Short communication

The impact of flavoring on the rewarding and reinforcing value of e-cigarettes with nicotine among young adult smokers

Janet Audrain-McGovern [a,*], Andrew A. Strasser [a], E. Paul Wileyto [b]

[a] Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, United States
[b] Department of Biostatistics and Epidemiology, Perelman School of Medicine, University of Pennsylvania, United States

ARTICLE INFO

ABSTRACT

Objective: Flavored e-cigarette use has risen rapidly, especially among young adults who also smoke cigarettes. We sought to determine whether flavoring enhances the subjective rewarding value, relative reinforcing value, and absolute reinforcing value of an e-cigarette with nicotine compared to an unflavored e-cigarette with nicotine.

Methods: Using a within-subjects design, young adult smokers (n = 32) participated in three human laboratory sessions. Session 1 evaluated the rewarding value of flavoring by having participants rate unflavored and flavored e-cigarettes with nicotine. Session 2 assessed the relative reinforcing value of a flavored vs unflavored e-cigarette via a choice task that evaluated the willingness to "work" to hit targets on a computer screen to earn flavored or unflavored e-cigarette puffs. Session 3 measured the absolute reinforcing value of flavored versus unflavored e-cigarettes via a 90-min ad-libitum vaping session where puffs from each e-cigarette were counted.

Results: Subjective reward value was higher for the flavored versus the unflavored e-cigarette ($\beta = 0.83$, CI 0.35–1.32, p = 0.001). Participants worked harder for flavored e-cigarette puffs versus unflavored e-cigarette puffs (breakpoint = 5.7; 597 responses versus 127 responses; $\beta = 460.733$, CI 246.58–674.88, p < 0.0001). Participants took twice as many flavored puffs than unflavored e-cigarette puffs (40 vs 23 puffs; IRR = 2.028, CI 1.183–3.475, p = 0.01).

Conclusions: Flavoring enhances the rewarding and reinforcing value of e-cigarettes with nicotine, and thus their abuse liability in young adult smokers. Further research is necessary to determine whether the use of flavoring in e-cigarettes impacts cigarette smoking behavior among young adults.

© 2016 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Electronic cigarette (e-cigarettes) use has risen rapidly, especially among young adults (14.2%) who also smoke combustible cigarettes (59.3%; Berg, 2016; Kalkhoran and Glantz, 2016; McMillen et al., 2015). The availability of flavoring is the most frequently reported reason young people give for initiating and continuing to use e-cigarettes (Pesko et al., 2016; Villanti et al., 2013). While this research highlights a preference for flavoring among young adults, the factors that underlie such preferences has yet to be investigated. Flavoring may increase the subjective rewarding value, the relative reinforcing value, and the absolute reinforcing value of e-cigarettes with nicotine compared to unfla-

vored e-cigarettes with nicotine. We sought to examine these indices of abuse liability.

2. Methods

2.1. Participants and procedures

Young adult cigarette smokers were recruited from the community through print advertisements. Eligible smokers were between the ages of 18–30 years old, currently smoked ≥5 cigarettes a day for at least one year, and had used an e-cigarette at least once. Smokers who had a carbon monoxide (CO) breath sample <10 ppm, a positive urine screen for illicit drugs, psychotropic medication, or pregnancy were excluded. Smokers were also excluded from participation if they currently used nicotine products other than cigarettes, reported a psychiatric disorder (excluding nicotine dependence), and had never used an e-cigarette or used e-cigarettes daily. Young adult combustible cigarette smokers have

Table 1
Sample Characteristics (N = 32).

Demographics	
Sex	–
Female, n (%)	12 (38.0)
Male, n (%)	20 (62.0)
Age, M (SD)	25.0 (3.0)
Race/Ethnicity, n (%)	–
Asian	2 (6.0)
Black/African American	14 (44.0)
White	14 (44.0)
Multi-ethnic/Multi-Racial	2 (6.0)
Hispanic Ethnicity, n (%)	5 (16.0)
Highest education, n (%)	–
Some high school	1 (3.0)
High school graduate	7 (22.0)
Some college	17 (53.0)
College graduate	7 (22.0)
Smoking/E-cigarette History	
Cigs per day, M (SD)	11.4 (8.7)
Menthol Smoker, n (%)	18 (56.2)
Nicotine Dependence, M (SD)	3.66 (2.5)
Lifetime E-cig Use, M (SD)	12.0 (15.4)

Note. Lifetime e-cigarette use was the number of times.
(episodes) that an e-cigarette was used.

the highest rate of e-cigarette use (Berg, 2016; Kalkhoran and Glantz, 2016; McMillen et al., 2015). We recruited a sample that was neither naïve to e-cigarettes nor regular consumers to elucidate how flavoring may underlie e-cigarette uptake in young adult smokers. This sampling approach was approved by the Institutional Review Board.

Individuals were prescreened for inclusion and exclusion criteria via telephone and those meeting initial criteria attended a screening visit. After providing written informed consent, potential participants provided a CO to verify smoking status and a urine sample for a drug screen and pregnancy test. E-cigarette use was quantified by asking "How many times in your lifetime (past month, past week) have you used an e-cigarette, e-hookah, vape pen or personal vaporizer?" Pictures of each of these were included to promote clarity. Participants received $200 compensation for the completion of three laboratory visits. The second and third laboratory visits were separated by at least two days to allow smoking and nicotine intake to normalize after a 12-h smoking abstinence period and a two-hour laboratory visit that prohibited smoking. Table 1 provides a summary of the sample characteristics (n = 32).

2.1.1. Rewarding value of E-cigarette flavoring. At the initial visit, participants first received instructions for use and then had an opportunity to familiarize themselves with the tank-style e-cigarette by taking two puffs from a nonflavored e-cigarette without nicotine. The "e-GO" tank-style e-cigarette had a single 2.2-2.4 ohm resistance coil that could not be adjusted, 650 mAh rechargeable lithium ion battery and a 2.4 ml refillable e-liquid tank.

Participants then sampled three tank-style e-cigarettes; one contained unflavored e-liquid, one contained a fruit-flavored (green apple) e-liquid, and one contained a dessert-flavored e-liquid (chocolate). All three contained nicotine. The flavored and unflavored e-liquid was a 50/50 PG/VG blend containing 6, 12, or 18 mg/ml of nicotine depending on the nicotine content of the participant's usual cigarette brand and their smoking rate. For example, if a participant reported smoking 15 cigarettes per day and their usual brand had 0.8 mg/cig (e.g., Marlboro Light, Newport 100s), we assigned that participant to receive a 12 mg/ml e-liquid (e.g., 0.8 × 15 = 12). Of the 32 participants, 14 received the 6 mg e-liquid, 12 received the 12 mg e-liquid and 6 received the 18 mg

e-liquid. None of the participants reported that they found the e-cigarettes aversive.

Participants took two puffs from the nicotine alone e-cigarette, the fruit flavored e-cigarette, and the dessert flavored e-cigarette. We selected green apple and chocolate because sweet flavors are popular among e-cigarette users (Berg, 2016), promoting generalizability and the avoidance of exposure to aversive flavoring. The exposure to the three e-cigarettes was separated by 20 min each and the order of the three exposures was counterbalanced (Ray et al., 2006; Rukstalis et al., 2005). After each of the three e-cigarette exposures, participants completed measures of subjective reward.

2.1.2. Relative Reinforcing Value of E-cigarette Flavoring. For the second visit, participants arrived at the laboratory at 9:00 a.m. after overnight (12-h) abstinence (CO-verified <10 ppm). In preparation for the assessment of the relative reinforcing value of flavor (RRVF), participants received an introduction to a validated behavioral choice paradigm (Lussier et al., 2005; Perkins et al., 1994, 2009; Yoon et al., 2009) whereby they had the chance to earn points for flavored or unflavored e-cigarette puffs. The goal was to determine the motivation to use a flavored e-cigarette rather than to quantify the reinforcing value of specific flavors. The e-cigarette flavor with the highest rewarding value (measured at visit 1) served as the flavor for this assessment.

Assessment of the RRVF was accomplished by asking the participants to perform work, in the form of moving a computer mouse to hit targets on one of two computer screens, to earn points toward flavored or unflavored e-cigarette puffs. Using a concurrent schedule (Audrain-McGovern et al., 2015, 2014; Perkins et al., 1994; Perkins et al., 2002), participants were told that they could switch from working on one screen to the other as often as they wished. Participants were instructed to move the computer mouse to have the cursor hit the targets (either an apple/piece of chocolate or a water droplet alongside an e-cigarette; Norman and Jongerius 1985; Perkins, 2009; Perkins et al., 1994). Consistent with relative reinforcement paradigms, the reinforcement schedule in the unflavored e-cigarette earning screen remained constant at a fixed ratio FR-25 (25 targets achieved to earn a point) while the reinforcement schedule for the flavored e-cigarette increased (required more effort) with a progressive ratio schedule of PR–25 x over 10 trials, such that 25, 50, 75, 100, 125, 150, 175, 200, 225, and 250 targets had to be achieved to earn a point (Audrain-McGovern et al., 2015, 2014; Bickel et al., 2000; Epstein et al., 2007). As such, this task determined how reinforcing flavored puffs were relative to unflavored puffs by the willingness of the participant to work increasingly harder for them. RRVF was defined by the breakpoint or the highest trial (out of 10 trials) that was completed for flavored e-cigarette puffs.

The computer task was performed until a participant completed 10 trials and accumulated a total of 10 points from which they earned either one puff of an unflavored e-cigarette for each point (i.e., up to 10 puffs of an unflavored e-cigarette) or one puff of a flavored e-cigarette for each point (i.e., up to 10 puffs of a flavored e-cigarette). E-cigarette puffs were taken at the end of the procedure to prevent satiation from influencing responding in subsequent trials. To ensure that responding in the choice task was based on reinforcer preference rather than departure from the laboratory, the choice task was followed by a 1-h wait in the laboratory.

2.1.3. Absolute Reinforcing Value of E-cigarette Flavoring. For the third visit, participants arrived at the laboratory at 9:00 a.m. after overnight (12-h) abstinence (CO-verified <10 ppm). The absolute reinforcing value of flavored e-cigarettes as measured by a 90-minute ad libitum vaping paradigm in the laboratory, provided a measure of overall consumption (Arnold and Roberts, 1997). At this visit, participants had the opportunity to self-administer the unflavored or the flavored e-cigarette that the participant sampled at visit 1 and chose for the RRVF task at visit 2.