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Effects of flavourants and humectants on waterpipe tobacco puffing behaviour, biomarkers of exposure and subjective effects among adults with high versus low nicotine dependence

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Abstract

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Introduction—Flavourants and humectants in waterpipe tobacco (WT) increase product appeal. Removal of these constituents, however, is associated with increased intensity of WT puffing, likely due to reduced nicotine delivery efficiency. To clarify the potential public health outcomes of restrictions on flavourants or humectants in WT, we evaluated the effects of these constituents on puffing behaviours, biomarkers of exposure and subjective effects among adults with high versus low WT dependence.

Methods—N=39 high dependence and N=49 low dependence WT smokers (Lebanese Waterpipe Dependence Scale scores ≥10 = high dependence) completed four smoking sessions in a cross-over experiment. Conditions were preferred flavour with humectant (+F+H), preferred flavour without humectant (+F−H), unflavoured with humectant (−F+H) and unflavoured without humectant (−F−H). Measures of puff topography, plasma nicotine and expired carbon monoxide (eCO) boost, and subjective effects were assessed.

Results—Level of WT dependence modified the effect of WT condition on average flow rate, average puff volume and eCO boost. Although, overall, participants puffed the +F+H WT least intensely and −F−H WT most intensely, this association was strongest among WT smokers with high dependence. Participants preferred smoking the +F+H WT and achieved the largest plasma nicotine boost in that condition.

Discussion—Findings underscore the complexity of setting product standards related to flavourants and humectants in WT. Future research evaluating whether WT smokers with high dependence would quit or reduce their WT smoking in response to removal of flavourants or humectants from WT is necessary to appreciate the full public health effects of such policies.

INTRODUCTION

The prevalence of waterpipe tobacco (WT) use remains high globally and is increasing in several countries.[1] In the USA, an estimated 2.6 million adults smoke tobacco in pipes or waterpipes.[2] Like other smoked tobacco products, WT smoking is associated with long-term health risks, including lung cancer,[3 4] oral cancer,[4] chronic obstructive pulmonary disease[4] and cardiovascular disease.[4 5] Due to nicotine exposure, WT smoking might also confer increased risk of health consequences that emerge during youth and young adulthood, such as impairment of brain development,[6] behavioural changes,[7] and development of nicotine dependence.[8]

One of the reasons WT smoking continues to surge in spite of the negative health consequences is the presence of characterising flavours in WT. In addition to leading some smokers to believe that flavoured WT is less harmful than unflavoured tobacco,[9] smoking flavoured WT is an easier and more satisfying activity.[10] Flavoured WT is especially appealing to youth,[11] with 89% of people in the USA who initiated WT smoking during youth starting with flavoured WT.[12] Although flavoured WT is generally preferred, WT smokers tend to puff unflavoured WT more intensely.[10 13 14] For example, laboratory smoking studies have identified statistically significant increases in average puff volume[10 13] and total puff volume,[14] and thus greater exposure to toxicants, when participants smoked unflavoured WT compared with their preferred flavour.

These laboratory smoking studies also found that the increased intensity of puffing unflavoured WT did not translate to an increase in plasma nicotine boost relative to smoking flavoured WT.[10 13 14] This result is likely due to the increased concentration of humectants, including glycerol and propylene glycol, in flavoured WT. Although humectants are used in most flavoured and unflavoured WT sold in the USA, recent analysis of WT from an internationally popular WT brand identified that flavoured WT had approximately 20 times the level of humectants as unflavoured WT.[15] Not only do these humectants add moisture to the WT, but they also sweeten it while increasing smoke production and nicotine delivery efficiency.[16] WT smokers compensate by puffing more intensely when faced with lower nicotine in the mainstream smoke they are inhaling.[17] Thus, smokers likely puffed harder when they were smoking unflavoured WT, in part, because they had some level of nicotine dependence and were trying to compensate for the reduced transfer of nicotine to the smoke as a result of low humectant content. Prior work[14] that evaluated both the effects of flavourants and humectants on WT smoking supported this theory. Specifically, although participants preferred smoking WT with flavourants and humectants, they smoked WT without characterising flavours or humectants most intensely.[14] Importantly, their plasma nicotine boost was lowest, but their expired carbon monoxide (eCO) boost was highest, when smoking WT without humectants.[14]

Flavourants and humectants in WT have been largely unregulated. In Germany, humectant concentration of WT must be below 5%[18]; however, humectants are sold separately and are commonly mixed into the WT by the user. The US Food and Drug Administration (FDA) has had the authority to regulate WT since 2016,[19] but no regulatory action related to flavourants or humectants in WT has been taken. Given the increased appeal of flavoured and high humectant WT, but more intense puffing of unflavoured and low humectant WT, it is unclear what public health effect a regulatory action limiting characterising flavours or humectants would have on the prevalence and health effects of waterpipe smoking. In fact, it is possible that these regulations would differentially affect WT smokers according to their level of WT dependence due to differences in their smoking patterns and craving for nicotine.[20–22] For example, when smoking their preferred brand of WT, smokers with high dependence (vs low dependence) inhaled more slowly, but also for longer and more frequently.[20] High frequency smokers (vs low frequency smokers) were also more likely to increase the intensity of their puffing when smoking a nicotine-free (compared with preferred brand) waterpipe product,[21] but less likely to change the intensity of their puffing when smoking unflavoured (compared with preferred flavour) WT.[22]

In summary, existing research has identified heterogeneous effects of flavourants and nicotine content on WT smoking topography according to level of dependence and frequency of use. An important research gap, however, is the potential heterogeneous effect of humectants on WT smoking among smokers with differing levels of dependence. With the potential to make WT less appealing and less addictive by regulating the humectant concentration of WT, this gap is an important one. The current study builds on our prior work that evaluated the effects of both flavourants and humectants subjective effects, smoking topography and biomarkers of exposure by studying these outcomes specifically among WT smokers with high vs low dependence. We hypothesised that smokers with high WT dependence will be more likely to increase the intensity of their puffing as flavourants and humectants are removed from WT to improve nicotine delivery, but that all smokers will prefer WT with flavourants and humectants.

METHODS

Setting and participants

Details about recruitment procedures have been reported previously.[14] Briefly, all study procedures occurred from May 2017 to January 2018 in Oklahoma City, Oklahoma. Participants (N=89 participants in N=44 dyads) were recruited via convenience sampling methods, including internet advertisements and word of mouth. Eligibility criteria included (1) current WT smoking for at least the past 6 months, (2) being between the ages of 18 and 50 years and (3) agreeing to abstain from tobacco (confirmed by eCO <10 ppm at start of visit), nicotine and marijuana use for 12 hours prior to each study visit. Exclusionary criteria included (1) self-reported lung disease; (2) cardiac events or distress in the past 3 months; (3) pregnancy, breast feeding or planning to become pregnant and (4) past 30-day use of illicit drugs (excluding marijuana).

Design and procedures

We used a randomised cross-over design, with randomisation to type of WT tobacco (described below) counterbalanced and occurring at the dyad level. Dyads participated in four clinic visits, during which they completed a presmoking questionnaire, smoked WT from separate waterpipes, then completed a postsmoking questionnaire. Dyads completed all four clinic visits at the same time of day, with up to 2 hours of flexibility as necessary. WT tobacco conditions included (1) preferred characterising flavour and high humectant (+F+H), preferred characterising flavour and low humectant (+F−H), no characterising flavour and high humectant (−F+H), and no characterising flavour and low humectant (−F−H). After completing the study, we identified that the −F+H and −F−H products did not differ in level of nicotine, and both had humectant contents of less than 5%.[14] Thus, we collapsed these smoking conditions for each participant and relabelled them as −F−H for analyses. Because this condition was repeated, a main effect for time point was included in all statistical models.

WT smoking sessions occurred in a controlled laboratory setting in a room under negative pressure. All participants smoked ad libitum for up to 1 hour; a subset of participants (N=50 participants in N=25 dyads) completed a standardised puffing session before ad libitum smoking. During the standardised puffing session, participants were instructed to puff every 30 s for 5 min. Participants sat next to their dyad partner for smoking sessions. One piece of lit charcoal was placed on top of the perforated foil on the waterpipe; additional preweighted, lit charcoal was provided on request. Smoking topography was measured continuously for each participant. Venous blood samples and eCO were collected immediately before and after each smoking session. Participants received US$50 for attending each clinic visit and an additional US$50 as a bonus for completing all clinic visits.

Participants provided informed consent prior to completing study procedures.

Materials

Participants smoked WT from one-hose Mya waterpipes. Water level, foil type and leather hoses were consistent across each smoking session. New, sterile, disposable mouthpieces were used for each smoking session. Ten grams of WT were placed in a glazed ceramic bowl atop the waterpipe and covered with prepunched aluminium foil. Charcoal briquettes were weighed, then lit and placed on top of the foil. A pressure transducer integrated into the waterpipe hose was used to measure smoking topography.

For the two conditions where participants smoked their preferred flavour of WT (ie, +F+H and +F−H), each participant chose his or her own preferred flavour from six Nakhla flavoured tobacco options: double apple (35%), strawberry (35%), mandarin (12%), lemon (12%), apple (4%) or vanilla (2%). Flavour choice was made during screening, and the same flavour was used for both sessions. Participants within dyad were permitted to smoke different WT flavours. For the two conditions where participants smoked WT without characterising flavours, Nakhla Zaghloul WT was smoked. Although it did not have characterising flavours, Nakhla Zaghloul nonetheless differs from other unflavoured WT smoked in the Middle East and Asia that use dry leaves.[23]

Measures

Dependent variables—We evaluated four domains as dependent variables: (1) smoking topography, (2) biomarkers of exposure, (3) subjective drug liking and (4) behavioural intentions. For smoking topography, measures included average flow rate, interpuff interval, puff volume and puff duration; maximum puff volume; puff time and smoking time; and total inhaled volume and number of puffs. For biomarkers of exposure, measures included eCO boost and plasma nicotine boost. eCO, a biomarker of smoke exposure, was assessed using a handheld monitor (Smokerlyzer Micro, Bedfont Scientific) immediately before and after the smoking session. For plasma nicotine, venous blood was drawn immediately prior to and following (within 5 min) the ad libitum smoking session. Plasma nicotine analyses were completed using liquid chromatography tandem mass spectrometry. eCO and plasma nicotine boosts were calculated by subtracting the presmoking levels from the postsmoking levels. Subjective drug liking was measured after the smoking session with six items: enjoyment, interest in future use, liking, finding the product pleasurable, finding the product satisfying and willingness to use in the future.[13] Responses were recorded using a Visual Analogue Scale ranging from 0 ('not at all') to 100 ('extremely'). Behavioural intentions[24] to continue using WT were also measured after the smoking session. Participants reported how likely they were to:'try this product again,' 'pay to smoke this product at a waterpipe lounge/bar,' 'purchase this product for personal use,' and 'use this product regularly.' Responses were recorded using a 5-point Likert scale ranging from 'extremely unlikely' to 'extremely likely.' To increase the cell sizes for modelling, responses were dichotomised to two groups: extremely unlikely/unlikely/neutral versus likely/extremely likely.

Independent variables—Independent variables included WT condition (described above) and level of WT dependence. WT dependence was measured prior to smoking at the first visit using the Lebanese Waterpipe Dependence Scale-11, which measures frequency and context of smoking, cessation self-efficacy, motivations for smoking and to what extent participants would sacrifice food or income to smoke.[25] Participants with scores ≥10 were classified into the high dependence group, as 10 is the threshold for clinical dependence.[25]

Covariates—Covariates were self-reported at the first study visit. Measures included age (dichotomised to 18–24 and 25+), race and ethnicity (collapsed to non-Hispanic white, non-Hispanic black and other), sex (male or female), education level (collapsed to high school or General Equivalency Diploma [GED], some college or associate's degree and bachelor's degree or higher), yearly household income (dichotomised to <US$50 000 and ≥US$50,000), and use of other tobacco products (ie, use of cigarettes, electronic cigarettes, cigars, cigarillos, little cigars, snus or smokeless tobacco monthly or more vs less).

Data analysis

First, distributions of continuous dependent variables (ie, topography, plasma nicotine boost, eCO boost and subjective drug liking) were evaluated. Topography measures were then winsorised at the 1st and 99th percentiles to address potential outliers while maintaining sample size. Next, distributions of covariates were compared by level of WT dependence using χ^2 tests or Fisher's exact tests, depending on cell size. Covariates that were imbalanced across WT dependence groups were controlled in adjusted analyses. Finally, we used mixed-effects linear regression (for topography, biomarkers of exposure, and subjective drug liking dependent variables) and logistic regression (for behavioural intentions dependent variables) to model the joint effects of WT dependence and WT condition on our dependent variables. We specified random intercepts for dyad and participant in all models. Assumptions of homoscedasticity and normality of errors were checked. Likelihood ratio tests were used to compare models with WT-condition-by-dependence product interaction terms to reduced models without the product interaction terms. The alpha level was set to 0.05 for initial analyses and Holm's procedure was used to adjust the alpha for post hoc pairwise comparisons.[26]

RESULTS

Participant characteristics

Characteristics of study participants have been reported previously.[14] Briefly, overall, the sample was majority male, young adult (vs older adults) and non-Hispanic white (table 1). Compared with participants with low WT dependence (N=49), participants with high WT dependence (N=39) were more likely to be younger adults (p=0.03) and to use other tobacco products monthly or more often (p=0.01). As a result, these variables were controlled in adjusted analyses.

Unadjusted distributions of dependent variables by WT condition and dependence level

Smoking topography—Among smokers with high WT dependence, descriptive analyses revealed that intensity of puffing increased as flavourants and humectants were removed/reduced from the WT (table 2). Specifically, mean values of average flow rate, average puff duration and average puff volume were lowest in the +F+H condition and highest in the −F−H condition, with mean values in the +F−H condition falling in between. The summary measures of total inhaled volume and total number of puffs generally followed the same pattern, with the highest mean values occurring in the −F−H condition. These summary measures also had notable variability in the +F+Hcondition. For total inhaled volume, the range was 3.9–206.6 L. For total number of puffs, the range was 7–346.

Among smokers with low WT dependence, a similar, but more attenuated, pattern was observed for topography measures. For example, the mean difference between the +F+H and −F−H conditions with respect to average flow rate was 1.4 L per minute among low dependence smokers, but 3.5 L per minute among high dependence smokers (table 2).

Biomarkers of exposure—Overall, participants had the greatest plasma nicotine boost when smoking +F+H WT—with values roughly double that observed in the other conditions. Among high dependence smokers, the +F−H condition resulted in the lowest plasma nicotine boost; among low dependence smokers, both the +F−H and −F−H conditions resulted in similar plasma nicotine boosts. eCO results confirmed the topography findings, with both user groups having the highest eCO boost when smoking the −F−H WT, and the variability being greatest among high dependence smokers.

Subjective drug liking and behavioural intentions—According to our measures of subjective drug liking and behavioural intentions, both high and low dependence WT smokers preferred the +F+H WT (table 2). Among high dependence smokers, however, there was little difference in subjective drug liking between the +F+H and +F−H conditions; when flavourants were removed (ie, −F−H WT), subjective drug liking decreased more substantially.

Low dependence smokers liked the +F+H WT more than high dependence smokers on average. There was little difference in their subjective drug liking of +F−Hand −F−H WT flavours when compared with high dependence smokers, however. Although they reported liking the +F+H WT more, low dependence smokers generally had similar behavioural intentions for use of this type of WT as high dependence smokers. They had reduced behavioural intentions for the +F−H and −F−H WT conditions compared with high dependence smokers.

Evaluation of interaction between WT dependence and WT condition on dependent variables

Level of WT dependence modified the effect of WT condition on average flow rate and average puff volume in adjusted analyses (table 3). Specifically, the variability in average flow rate and average puff volume was greater for high dependence than low dependence smokers (figure 1). This resulted in a greater variability in eCO boost for high dependence smokers, with the greatest eCO boost occurring in the −F−H WT condition (table 3, figure 1). Overall, −F−H tobacco was smoked most intensely, and +F+H WT was smoked least intensely by all smokers, but differences were greatest for high dependence smokers.

Post hoc pairwise comparisons revealed that, among high dependence smokers, the largest differences in average flow rate and average puff volume occurred when comparing WT with and without humectants (ie,+F−Hvs +F+Hand −F−H vs +F+H; all p’s<0.001; figure 1). No differences were detected in average flow rate and average puff volume when comparing WT conditions with and without flavourants (ie, +F−H vs −F−H; p=0.44 and p=0.78, respectively). The opposite pattern was observed among low dependence smokers. Their largest differences in average flow rate and average puff volume were observed when comparing WT with and without flavourants (all p's<0.02), and no differences were detected when comparing flavoured WT with and without humectants (p=0.77 and p=0.21, respectively).

Notably, level of WT dependence did not modify the effect of WT condition on plasma nicotine boost in adjusted analyses (table 3; figure 1). It also did not modify the effect of WT condition on subjective drug liking or behavioural intentions.

DISCUSSION

This was the first study to evaluate the effects of WT flavourants and humectants on smoking behaviours, biomarkers of exposure, and subjective effects among adults with high and low WT dependence. We identified that removal of flavourants and humectants from WT had a larger effect on the smoking behaviours of high dependence smokers than low dependence smokers. High dependence smokers had greater increases in the intensity of their puffing as flavourants and humectants were removed/reduced. Both high and low dependence smokers preferred the +F+H WT, however, and intentions to use the −F−H WT in the future were quite low (eg, 38.7% of high dependence and 27.3% of low dependence smokers said they would try the product again). Moreover, plasma nicotine boost was highest for both groups of smokers when they smoked the +F+H tobacco. This pattern of results suggests that regulations restricting or banning flavourants and humectants from WT could make the product less appealing and less addictive for new smokers and WT smokers with high or low dependence, but might lead to increased toxicant exposure in high dependence smokers if they do not reduce or quit WT smoking.

Our prior work identified that removal/reduction of flavourants and humectants increased intensity of puffing among WT smokers overall,[14] and the current study found that the specific component removed from WT (ie, flavourants or humectants) differentially affected the puff topography of high dependence versus low dependence smokers. For high dependence smokers, the greatest increase in puff intensity appeared to occur when humectants were reduced, although the absence of a −F+H condition prevented us from directly estimating the effect of humectants on puffing behaviour when flavourants were absent. Considering that humectants increase the nicotine delivery efficiency of WT,[16] these results are in agreement with what has been hypothesised by other studies[21 22]: that high dependence smokers likely increased the intensity of their puffing to improve nicotine delivery. Relatedly, the effect of removing flavourants was likely less important for these participants than the loss of nicotine delivery efficiency from humectant reduction. Increases in total particulate matter and fraction of the nicotine in burned tobacco (ie, greater 'transfer efficiency') are transferred to the mainstream smoke from WT with higher levels of huemctants.[16 27] For low dependence smokers, the greatest increase in puff intensity occurred when flavourants were removed. The reason behind these results is less clear, but could be related to the decreased smoke production reported by participants and research assistants when smokers were smoking WT in the −F−H condition.[14]

The mechanism behind the greater nicotine transfer efficiency associated with humectants in WT is not yet known. Nicotine may reside solely in the unburned tobacco leaf, and, simplistically stated, when heated to 160°C–220°C (ie, temperatures reached in the head of a waterpipe[28]) will thermally transfer to the gas phase,[29] where it can readily dissolve into the glycerol (the primary humectant) and water present in the mainstream smoke. In addition, nicotine may already be solvated by the glycerol in the WT, given the mechanical mixing that is required to incorporate such high concentrations of humectants and syrups during manufacturing. Given nicotine's complete miscibility in both glycerol and water, the greater nicotine transfer efficiency associated with higher humectant content may be due to the nicotine mass contributions from glycerol and water.

Along with our finding that participants generally did not like the −F−H WT or intend to use it in the future, results highlight the complexity of setting product standards related to characterising flavours and humectants for WT. Among smokers with high WT dependence, removal of flavourants or humectants could increase smokers' exposure to toxicants as a result of more intense puffing. On the other hand, the decreased palatability and nicotine delivery efficiency of these products might result in these smokers switching to another tobacco product to satisfy their nicotine craving, or quitting tobacco products altogether. Most importantly, the decreased appeal may result in fewer people initiating WT smoking. Among smokers with low WT dependence, we would expect a smaller increase in exposure to toxicants as a result of more intense puffing because their smoking behaviours were more stable across conditions. As these smokers also did not like the −F−H product, the public health benefits of removing flavourants and humectants from WT for low dependence smokers are clearer.

Results of this study are subject to several limitations. First, all participants were recruited via convenience sampling and lived in one US city; thus, results might not generalise to other populations in the USA or globally. Second, due to the similarities in product characteristics that we detected after study completion, we could not directly evaluate the effect of removing flavourants, but not humectants, from WT (ie, a −F+H condition), which should be explored in future work. Third, although behavioural intentions are predictive of future behaviour,[24] we did not directly test whether participants would actually stop using WT under natural conditions if flavourants and humectants were removed. Future longitudinal work evaluating WT smoking behaviours when smokers only have access to WT without flavourants and/or humectants in their natural environments would be useful to understand the public health effects of such product standards.

CONCLUSION

Only one country, Germany, has established a product standard that limits the humectant concentration of WT.[18] In the USA, the FDA must have proof that new product standards on tobacco products would benefit population health.[30] This study was the first to evaluate how toxicant exposures and puffing behaviours may change as a result of removing flavourants and reducing humectants from WT might be for different types of WT smokers, but future work will be crucial to put our findings into context. For high dependence smokers, would removal of flavourants and/or humectants (leading to reduced nicotine delivery efficiency) cause tobacco cessation or switching to other tobacco products? How much would the removal of flavourants and/or humectants result in decreased initiation or progression of WT smoking among youth and young adults? For smokers who would continue to smoke WT without flavourants or humectants, what are the long-term health risks of smoking WT more intensely?

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What this paper adds

- Flavourants and humectants increase the appeal of waterpipe tobacco (WT) by improving palatability and nicotine delivery efficiency.
- Experimental studies have identified that WT smokers puff WT without flavourants or humectants most intensely, even though they like it the least.
- No study has evaluated whether removal/reduction of flavourants and humectants from WT would differentially affect puffing behaviours or product liking for WT smokers who have high versus low WT dependence.
- We evaluated whether level of WT dependence modified the associations between flavourants/humectants in WT and WT smoking behaviours, biomarkers of exposure and subjective effects.
- We identified that removal of flavourants and humectants was associated with reduced product liking for all WT smokers, but that WT smokers with high dependence increased the intensity of their puffing in this condition more than WT smokers with low dependence.

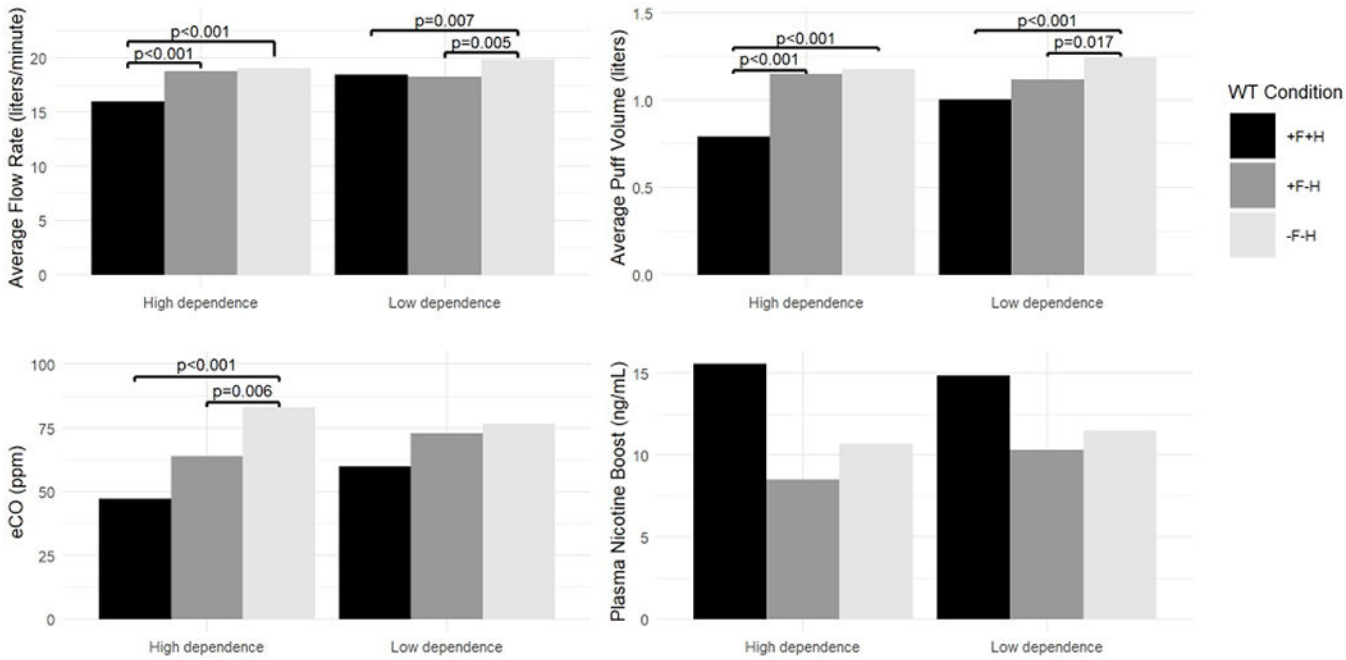

Figure 1.

Adjusted effects of waterpipe tobacco (WT) condition on puff topography and biomarkers of exposure among high and low dependence WT users, Oklahoma City, Oklahoma, 2017–2018[a]. [a]Post hoc pairwise comparisons were not estimated for the plasma nicotine results because there was no evidence of a statistical interaction between WT condition and dependence. eCO, expired carbon monoxide.

Table 1

Participant characteristics by waterpipe tobacco (WT) dependence level, Oklahoma City, Oklahoma, 2017–2018

	High dependence* **n=39**	**Low dependence*** **n=49**	**P value**
Sex (n(%))			0.82
Male	24 (61.5)	29 (59.2)	
Female	15 (38.5)	20 (40.8)	
Age group (n(%))			0.026
18–24 years	29 (74.4)	25 (51.0)	
≥25 years	10 (25.6)	24 (49.0)	
Race and ethnicity (n(%))			0.46
Non-Hispanic white	19 (48.7)	29 (59.2)	
Non-Hispanic black	5 (12.8)	3 (6.1)	
Other	15 (38.5)	17 (34.7)	
Education level (n(%))			0.052
High school or GED	15 (38.5)	12 (24.5)	
Some college or associate's degree	19 (48.7)	20 (40.8)	
Bachelor's degree or higher	5 (12.8)	17 (34.7)	
Yearly income (n(%))			0.15
<US$50 000	23 (59.0)	36 (73.5)	
≥US$50 000	16 (41.0)	13 (26.5)	
Use of other tobacco products† (n(%))			0.014
Less than monthly	14 (35.9)	31 (63.3)	
Monthly or more	24 (61.5)	18 (36.7)	
Missing	1 (2.6)	0 (0.0)	

*Level of WT dependence was established using the Lebanese Waterpipe Dependence Scale-11.[25] Participants with scores ≥10, which indicate clinically relevant WT dependence, were classified in the high dependence group.

†Other tobacco products included cigarettes, electronic cigarettes, cigars, cigarillos, little cigars, snus and smokeless tobacco.

GED, General Equivalency Diploma.

Table 2

Unadjusted distributions of study outcomes by waterpipe tobacco condition and dependence level, Oklahoma City, Oklahoma, 2017–2018

	High dependence			Low dependence		
	+F+H	**+F−H**	**−F−H**	**+F+H**	**+F−H**	**−F−H**
Topography outcomes (mean (SD))						
Average flow rate (L/min)	14.2 (5.3)	17.0 (5.3)	17.7 (4.8)	15.5 (5.0)	15.1 (4.3)	16.9 (4.5)
Average interpuff interval (s)	40.1 (29.1)	35.8 (29.5)	33.0 (28.0)	44.4 (26.3)	41.5 (25.2)	44.6 (28.4)
Average puff duration ()	2.4 (1.0)	3.3 (1.5)	3.4 (1.2)	3.0 (1.0)	3.2 (1.3)	3.4 (1.2)
Average puff volume (L)	0.6 (0.4)	1.0 (0.5)	1.0 (0.5)	0.8 (0.4)	0.8 (0.4)	1.0 (0.5)
Maximum puff volume	1.3 (0.8)	1.7 (0.8)	2.1 (0.9)	1.6 (0.7)	1.9 (2.0)	2.4 (2.2)
Total puffing time (min)	3.0 (2.8)	3.0 (2.2)	4.7 (3.4)	3.4 (2.2)	3.5 (2.3)	3.7 (2.4)
Total smoking time (min)	35.4 (16.5)	29.9 (18.1)	39.4 (17.0)	43.1 (15.2)	40.6 (13.1)	41.4 (17.0)
Total inhaled volume (L)	46.0 (57.1)	50.5 (41.2)	81.8 (60.2)	54.3 (42.7)	52.3 (35.6)	65.0 (47.2)
Total no of puffs	72.4 (66.9)	56.2 (51.7)	88.1 (71.7)	66.6 (40.0)	62.4 (31.2)	67.5 (47.7)
Biomarkers of exposure (mean (SD))						
Plasma nicotine boost (ng/mL)	13.0 (27.6)	4.4 (5.4)	7.0 (6.5)	11.6 (9.4)	7.0 (5.4)	6.7 (6.7)
eCO boost (ppm)	27.0 (38.1)	41.9 (41.9)	69.5 (55.7)	36.0 (29.1)	41.8 (36.4)	45.8 (42.8)
Subjective drug liking (mean (SD))						
Enjoyed product	51.7 (28.3)	50.4 (36.8)	39.4 (29.3)	63.6 (28.4)	50.1 (27.9)	41.8 (29.2)
Interested in using product in future	50.3 (33.5)	46.2 (34.5)	39.4 (29.9)	59.2 (33.2)	44.5 (26.4)	33.0 (30.5)
Liked product	53.2 (28.4)	49.7 (36.4)	40.7 (29.1)	62.4 (29.6)	50.6 (28.6)	38.5 (29.1)
Found product pleasurable	53.2 (28.7)	50.3 (34.4)	42.8 (29.2)	61.5 (28.0)	49.6 (26.7)	41.1 (28.8)

	High dependence			Low dependence		
	+F+H	**+F−H**	**−F−H**	**+F+H**	**+F−H**	**−F−H**
Found product satisfying	52.4 (30.8)	48.7 (34.2)	43.0 (30.3)	62.0 (28.3)	49.0 (28.4)	42.1 (29.1)
Willingness to use product in future	55.9 (35.0)	53.1 (34.7)	44.8 (32.7)	63.3 (33.5)	49.8 (27.2)	39.8 (31.9)
Behavioural intentions (% likely or extremely likely)						
Try product again	59.4	53.9	38.7	72.9	37.5	27.3
Pay to smoke product in hookah lounge/bar	53.1	42.3	29.0	56.3	27.5	19.3
Purchase product for personal use	40.6	30.8	27.4	41.7	17.5	11.4
Use product regularly	31.3	19.2	12.9	29.2	20.0	6.8

eCO, expired carbon monoxide.

Table 3

Evaluation of statistical interaction between level of waterpipe tobacco condition and dependence level, Oklahoma City, Oklahoma, 2017-2018*

	$\chi^{2(2)}$	P value
Smoking topography		
Average flow rate	9.34	0.0094
Average interpuff interval	1.94	0.38
Average puff volume	9.64	0.0081
Average puff duration	5.66	0.059
Maximum puff volume	0.20	0.91
Total puffing time	5.06	0.080
Total smoking time	5.47	0.065
Total inhaled volume	3.59	0.17
Total number of puffs	1.89	0.39
Biomarkers of exposure		
Plasma nicotine boost	0.56	0.75
eCO boost	9.74	0.0077
Subjective drug liking		
Enjoyed product	2.02	0.36
Interested in using product in future	5.08	0.079
Liked product	2.98	0.23
Found product pleasurable	2.66	0.26
Found product satisfying	3.28	0.19
Willingness to use product in future	2.47	0.29
Behavioural intentions		
Try product again	5.52	0.063
Pay to smoke product in hookah lounge/bar	3.48	0.18
Purchase product for personal use	4.58	0.10
Use product regularly	1.60	0.45

*Likelihood ratio tests were used to evaluate statistical significance of interaction terms in full versus reduced mixed-effects regression models.

eCO, expired carbon monoxide.