would otherwise be off-putting. To test these competing hypotheses, we tested whether certain sensory attributes from eCigs, like harshness/irritation and sweetness, would predict eCig liking, and if liking would predict acute intake in a controlled laboratory setting.

Methods

Participant Recruitment

Potential participants were recruited via multiple methods, including paper flyers posted on and around our university campus, paid targeted ads on social media (Facebook), and email announcements to an existing opt-in database of 1200+ age diverse individuals who have previously expressed interest in participating in studies by the Sensory Evaluation Center at Penn State. Interested individuals completed a screening questionnaire and were invited to participate based on eligibility criteria. Inclusion criteria consisted of 1) self-identified as male, 2) aged 18 to 45, 3) ability to speak English fluently, and 4) had either smoked at least one cigarette in the past 30 days OR used an electronic cigarette (eCig) in the past 6 months. Individuals were also excluded from participation if they 1) were using nicotine replacement therapy or other pharmaceuticals for smoking cessation, or 2) had a history of any respiratory illness or any other illnesses exacerbated by smoking. The choice to test only males was made for several reasons. Foremost, we wished to increase sample homogeneity, given the pilot nature of the study. Due to greater prevalence of use (^{11,12}), we anticipated it would be easier to recruit men for the study; this also reduced burden on both the participant and experimenter by precluding the need to screen for pregnancy prior to vaping in the laboratory.

Study Design

Participants who met eligibility criteria were scheduled for a single laboratory visit. A between subjects 2 by 2 design – with two nicotine concentrations (6mg/ml and 18mg/ml) and two commercially sourced flavors (Cherry Crush and Smooth Chocolate)

– was used, all at a 50/50 ratio of propylene glycol and vegetable glycerin. These concentrations were selected as low and high levels that are commonly used by current eCig users (see 5). Participants were randomly assigned to one of four experimental conditions: Low Nicotine/Cherry Crush, Low Nicotine/Smooth Chocolate, High Nicotine/Cherry Crush, or High Nicotine/Smooth Chocolate. They vaped the randomly assigned nicotine concentration/flavor combination under supervision of the experimenter and completed several questionnaires (detailed below). The electronic nicotine delivery system (VaporFi Rocket 3 Vape Pen equipped with 0.1ohm atomizers, set to fire at 300W) and e-liquids were commercially available products purchased from an online retailer (VaporFi; Miami Lakes, FL); these were used as provided by the manufacturer without modification. In this device, the coil is integral to the tank, and 3 drops of e-Liquid were added to the coil on first use.

Procedure.

We filled the e-cigarette tank with the appropriate e-liquid flavor/nicotine combination, and weighed it on an analytical balance (Ohaus, Model PA114, Parsippany NJ) at the beginning and end of the test session; the amount vaped was calculated by difference. Total nicotine intake was then expressed in terms of milligrams of nicotine vaped – this was done by first converting the weight of e-liquid vaped to milliliters by using the mean density of a 50/50 PG/VG blend (1150 mg/mL). This volume was then multiplied by the concentration of nicotine in the e-liquid (either 6 or 18 mg/mL) stated on the label. Thus, these calculations assume a) contributions of the added flavor and nicotine to the density of an e-liquid are negligible, and b) the actual amounts of nicotine in the e-liquid match the amount stated on the label. No attempt was made to

verify this via analytical chemistry.

All testing occurred in a custom-built smoking research facility located in the Chandlee Laboratory on the Penn State campus. All study procedures were approved by the Penn State Institution Review Board (Protocol #00007087). After signing IRB approved informed consent documents, participants were given a 9.7in tablet computer (Apple iPad Air, Apple, Inc, Cupertino, CA) displaying directions for the experiment, which they were asked to read carefully before starting the experiment. These directions included a brief overview of the study and provided detailed instructions on how to perform the task. Using the iPad, participants first completed a series of questionnaires, which included demographic information, questions regarding frequency and nature of nicotine-containing product use, the Fagerstrom Test for Nicotine Dependence (FTND)¹³ and the Arnett Inventory of Sensation Seeking (AISS)¹⁴.

Following completion of the questionnaires, participants were instructed on how to use a general Labeled Magnitude Scale (gLMS)¹⁵ and underwent a brief orientation on use of the scale. The gLMS is a 100-point scale with semantic labels along the line. On the left end, it is labeled with 'NS' (no sensation) at 0, and the right side is labeled 'strongest imaginable sensation of any kind' at 100. Additional adjectives – 'BD'; barely detectable, 'weak', 'moderate', 'strong' and 'very strong' – are placed at 1.4, 6, 17, 35 and 51, respectively; these numbers were not visible to participants. The gLMS generates ratio level data similar to the method of magnitude estimation, but is easier to use, and does not require adjustment for differences in number usage¹⁵⁻¹⁷. Participants were instructed to not let whether or not they liked or disliked a sensation to influence their intensity ratings. The scale orientation included practice rating 15 remembered or

imagined sensations, and these included both food and non-food items to emphasize that the scale should be used in context of all possible all sensations ¹⁷.

Affective (liking) ratings were collected using a 200 point horizontal generalized bipolar hedonic scale. This scale is labeled ‘strongest disliking of any kind’ on the left (-100) and ‘strongest liking of any kind’ on the right (+100), with ‘neutral’ at 0 at the center point. These scales have been used previously by our team (e.g. ^{18,19}) and similar scales have been used in other eCig research ⁴. Orientation for the liking scale involved rating 8 remembered experiences. Participants were instructed to keep the extremes (strongest liking or strongest disliking of any kind) consistent across items. Finally, prior to vaping, participants were asked how much they currently wanted a cigarette on a visual analog scale; no specific instructions were given to participants on abstaining from nicotine products prior to visiting the lab. All questionnaires and ratings were collected using the Compusense Cloud platform (Guelph, ONT), as part of the Compusense Academic Consortium.

Participants were asked to vape freely for 10 minutes (meaning they could self-regulate, vaping as much or as little as they wished during this period). After the first puff, participants made intensity ratings for sweetness, bitterness, coolness, harshness/irritation, and overall flavor on separate general Labeled Magnitude Scales; they also rated overall liking on the bipolar hedonic scale. At the end of the 10-minute free vaping period, the participant was asked to make another set of ratings. We did not expect any effects for the bitterness or coolness measures – they were included to minimize dumping effects (see ²⁰). After all sensory ratings were completed, participants were asked ‘how much do you currently want a cigarette?’ on a visual analog scale. Last,

all participants completed an Adverse Events Checklist with the experimenter to assess general and respiratory health before leaving the laboratory.

After the participant left, the experimenter removed the e-liquid tank from the electronic cigarette and re-weighted it to determine the amount of liquid the participant had vaped. The amount was determined by difference from the pre-weight and recorded.

Statistical Methods

Psychophysical ratings and questionnaire data were exported from Compusense Cloud; e-liquid usage was tabulated in Microsoft Excel. All analyses were performed in SAS 9.4 (Cary, NC). Separate linear regression models were run using *proc reg* to test whether amount vaped could be predicted by liking at first puff and at the end of 10 minutes. Additionally, *proc reg* was used to examine whether there was a relationship between first puff liking ratings and liking ratings at the end of the 10-minute session. Linear regression models were run using *proc reg* to determine whether liking was predicted by either sweetness or harshness/irritation ratings, collapsed across all conditions. ANOVA models testing the effects of nicotine (6 vs. 18 mg/mL) and flavor (Cherry v. Chocolate) were performed using *proc mixed*. A mixed model with flavor and nicotine as between subjects factors and time as a repeated measure was created: Liking = NicotineLevel + Flavor + Time + NicotineLevel by Flavor + NicotineLevel by Time + Time by Flavor + NicotineLevel by Flavor by Time. Next, *proc reg* was used to examine whether there was a relationship between liking ratings and amount of e-liquid vaped within that condition. Finally, effects of nicotine level and flavor on perceived sensations were tested in separate models (e.g., [Sensation] = NicotineLevel + Flavor +

NicotineLevel by Flavor). Fagerstrom scores were collected but are not reported here: due to a coding error, the wording of the FTND in the computerized questionnaire referred only to combustible tobacco cigarettes, without consideration of vaping. Because we cannot know which participants answered the questions narrowly (i.e., cigarettes only) versus in the broader context of eCig usage, we discarded these data.

Participant Characteristics

Most participants (total $n = 39$) self-reported their ethnicity as Caucasian, and they had a mean age of 22.7 years. Consistent with recruitment criteria, 100% had used eCigs at some point in their life, and 64.1% were regular eCig users, based on self-report via a yes/no question (“Do you vape/use electronic cigarettes regularly?”). Approximately one-fifth (20.5%) were regular smokers, and 7.7% were regular hookah users (via simple yes/no questions worded as above). Full demographic details are available in Supplemental Table 1. All participants were enrolled and tested between February and September 2018. The study was originally powered for 74 participants across all conditions to observe a medium effect in a between groups ANOVA; however, the study was terminated early due to difficulty recruiting participants who met inclusion criteria.

Results

Intensity Ratings, as function of assigned condition

First, we tested if assigned nicotine level and/or flavor influenced first puff ratings for Sweetness and Harshness/Irritation, via separate ANOVA models for each sensation (time was a repeated measure, and concentration was between subjects). As shown in Figure 1, harshness increased with nicotine level [$F(1,35) = 6.95$; $p = 0.0124$]. Conversely, in the parallel model for sweetness, there was no effect of nicotine level

[$F(1,35) = 0.01$; $p = 0.94$]. Notably, flavor did not affect sweetness or harshness ratings in either model, as both the main effects and interactions of flavor were not significant.

Figure 1: Effect of nicotine level on harshness/irritation (solid circles with solid line) and sweetness (open boxes with dashed line); values are jittered slightly to avoid overlap. Gray symbols show means collapsed across flavor, as main effects of flavor and interactions with flavor were not significant. For illustration only, brown and red symbols indicate within condition means for the chocolate and cherry conditions.

Liking ratings were generally stable over time

Liking ratings were stable across 10 minutes of ad libitum vaping. The best fit line had a slope slightly under 1, implying there is a small decrease in liking with exposure (see Supplemental Figure 1); however, this effect is quite small (i.e., a first puff liking of 20 would drop to ~17 by the end of the session).

Liking as a function of Harshness/Irritation and Sweetness

We anticipated harshness/irritation and sweetness ratings would have the largest effect on liking. As shown in Figure 2 (left), harshness/irritation ratings at first puff explained 27.8% of the variance in liking ratings at first puff; for each 10 point increase in harshness, liking ratings dropped by 9.8 points [$F(1,37)=14.23$; $p = 0.0006$]. An opposite effect was observed for sweetness: sweetness ratings at first puff explained 13.7% of the variance in first puff liking, and each 10 point increase in sweetness increased liking by 10.0 points [$F(1,37)=5.89$; $p = 0.0202$]. We did not test ratings after 10 min, given the stability over time shown previously in Supplemental Figure 1.

Figure 2: Liking/Disliking rating as a function of Harshness/Irritation (left) and Sweetness (right). Red and brown symbols indicate cherry and chocolate, respectively, while open and closed symbols represent low and high nicotine levels. Notably, the majority of the ratings were below zero, indicating they are disliked.

Liking Ratings as a function of assigned condition

To test the effect of condition on liking, a mixed model with flavor and nicotine as between subjects factors and time as a repeated measure was created. As expected, the

Nicotine by Flavor interaction was significant [$F(1, 35) = 7.56, p = 0.0094$], as was the main effect of Nicotine [$F(1,35)= 4.86; p = 0.0342$] (not shown); no other main effects or interactions were significant (all p 's $>.15$). As shown in Figure 3, participants in the high nicotine chocolate condition gave significantly lower ratings than those in the high nicotine cherry condition (Tukey-Kramer $p = 0.0277$). Also, those in the high nicotine chocolate condition gave significantly lower ratings than those in the low nicotine chocolate condition (Tukey-Kramer $p = 0.0076$); the difference between the low nicotine cherry group and the high nicotine chocolate group was not significant (Tukey-Kramer $p = 0.0669$). No other pairwise comparisons were significant (all p 's >0.79). Taken together, these results suggest that the high nicotine cherry condition was less disliked, and high nicotine chocolate more disliked, than the other conditions.

Figure 3: Mean liking ratings as a function of assigned condition. Red and brown indicate cherry and chocolate, respectively; open and closed shapes indicate 6mg/mL and 18mg/mL, respectively.

Amount Vaped, as a function of liking

We then used linear regression to test whether liking influenced the amount participants vaped over the 10-minute session. As depicted in Figure 4, as first puff liking increased, the amount of eLiquid vaped (in mL) increased ($R^2=0.26$; $p < .0001$). Critically, however, first puff liking did not predict the amount of nicotine (in mg) vaped ($R^2=0.06$; $p = 0.13$) over 10 minutes, as shown in Supplemental Figure 2.

Figure 4: Amount of eLiquid (in mg) vaped over 10 minutes as a function of liking on the first puff. Red and brown indicate cherry and chocolate, respectively; open and closed shapes indicate 6mg/mL and 18mg/mL, respectively.

Amount Vaped, as a function of assigned condition

Last, we tested whether amount vaped across the session differed by assigned condition. As shown in Supplemental Figure 3, the amount of eLiquid vaped dropped as nicotine level increased [$F(1,35) = 4.67$; $p = 0.038$], but flavor (cherry v. chocolate) did not influence amount vaped [$F(1,35) = 0.48$; $p = 0.49$], and the interaction was not significant. Conversely, the amount of nicotine vaped (in mg) did not vary by nicotine level [$F(1,35) = 2.40$; $p = 0.13$] or flavor [$F(1,35) = 0.99$; $p = 0.33$]. Collectively, this suggests that our participants titrated their nicotine intake, regardless of assigned condition, and that liking does not influence the amount of nicotine they consumed.

Discussion

Based on national surveillance data in the United States, eCig use is on the rise, and added non-tobacco flavors have become a double-edged sword in terms of their public health implications ¹. While some individuals may find such non-tobacco flavors appealing as they attempt to cut back on nicotine intake, thereby supporting smoking cessation, there is also growing consensus that added flavors (especially sweet, fruity options) may appeal to youth who would not otherwise smoke. The present study sought to determine how added flavors influenced the acceptability/liking and acute intake of different nicotine concentrations in a laboratory setting. Initially, we hypothesized eCig users might be more accepting of a lower nicotine level when paired with a well-liked flavor; however, present data does not support this. Rather, high-nicotine cherry was less disliked than high nicotine chocolate. As expected, we also found that two sensory attributes – harshness/irritation and sweetness – each contributed to liking, with

opposing effects. More notably, we found evidence that while nicotine level influences harshness, overall liking does not influence total nicotine intake with the session.

Data from Pullicin et al. (2019) shows that as nicotine concentration increases, liking drops ⁷, consistent with other data showing that as nicotine concentration increases, so does perceived harshness ^{21,22}. Here, we recapitulate and extend these findings: greater harshness/irritation associated with lower liking, however lower liking did *not* associate with total nicotine intake. Also, we found that liking was lower in the high nicotine condition – which had higher harshness ratings – but only for a less liked flavor (chocolate). Collectively, this suggests that a well-liked flavor (e.g., cherry) may potentially increase the tolerance for nicotine concentrations that would be otherwise aversive. This implies that instead of facilitating nicotine reduction in smoking cessation (i.e., tapering), the widespread availability of fruity flavors may instead reduce the innate aversiveness of higher levels of nicotine. While pilot study cannot speak directly to whether flavor induced reductions in aversiveness affect eCig initiation and abuse liability, product features that potentially reduce barriers to initiation are concerning.

Flavor perception is an amalgamation of multiple sensory inputs, including taste, smell, and chemical touch (chemesthesis), which interact with one another. One key aspect of this integration is a phenomenon known as mixture suppression. For example, when bitterness is mixed with sweetness, perceived sweetness and bitterness of the mixture is less than either one in isolation ^{23,24}. Likewise, smell shows similar effects in mixtures. In 1974, Cain and Drexler ²⁵ distinguished between masking (the modification of odor quality to make it more acceptable) and counter-action (the reduction of malodor intensity to an acceptable level). Soon after, Lawless demonstrated individual components of a mixture are not only less intense when combined than when evaluated

separately, but also that mixing them influences pleasantness directly ²³. That is, when a pleasant stimulus is added to an unpleasant stimulus, some pleasantness is added directly, because of the presence of the pleasant stimulus itself, and some indirectly by decreasing the perceived intensity of the unpleasant stimulus. Here, we find evidence that the relatively well-liked cherry flavor directly improves liking of the harsh high nicotine condition (see Figure 3); this improvement seems to be due to the pleasantness of the cherry, but not masking or mixture suppression, as harshness itself was not reduced (i.e., the flavor by nicotine interaction for harshness was not significant). Indeed, there was no evidence of an effect of nicotine level or flavor on sweetness, while there was an effect of nicotine level on liking: thus, any change in liking is not mediated by changes in sweetness or harshness. This improvement is also distinct from mixture suppression that might come from adding a high potency sweetener. That said, Rosbrook and colleagues failed to find an effect of added sucralose (a high potency sweetener) on either harshness/irritation or liking ²⁶. Currently, it is unknown whether common ingredients in e-liquids like menthol or vanillin reduce negative sensations (via masking/mixture suppression) or merely add pleasantness directly, as occurred in our data. Elsewhere, added vanillin increases liking for sampled ethanol without modifying burn ²⁷; it remains to be determined whether adding vanillin to nicotine vapor might reduce harshness/irritation and/or increase pleasantness directly.

Notably, participants in this pilot study titrated their nicotine intake, regardless of the assigned flavor condition (see Figure 4, and Supplemental Figures 2 and 3). Collectively, these data suggest assigned flavor does not affect total nicotine intake in an acute lab setting. That said, our population consisted of current smokers or eCig users, so we cannot comment directly on the role of flavor in eCig initiation and early use from

these data. Meernik and colleagues conducted a systematic review of eCig literature, and found that multiple studies identify flavor as a reason for eCig appeal and use in both adults and youth ²⁸. Further, among youth, fruit, sweets, and beverage flavors significantly increased probability of choosing electronic nicotine delivery systems (ENDS) ²⁹.

Some limitations of the present study should be noted. Here, we only looked tested two flavors, and there are thousands of flavor options on the market in a wider variety of categories than what we included here. For example, Krüsemann and colleagues developed a flavor wheel to classify e-liquid flavors ³⁰, and they identified 13 main categories: tobacco, menthol/mint, nuts, spices, coffee/tea, alcohol, other beverages, fruit, dessert, candy, other sweets, other flavors, and unflavored. With so many options, it is likely that there is a flavor for nearly anyone who is interested in vaping. In our study, participants were randomly assigned to a condition, and we did not try to account for any existing flavor preferences a participant might have. In open ended comments, 12 participants mentioned using ‘mint’ flavored e-Liquid, while 9 mentioned ‘fruit’; ‘cherry’ was mentioned only once, and ‘chocolate’ was never mentioned. Further, nicotine level was also randomly assigned, without consideration of the level they typically used. Thus, the condition they were assigned to might have been a less liked flavor, or higher in nicotine than what they typically used. Spontaneous comments from the participants indicated the 18mg/ml nicotine level was too excessive for some individuals. Also, the wording used (“harshness/irritation”) may have primed participants to view this sensation from eCigs as negative; however, it is sometimes referred to as “throat hit”(e.g., ²²) which may have a more positive connotation for experienced nicotine consumers. Nor did we ask participants to abstain from nicotine

intake prior to the study, so individuals may have differed in the amount of time since they last vaped or smoked. Familiarity may also have played a role in liking: if an individual had been using cherry e-liquid prior to the study, it may have been rated more highly than would an unfamiliar chocolate flavor. Only men were tested here, so these findings may not generalize to women. We note this is a substantial limitation that must be addressed with additional research. Finally, due to an error in ballot construction, the wording of the Fagerstrom Test for Nicotine Dependence referred only to combustible tobacco cigarettes, which may have been confusing for participants who were eCig-only users; accordingly, these data were discarded. Knowing the level of dependence would be useful in future studies.

In conclusion, flavor has been well established previously as a key factor in the appeal of electronic cigarettes. Here, we contribute to this body of work by showing that acute liking did not predict greater nicotine intake in individuals who regularly vape, as it appears they can titrate their nicotine intake regardless of flavor. As expected, we find that more harshness/irritation reduces liking, while greater sweetness increases liking. Also, a well-liked flavor may make higher nicotine levels more tolerable by adding pleasantness directly. While diverse e-liquid flavors have been justified as a means to support smoking cessation, it is evident that some flavors can increase acute liking, even at high nicotine levels; whether such increases in acute liking translate to increased eCig initiation and abuse liability is currently unknown. A major concern with the prevalence of desirable eCig flavors is the appeal to individuals who otherwise might not consider using combustible nicotine containing products, especially if well liked flavors mitigate otherwise aversive sensations, thereby making the overall experience of eCig use more pleasant in young adults.

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Conflict of interest disclosure

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Baker et al. Supplemental Figures

Supplemental Figure 1: Liking ratings were generally stable over 10 minutes of ad libitum vaping.

Supplemental Figure 2: Amount vaped as a function of liking, measured in mg of nicotine. First puff liking did not predict total nicotine intake.

Supplemental Figure 3: Amount of eLiquid vaped over 10 minutes, as a function of assigned condition.