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Dual Use of Cigarettes, Little Cigars, Cigarillos, and Large Cigars: Smoking Topography and Toxicant Exposure

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Abstract

Objective—Smoking topography variables and toxicant exposure (plasma nicotine and exhaled CO) were examined in 3 groups of study participants that smoked both cigarettes and either filtered little cigars (Winchester), cigarillos (Black & Mild), or large cigars (Phillies Blunt).

Methods—Laboratory ad lib smoking of the cigar products was collected with a smoking puff analyzer; plasma levels of nicotine and exhaled CO were collected before and after smoking.

Results—Although there were no statistically significant differences in demographic and cigarette smoking topography among the groups, there were significant differences in how the different cigar products were smoked. Plasma nicotine boost was similar after all products but exhaled CO was greater after the cigarillo and large cigar than the little cigar. Some of the differences were due to the differences in article size but other differences were apparent even after adjustment for the amount of tobacco burned or the mouth intake (puff volume).

Conclusions—The topography findings of differences among products challenge the practice of grouping cigars as a single entity in surveys, regulatory decisions, and discussions of toxicant exposure. The results add to the discussion of distinctions among products in the scientific assessment of public health risk and regulatory decisions.

Keywords

little cigars; cigarillos; large cigars; tobacco; smoking; topography; toxicant exposure

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Human Subjects Statement

This study was approved by Battelle Memorial Institute's Institutional Review Board.

Conflict of Interest Statement

The authors have no conflicts of interest.

The way smokers consume combustible tobacco products is individualized.^{1,2} Two smokers of the same tobacco product may take different number of puffs, with various volume, velocity, and duration. Because of that unique product-user interaction, smokers may be potentially exposed to various levels of tobacco smoke constituents, even while smoking the same tobacco product. Many published studies show that measuring smoking behavior (topography) provides a valid and reliable index of smoking and an indirect measure of smoke exposure.^{3–6} Smoking topography is also a useful tool for assessing harm related to smoking, or even can be used to predict abstinence after using nicotine replacement therapy.⁷

Smoking topography is well described in the literature for combustible cigarettes. Data show that smoking topography may depend on many different factors including: sex,^{8,9} age,⁹ race, nicotine metabolism ratio, CYP2A6 genotype,⁸ or health status.^{10,11} However, to date, data available on smoking topography of other tobacco products (particularly cigars) is limited.

Assessing cigar smoking topography is challenging because there are multiple types of cigars available in the United States (US), including filtered small cigars, little cigars, cigarillos, and traditional large cigars. In 2014, large cigars and cigarillos made up 96% of the market share whereas little cigars comprised the other 4%.¹² Little cigars resemble cigarettes in size, tobacco weight, and shape; large cigars can be up to 20 or more times heavier than little cigars. Thus, it is important to differentiate these products and understand the distinct smoking topography and harm associated with the use of each.

Significant progress has been made in reducing cigarette smoking among US adults over the past 5 decades;¹³ however, cigar smoking is increasing in popularity. According to the US Centers for Disease Control and Prevention (CDC), in 2013, an estimated 12.4 million people in the US aged 12 years or older (or 5.2%) were current cigar smokers.¹² The CDC also reports that 8.2% of all students in grades 9–12 and 1.9% of all students in grades 6–8 were cigar smokers in 2014.¹²

The emergence of cigars raises new concerns. However, it was only as of May 2016 when cigars were included under FDA regulation.¹⁴ Nevertheless, cigars still are not regulated with the same restrictions as cigarettes. For example, in contrast to cigarettes, cigars are available in a wide variety of flavors. Cigars also can be sold singly or through other different options whereas cigarettes are sold in the US in packages of 20. Some cigar smokers, former/current cigarette smokers, and the nonsmoking public misperceive cigar smoking as being less harmful than cigarette smoking^{15–17} even though cigar consumption is associated with a risk of heart disease, pulmonary disease, and many types of cancer.^{12,18}

We have published previous papers comparing puffing topography, biomarkers of acute exposure [exhaled carbon monoxide (CO_{ex}) and plasma nicotine] and physiologic effects from usual brand cigarette and 3 separate types of cigar products: little cigars,⁵ cigarillos,³ and large cigars.⁶ This study, a secondary analysis, was designed to determine whether there were differences between smoking topography and toxicant exposure for cigar products in research study participants that smoke both cigarettes and cigars.

METHODS

Participants

Research volunteers were recruited from the Baltimore metropolitan area using newspaper advertisements, Craigslist, and snowball recruitment techniques between March 2013 and January 2015 to participate in one of 3 separate studies of dual use of cigarettes and cigars; 21 persons smoked little filtered cigars, 24 smoked cigarillos, and 17 smoked large cigars. All participants smoked at least 10 cigarettes per week and smoked at least one cigar product per week.

Procedure

The details of the procedures are described in previous publications^{3,5,6} and they were identical for each of the participant groups. Briefly, participants reported for 2 visits to the laboratory of approximately 2 hours each. Those that completed the study were compensated \$165. On their first visit, they signed an informed consent document that had been approved by the Battelle IRB. They answered questions about their demographics, smoking history, and nicotine dependence (FTND). A urine sample was collected for subsequent cotinine analysis and corrected for creatinine clearance. At one of the visits, they smoked their usual brand of cigarette. At the other visit they smoked either a Winchester filtered little cigar, a Black & Mild cigarillo, or a Phillies Blunt large cigar dependent on the size of the product they usually smoke. All laboratory-provided cigars were unflavored. Cigars were fitted to the mouthpiece of a Smoking Puff Analyzer (SPA/D) smoking topography machine (Sodim Instruments, MebTEC, Mebane, NC). All smoking was *ad lib*. Before smoking, participants that smoked either large cigars or cigarillos were shown a picture of the cigar article and they indicated how much of the product they usually consumed in a single smoking session. Cigars were weighed before and after smoking to calculate the amount of tobacco consumed.

Measures

Demographic and tobacco use characteristics—Personal smoking history and demographic information were collected at the first visit. The Fagerstrom Test for Nicotine Dependence (FTND) was used to assess cigarette dependence.¹⁹ Cotinine also was assessed at the first visit to provide an assessment of chronic nicotine exposure. Urine samples were analyzed by Labstat International ULC (Kitchener, Ontario, Canada). The lower LOQ for the cotinine assay was 8.78 ng/mL.

Outcome measures: smoking topography—Smoking topography was assessed from the SPA/D smoking topography unit. The article was inserted into the mouthpiece. Adapters were made so that the mouthpiece accommodated the various diameters of the products. The topography measured number of puffs, average puff volume (APV), total puff volume (TPV), puff duration (PD), puff velocity (PVel), and interpuff interval (IPI). Smoking topography of cigarette smoking has been found to be reliable and constant over time and not affected by smoking through a topography mouthpiece.^{4,20,21}

Outcome measures: toxicant exposure—Blood samples were collected before smoking and 5 and 10 minutes after smoking ended. The samples were centrifuged and the plasma was stored frozen until analysis for nicotine content by Virginia Commonwealth University using GC/MS methods. The lower limit of quantification (LOQ) of the measurement was 2.5 ng/mL. The difference between plasma nicotine before smoking and after smoking was calculated to determine the nicotine plasma boost – the absolute increase in plasma nicotine concentration.

Exhaled carbon monoxide (COex) was measured before and 2 minutes after smoking ended using a Breath CO Monitor (Vitalograph Inc., Lenexa, KS). Similarly, the difference between COex before smoking and after smoking was calculated to determine COex boost.

Outcome measures: subjective effects—The effect of the products to reduce tobacco craving was assessed using the brief form of the Questionnaire on Smoking Urges (QSU)^{22–24} and administered before smoking and 5 minutes after smoking ended. This 10-item questionnaire samples 2 dimensions of smoking urges – those that address the perceived positive effects of smoking (Factor 1) and the anticipated relief of tobacco withdrawal and craving (Factor 2). The total QSU score is the sum of the factor scores.

Product satisfaction and immediate effects were assessed using the Duke Sensory Questionnaire (DSQ) and the Cigarette Evaluation Scales (CES). These instruments were administered approximately 10 minutes after the completion of smoking, and both utilize a 7-point Likert scale in which 1 = “not at all” and 7 = “extremely.”

The (DSQ) contains 9 questions related to puff liking and satisfaction, nicotine in puffs, and puff strength (on the tongue, nose, mouth and throat, windpipe, chest), and similarity to own brand.²⁵ The CES was modified to query cigar smoking. It contains 11 questions related to product satisfaction, taste, and effects (ie, dizziness, calmness, concentration, wakefulness, hunger reduction, nausea, irritability, enjoyment of sensations, and reduction of craving).²⁶ Composite scores for satisfaction (satisfaction and good taste), psychological reward (calmness, concentration, wakefulness, hunger reduction and irritability), and aversion (dizziness and nausea) also were generated.

Outcome measures: initiation and continuation—Participants’ reasons for initiating and continuing the use of their respective cigar products was assessed using a brief qualitative questionnaire at the conclusion of the second visit.

Statistical Analysis

To account for the difference in product sizes and consumption, both plasma nicotine and COex boosts were adjusted for the amount of tobacco smoked (ng/mL/gm and ppm/gm of tobacco, respectively) and for mouth level exposure by adjusting for total PV (ng/mL/L and ppm/L of total PV). For each person, the CO and nicotine boost were divided by TPV (in liters) or the grams of tobacco consumed to give a ratio for that person that was reflective of the change in CO or plasma nicotine as a function of the amount of product burned or the amount of smoke puffed.

Two types of ANOVA models were utilized in the analyses of this data. One-way ANOVA models were fitted to the data collected once during each visit (ie, puff topography measures, DSQ, CES, and adjusted toxicant exposure). A 2×3 ANOVA model with fixed effects for time point (pre- and post-smoking) and cigar type (little cigar, cigarillo, and large cigar) and the interaction between time point and cigar type was fitted to the data for each dependent variable measured before and after smoking. ANOVA models are presented along with estimated marginal means and their 95% confidence intervals. The estimated marginal means are the means derived from the statistical model, and in the case of models with multiple effects, are means adjusted for other effects in the statistical model (as opposed to simple arithmetic means. F-values and p-values also have been included in the tables. A statistically significant ($p < .05$) test of an effect in an ANOVA model was followed by pairwise *post hoc* t-tests between the means. All data analyses were conducting using Stata version 13.1.

RESULTS

Participant Demographics and Smoking Characteristics

Table 1 displays the summary statistics for the demographic characteristics of the groups. They were mostly male, African-American, and lower income. The average age of participants in this sample was 41.0 years. Participants mostly preferred menthol cigarettes, smoked an average of 18.9 cigarettes per day, and began smoking around 13 years old. Each group had similar FTND scores that averaged 6.7 – a level that indicates significant nicotine dependence.²⁷ Little cigar and cigarillo smokers mostly preferred flavored cigars, whereas large cigar smokers mostly preferred unflavored cigars. The average age of cigar initiation was 25.8 years (33.9 for little cigars, 23.2 for cigarillos, and 19.7 for large cigars).

Outcome Measures

Cigarette smoking: puff topography and toxicant exposure—Puff topography of cigarette smoking was compared across the 3 groups of cigarette and cigar dual users (Table 2). There were no significant differences among the 3 cigar groups for any of the cigarette puff topography and nicotine exposure (all p s $> .072$). However, groups did differ slightly on CO exposure. Summary statistics for these outcomes can be found elsewhere.^{3,5,6}

Cigar smoking: puff topography—One-way ANOVA models revealed statistically significant differences among the 3 cigar groups on all puff topography parameters. Persons who smoked cigarillos and large cigars took significantly more puffs than those that smoked little cigars ($p < .001$). Persons who smoked cigarillos took significantly more time to smoke than those that smoked little cigars and large cigars ($p < .001$). The PVel for large cigar smokers was significantly greater than that of little cigar and cigarillo smokers ($p = .001$). The PD was significantly larger for cigarillo smoking than for little cigar smoking ($p = .004$). IPI was significantly longer for cigarillo smoking compared to large cigar smoking ($p = .044$). The total puff volume was significantly different for each of the cigar groups ($p < .001$).

Toxicant exposure—Table 3 shows the results of the ANOVA models for measures of toxicant exposure. There was a statistically significant effect of time for plasma nicotine and COex, suggesting that these measures increased from pre- to post-smoking across the cigar groups. There was also a significant interaction between time and product for COex suggesting that the change in COex from pre- to post-smoking was dependent on the product. This is further investigated in the one-way ANOVA model for COex presented in Table 3. COex increased significantly more after cigarillo and large cigar smoking than after little cigar smoking (24.8ppm and 23.5ppm vs 7.6ppm, respectively; $p < .001$). There was a significant effect for product, time, as well as the product X time interaction for the weight of tobacco. Significantly more tobacco was smoked during cigarillo and large cigar smoking than during little cigar smoking. Accounting for the weight of the filter, study participants smoked approximately 61% of the little cigar, 43% of the cigarillo, and 23% of the large cigar. There was a statistically significant correlation between the nicotine boost and the amount of tobacco consumed for cigarillo ($r = .58$, $p = .003$) and large cigar smoking ($r = 0.87$, $p = .003$) but not for little cigar smoking. When comparing the nicotine boosts from the cigarette and cigar conditions, only the large cigar group showed a statistically significant association ($r = 0.63$, $p = .007$).

After adjusting plasma nicotine boost for differences in consumption (ie, per gram of tobacco consumed and per L of total puff volume), there was a statistically significant effect for product type such that little cigars delivered significantly more nicotine per unit of consumption than cigarillos and large cigars. However, there was no difference in COex after adjusting for differences in consumption. Figure 1 shows the unadjusted and adjusted measures of toxicant exposure (ie, nicotine boost and COex boost).

Subjective effects—Subjective effects are presented in Table 4. There was a significant effect of time for each of the QSU 2×3 ANOVA models showing that smoking urge was reduced from pre- to postsmoking for each cigar group; the one-way ANOVA models of the DSQ revealed no statistically significant differences among the 3 cigar groups. However, little cigars were rated significantly lower than cigarillos and large cigars for satisfaction on the CES. Additionally, the change in QSU scores (Factor 1, Factor 2, and Total) did not significantly differ among the 3 cigar groups (all $ps > .971$).

Initiation and continuation—Study participants indicated their reasons for both initiating and continuing use of their respective cigars during a brief qualitative interview. The influence of peers was the most common reason for initiating cigar use cited by cigarillo and large cigar smokers (endorsed by 33% and 56% of the sample, respectively). However, cost was the most common reason for initiating cigar use cited by little cigar smokers (endorsed by 38% of the sample). Cost remained the most common consideration for continuing cigar use among little cigar smokers (endorsed by 52% of the sample). However, the appeal of flavoring was the most common reason for continuing the use of cigarillos and large cigars (endorsed by 42% and 31% of the sample, respectively).

DISCUSSION

The broad legal definition of a cigar, a tobacco rod encased in a wrapper that is at least partially composed of tobacco,²⁸ encompasses a wide variety of products that differ in size, design, filtration, flavor, cost, and packaging.¹² Furthermore, most people who smoke cigar products also smoke cigarettes.^{29,30} Despite the well-known diversity of both the product and the consumers they are often considered as a single entity in discussions of domestic smoking practices, epidemiological surveys, and regulation. Although this grouping may facilitate general discussion of cigars and use patterns, the results contained in this manuscript illustrate that differences among cigar products are manifest; they imply differences in toxicant exposure among cigar smokers and suggest that regulatory decisions about cigar smoking could be informed by consideration of these differences.

Three groups of dual users of both cigarettes and cigars were selected for 3 distinct laboratory studies where smoking of cigarettes and cigars was distinguished.^{3,5,6} Although, the present report centers on contrasting the results of the cigar smoking among the 3 groups, as mentioned above and in previous publications, the cigarette smoking in the groups was similar. Across the 3 groups there were no statistically significant differences in cigarettes per day, age of cigarettes initiation, measures of nicotine dependence (FTND) or smoking topography measures of PV, PD, IPI, total PV or total puffs. Despite similarities in cigarettes smoking, there were significant differences in smoking behavior among the cigar groups (Table 2). For example, PV and PD and other smoking topography variables were different among the 3 cigar classes. Some topography differences could be due to the size of the cigar article and other design features (eg, presence of a filter on the little cigar but not the other products); however, some variables that index the process of puffing (bringing smoke into the mouth) would seemingly be independent of the size of the article (eg, average puff volume). Importantly, topography differences cannot be attributed simply to differences in the size of the article in the mouth because all of the smoking was through a mouthpiece that was equal in size (at the mouth end) for all of the products.

When study participants smoked the cigars they all achieved a similar boost in plasma nicotine – a boost that appeared to be similar to the boost that they achieved after cigarette smoking. These data indicate that, like cigarette smokers, dual users of cigars and cigarettes smoke cigars to achieve a familiar level of nicotine. However, while achieving a familiar level of nicotine, there were significant and different increases in COex. Specifically, little cigar smokers had significantly lower levels of COex than cigarillos and large cigar smokers. These results indicate that in efforts to achieve levels of nicotine, cigar smokers (especially cigarillo and large cigar users) expose themselves to toxicant levels of CO and potentially other components of mainstream tobacco smoke.

To adjust nicotine and COex for differences in the size of the cigar articles and smoking behavior among the products statistically, we adjusted the plasma boost and COex per unit of consumption (per 1 gm of tobacco burned) and mouth level of exposure (per 1 liter of total puff volume). These comparisons suggested that CO exposure per unit of consumption was similar across the cigar groups whether smoking was adjusted for either amount or volume. On the other hand, little cigar smoking yielded higher levels of nicotine per unit of

consumption than either cigarillos or large cigars when smoking behavior was adjusted for grams of tobacco burned or total puff volume. These results tentatively suggest that little cigars are the most efficient nicotine delivery devices, whereas cigarillos and large cigars deliver more toxicants to achieve levels of nicotine, comparable to those resulting from little cigar smoking. These differences could occur because little cigars are sized and designed like cigarettes, and therefore, they are smoked like cigarettes. It is possible that, compared to other cigar articles, little cigars are inhaled more vigorously. Furthermore, mainstream smoke characteristics of little cigars may differ from that of large cigars or cigarillos. For example, Brunnemann and Hoffmann^{31,32} demonstrated that little cigar smoke generally has an acidic pH that is associated with easier inhalation than cigar products with a higher pH. Whatever the explanation, it is clear that all cigar products delivered significant and addictive quantities of nicotine and CO – findings that support the rationale for their regulation.^{3,5,6}

All of the cigar products reduced urges and craving for tobacco as measured by the QSU.^{22–24} This is a common finding among nicotine-delivering combustible products including bidis³³ and RYO.³⁴ E-cigarettes³⁵ and oral nicotine delivery products (Verve)³⁶ also reduce tobacco craving. Differences in product liking and puff evaluations were generally similar among the cigar products. These results were confounded by the experimental design decision to use only a single prototypical cigar product for all study participants. That decision resulted in differences in familiarity with referent cigar products among the groups – specifically, 62.5% (N = 15) of the cigarillo group ordinarily used Black & Mild (the referent product; 64.7% (N = 11) of the large cigar group ordinarily used Phillies Blunts (the referent product) but none of the little cigar group used the Winchester referent product.

The rapid and significant increase in plasma nicotine levels after smoking of cigar products among participants of all study groups strongly suggest that cigar smoking of any kind delivers nicotine in quantities that can engender and sustain nicotine addiction. This finding has implications for regulation of cigar products. There was another provocative, but limited qualitative finding in the present study that suggests that the cost of the product was an important determinant for initiation and continuation of use of little cigars, but not for cigarillo or large cigars. On the other hand, flavor of cigars seemed an important characteristic for the cigarillo and large cigar groups, but less so for the little cigar group. Although these findings are limited by sample size and group selection, they support findings from surveys^{37,38} and other qualitative data.³⁹ The results suggest that cigar regulation, like cigarette regulation, might center around cost and flavor.

Our studies were among the first that compared cigarettes to prototypical classes of cigars. The report by Koszowski et al⁴⁰ illustrates another purpose of the studies were to compare mainstream smoke constituents in the cigar products. That objective dictated that we choose a single referent prototypical cigar product for each of the groups. As noted above, there was an acknowledged difference in product familiarity with the cigar product among the experimental groups that could have influenced subjective, and possibly, the topography variables. Nevertheless, our findings add to the discussion of contemporary domestic cigar smoking and have implications for regulatory decisions. Current smoking surveys and

literature frequently combine the variables associated with cigar smoking into one or 2 groups. Our results show that there are significant differences among cigar products that go beyond differences in size and design; the various cigar classes are smoked differently and deliver differing level of CO and potentially other toxicants. The differences should be acknowledged in reports in the scientific literature and in regulatory decisions. The results contribute to the importance for a standardizing nomenclature of the cigar classes – the current classification is inadequate for either the users the scientific community or regulators to understand the nature of the product under consideration. Finally, in the deeming regulation announced in 2016, the FDA has asserted regulatory authority over cigars (and other products) that were not specifically named in the 2009 FSPTCA.¹⁴ The FDA has recognized the importance of a scientific basis for tobacco product regulation based on a public health standard. Our results support cigar regulation and add to the discussion of considerations of regulation across the wide variety of cigar products.

IMPLICATIONS FOR TOBACCO REGULATION

The domestic cigar market is comprised of a variety of smoking articles that differ in size, filtration, flavoring and product design but these products are often considered as a single entity. Our results show that there are significant differences in smoking topography and subsequent toxicant exposure among 3 prototypical cigar products. Even after adjustment for the amount of tobacco burned and the mouth level exposure, there were evident differences among the cigar products. The regulation of cigar products should acknowledge various cigar products as distinct entities.

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Figure 1.
Toxicant Exposure (Unadjusted and Adjusted)

Note.

*Adjusted for grams of tobacco consumed

^Adjusted for TPV

Table 1

Study Participant Demographics and Smoking Characteristics (N = 62)

DEMOGRAPHICS				
Variable	% (N) or Mean (SD)			
	Little Cigar N = 21	Cigarillo N = 24	Large Cigar N = 17	Total N = 62
Sex				
Male	71.4 (15)	91.7 (22)	94.1 (16)	85.5 (53)
Female	28.6 (6)	8.3 (2)	5.9 (1)	14.5 (9)
Race				
African American	61.9 (13)	79.2 (19)	76.5 (13)	73.6 (45)
Caucasian	33.3 (7)	12.5 (3)	17.7 (3)	21.0 (13)
Other	4.8 (1)	4.3 (2)	5.9 (1)	6.5 (4)
Education				
Less Than High School	28.6 (6)	25.0 (6)	11.8 (2)	22.6 (14)
High School Grad/GED	38.1 (8)	54.2 (13)	52.9 (9)	48.4 (30)
More Than High School	33.3 (7)	20.8 (5)	35.3 (6)	29.0 (18)
Income				
<\$20,000	76.2 (16)	66.7 (16)	76.5 (13)	72.6 (45)
\$20,000–\$35,000	14.3 (3)	16.7 (4)	23.5 (4)	17.7 (11)
>\$35,000	9.5 (2)	16.7 (4)	0	9.7 (6)
Age				
Mean (SD)	47.5 (9.5)	38.9 (12.3)	36.1 (7.9)	41.0 (11.2)
SMOKING CHARACTERISTICS				
Preferred Cigarette Flavor				
Menthol	81.0 (17)	87.5 (21)	94.1 (16)	87.1 (54)
Non-Menthol	19.0 (4)	12.5 (3)	5.9 (1)	12.9 (8)
Cigarettes Smoked Per Day				
Mean (SD)	17.4 (4.3)	19.0 (8.8)	20.5 (8.0)	18.9 (7.4)
Age of Cigarette Initiation				
Mean (SD)	12.4 (3.1)	13.9 (3.7)	13.4 (3.1)	13.3 (3.4)
Preferred Cigar Flavor				
Flavored	71.4 (15)	83.3 (20)	41.2 (7)	67.7 (42)
Unflavored	28.6 (6)	16.7 (4)	58.8 (10)	32.3 (20)

DEMOGRAPHICS				
Variable	% (N) or Mean (SD)			
	Little Cigar N = 21	Cigarillo N = 24	Large Cigar N = 17	Total N = 62
Age of Cigar Initiation				
Mean (SD)	33.9 (12.2)	23.2 (9.9)	19.7 (7.8)	25.8 (11.7)
Urinary Cotinine (µg/g) *				
Mean (SD)	1270.6 (728.4)	905.6 (969.3)	793.1 (408.8)	998.4 (782.7)
FTND				
Mean (SD)	6.8 (1.5)	6.5 (1.7)	6.9 (1.6)	6.7 (1.6)

Note.

* Corrected for creatinine

Puff Topography

Table 2

Outcome Measure	Estimated Marginal Means (95% CI)			F	p
	Little Cigar (N = 21)	Cigarillo (N = 24)	Large Cigar (N = 17)		
Number of Puffs ^{ab}	9.8 (6.2–13.4)	23.1 (19.7–26.5)	22.6 (18.6–26.6)	17.3	< .001
Total Time To Smoke (s) ^{ac}	239.3 (129.8–348.9)	607.4 (504.9–709.8)	370.6 (248.9–492.4)	12.5	< .001
Average Puff Volume (mL) ^{abc}	41.5 (34.2–48.8)	57.0 (50.1–63.8)	73.9 (65.8–82.0)	17.6	< .001
Puff Velocity (mL/s) ^{bc}	22.0 (18.2–25.8)	23.6 (20.1–27.2)	34.3 (30.1–38.5)	11.0	< .001
Puff Duration (s) ^a	2.0 (1.6–2.3)	2.8 (2.5–3.1)	2.5 (2.1–2.8)	6.1	.004
Interpuff Interval (s) ^c	20.8 (16.6–25.1)	24.5 (20.5–28.5)	16.6 (11.9–21.3)	3.3	.044
Total Puff Volume (mL) ^{abc}	399.0 (123.4–674.7)	1,252.3 (994.5–1,510.2)	1,659.8 (1,353.4–1,966.1)	20.3	< .001

Note.

^a denotes significant difference between little cigar and cigarillo smoking

^b denotes significant difference between little cigar and large cigar smoking

^c denotes significant difference between cigarillo and large cigar smoking

Toxicant Exposure

Table 3

Outcome Measure	Little Cigar	Cigarillo	Large Cigar	Product Main Effect F (p)	Time Main Effect F (p)	Product X Time Interaction F (p)
Plasma Nicotine (ng/mL)						
Pre-smoking	18.1 (11.2, 25.0)	11.5 (5.0, 17.9)	20.7 (13.0, 28.4)	2.14	37.2	0.23
Post-smoking	35.3 (28.4, 42.2)	31.7 (25.2, 38.1)	36.3 (28.6, 44.0)	(.122)	(<.001)	(.797)
Difference ^a	17.2 (10.0, 24.4)	20.2 (13.5, 27.0)	15.6 (7.6, 23.6)	0.42 (.657)	N/A	N/A
COex (ppm)						
Pre-smoking	28.1 (20.1, 36.0)	17.5 (10.0, 24.9)	22.3 (13.5, 31.1)	0.72	32.92	3.09
Post-smoking	35.7 (27.7, 43.6)	42.3 (34.9, 49.7)	47.4 (38.5, 56.2)	(.489)	(<.001)	(.049)
Difference ^{a,b}	7.6 (1.5, 13.7)	24.8 (19.1, 30.5)	23.5 (16.7, 30.3)	9.99 (<.001)	N/A	N/A
Tobacco Weight (g)						
Pre-smoking	0.9 (0.7, 1.1)	3.1 (2.9, 3.3)	6.6 (6.4, 6.8)	1436.97	213.70	15.05
Post-smoking	0.4 (0.2, 0.6)	1.8 (1.6, 1.9)	5.1 (4.9, 5.3)	(<.001)	(<.001)	(<.001)
Difference ^{a,b}	0.5 (0.3, 0.7)	1.3 (1.1, 1.5)	1.5 (1.3, 1.7)	28.72 (<.001)	N/A	N/A
Adjusted Plasma Nicotine^a						
Difference (ng/mL/g of tobacco smoked) ^{a,b}	32.5 (26.4, 38.7)	14.4 (8.9, 19.8)	7.8 (1.4, 14.3)	17.08 (<.001)	N/A	N/A
Difference (ng/mL/1L total puff volume) ^{a,b}	41.7 (35.0, 48.5)	15.3 (9.0, 21.6)	8.7 (1.2, 16.2)	25.72 (<.001)		
Adjusted COex^a						
Difference (ppm/g of tobacco smoked)	14.6 (10.3, 18.8)	18.0 (14.2, 21.8)	15.9 (11.4, 20.4)	0.76 (.474)	N/A	N/A
Difference (ppm/1L total puff volume)	18.5 (13.7, 23.3)	19.1 (14.6, 23.6)	16.2 (10.8, 21.5)	0.38 (.687)		

Note.

^a denotes significant difference between little cigar and cigarillo smoking for one-way ANOVAs

q denotes significant difference between little cigar and large cigar smoking for one-way ANOVAs
 χ^2 One-way ANOVA

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Table 4

Subjective Measures

Outcome Measure	Little Cigar Smoking	Cigarillo Smoking	Large Cigar Smoking	Product F-value (p-value)	Time F-value (p-value)	Interaction F-value (p-value)
Questionnaire on Smoking Urges (QSU) - Factor 1						
Pre-smoking	21.4 (17.5, 25.3)	23.0 (19.4, 26.5)	24.5 (20.3, 28.7)	1.18 (.310)	35.81 (<.001)	0.01 (.995)
Post-smoking	11.7 (7.8, 15.6)	13.6 (10.0, 17.1)	14.8 (10.6, 19.0)			
Difference ^a	-9.7 (-13.9, -5.5)	-9.4 (-13.2, -5.6)	-9.7 (-14.2, -5.2)	0.01 (.991)	N/A	N/A
Questionnaire on Smoking Urges (QSU) - Factor 2						
Pre-smoking	16.3 (12.8, 19.7)	18.6 (15.4, 21.8)	17.4 (13.6, 21.1)	0.89 (.414)	18.54 (<.001)	0.02 (.985)
Post-smoking	10.0 (6.5, 13.5)	12.1 (8.9, 15.3)	11.5 (7.7, 15.3)			
Difference ^a	-6.3 (-9.8, -2.7)	-6.5 (-9.8, -3.2)	-5.9 (-9.8, -2.0)	0.03 (.971)	N/A	N/A
Questionnaire on Smoking Urges (QSU) - Total						
Pre-smoking	37.7 (30.5, 44.8)	41.6 (35.1, 48.1)	41.9 (34.1, 49.6)	0.90 (.409)	28.79 (<.001)	0.00 (.999)
Post-smoking	21.7 (14.6, 28.8)	25.7 (19.2, 32.2)	26.3 (18.6, 34.0)			
Difference ^a	-16.0 (-23.5, -8.4)	-15.9 (-22.7, -9.0)	-15.6 (-23.7, -7.4)	0.00 (.998)	N/A	N/A
Duke Sensory Questionnaire (DSQ) ^a						
Puff liking	4.1 (3.5, 4.9)	5.0 (4.3, 5.6)	4.7 (3.9, 5.5)	1.36 (.263)	N/A	N/A
Puff satisfaction	4.2 (3.5, 4.9)	5.1 (4.5, 5.8)	4.9 (4.2, 5.7)	2.21 (.118)	N/A	N/A
Nicotine in puffs	5.3 (4.6, 5.9)	5.0 (4.4, 5.6)	4.8 (4.1, 5.5)	0.48 (.624)	N/A	N/A
Strength	20.2 (17.1, 23.4)	21.7 (18.8, 24.6)	22.9 (19.5, 26.4)	0.67 (.514)	N/A	N/A
Cigarette Evaluation Scale (CES) ^a						
Sensation	4.0 (3.0, 4.9)	4.5 (3.6, 5.4)	4.4 (3.4, 5.4)	0.43 (.656)	N/A	N/A
Craving reduction	4.6 (3.7, 5.5)	4.5 (3.6, 5.4)	4.8 (3.8, 5.8)	0.08 (.921)	N/A	N/A
Satisfaction ^{bc}	3.8 (3.1, 4.5)	5.2 (4.6, 5.8)	5.2 (4.4, 5.9)	5.55 (.006)	N/A	N/A

Outcome Measure	Little Cigar Smoking	Cigarillo Smoking	Large Cigar Smoking	Product F-value (p-value)	Time F-value (p-value)	Interaction F-value (p-value)
	Estimated Marginal Means (95% CI)					
			5% CI			
Psychological Reward	3.4 (2.2, 4.6)	3.7 (2.6, 4.8)	5.3 (4.0, 6.6)	2.75 (.072)	N/A	N/A
Aversion	1.8 (1.3, 2.3)	2.1 (1.6, 2.5)	1.9 (1.4, 2.5)	0.34 (.713)	N/A	N/A

Note.

^aOne-way ANOVA

^bdenotes significant difference between little cigar and cigarillo smoking for one-way ANOVAs

^cdenotes significant difference between little cigar and large cigar smoking for one-way ANOVAs