Short Communication

Smoking Topography Predicts Abstinence following Treatment with Nicotine Replacement Therapy

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Abstract

Objective: **Smoking topography refers to how a person smokes a cigarette and includes measures of the number of puffs and puff volume, duration, and velocity. This study examined the relationship between smoking topography and abstinence from cigarettes following nicotine replacement therapy. A secondary objective was to determine the relationship of smoking topography to carbon monoxide (CO) exposure.**
Method: **Participants (n = 113) smoked one of their preferred brands of cigarette through a smoking topography device prior to participating in an open-label trial of transdermal nicotine versus nicotine nasal spray. A subset of participants (n = 50) provided breath CO samples prior to and following smoking the cigarette.**
Results: **Mean V_{max} [odds ratio (OR), 1.12; 95% confidence interval (95% CI), 1.02-1.24; P = 0.02], mean puff volume (OR, 0.95; 95% CI, 0.91-0.98; P = 0.01), mean interpuff interval (OR, 1.06; 95% CI, 1.00-1.11; P = 0.03), and cigarette type (full flavor versus light/ultralight; OR, 0.35; 95% CI, 0.14-0.89; P = 0.03) were significant predictors of abstinence in a model controlling for treatment group and nicotine dependence. Controlling for time since last cigarette and initial CO level, mean puff velocity (β = 0.171; P = 0.01) was the only significant predictor of CO boost.**
Conclusion: **These results suggest that smoking topography may be useful to predict abstinence after using nicotine replacement therapy and to assess harm from smoking.** (Cancer Epidemiol Biomarkers Prev 2004;13(11):1800–4)

Introduction

There is significant variation between individuals in how a cigarette is smoked (1). A measure of how a cigarette is smoked is called smoking topography and includes such measures as the number of puffs and puff volume, duration, and velocity (2, 3). Smoking topography measures are related to actual cigarette nicotine yield (4, 5) as well as to overall exposure to carbon monoxide (CO; refs. 6-8) and exposure to tobacco carcinogens (4). Increases in puff volume generally produce an increase in CO (6, 8) and have been shown to increase exposure to several carcinogenic compounds found in cigarette smoke (4). However, type of cigarette (6, 7) and filter vent blocking (6) influence this relationship. There is evidence to suggest that males have greater puff volumes than females (9) and African American females tend to have greater puff volumes than Caucasian females (10). No studies have examined whether smoking topography influences liability to relapse or response to smoking cessation treatment.

The present study investigated whether measures of smoking topography predicted abstinence versus relapse among participants in an open-label randomized trial comparing nicotine patch with nicotine nasal spray (NS). These two forms of nicotine replacement therapy (NRT) have roughly equivalent efficacy and double the odds of smoking cessation relative to placebo (11-13). Pretreatment plasma nicotine and cotinine levels have been related to treatment outcome in some studies (14, 15) but not in others (16). Individual differences in smoking topography relate not only to nicotine levels (5) but also to the behavioral aspects of smoking. As such, this may provide additional information in the prediction of treatment outcome. We hypothesized that relapse rates would be higher among smokers who exhibit topography characteristics associated with greater cigarette consumption (e.g., increased number of puffs and puff volume, duration, and velocity).

A secondary goal of this study was to examine the association of smoking topography with smoke exposure as measured by increases in expired alveolar CO levels following smoking a cigarette. This measure has also been called CO boost (17). Although CO boost has been related in previous studies to total and average puff

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volume (8, 17), depth of inhalation, and puff duration (3), no previous studies examined the association of this marker with puff velocity. Based on this previous research, we hypothesized that mean puff velocity would also be a significant positive correlate of CO boost.

Materials and Methods

Subjects. Participants were recruited from a population of smokers enrolled in a smoking cessation trial using NRT (18). Eligible participants for this trial smoked ≥10 cigarettes per day for at least the prior 12 months. Exclusion criteria included age <18 years, pregnancy or lactation, current treatment or recent diagnosis of cancer, drug or alcohol dependence, current diagnosis or history of psychotic disorder, and current use of bupropion or other nicotine-containing products other than cigarettes.

All participants enrolled in the clinical trial during December 2002 and July to August 2003 were invited to participate in the smoking topography assessment. One-hundred percent (n = 113) of smokers included in the intent-to-treat analysis during this period completed the assessment. The CO boost measure was included only for the second cohort of smokers (n = 50; recruited July-August 2003).

Design and Procedures. Topography data were collected from participants 1 to 2 weeks prior to the initiation of NRT, during a weekday, between 4:30 and 6:00 p.m. Participants were asked to refrain from smoking for exactly 1 hour prior to attending the experimental topography session and to bring one of their own brand cigarettes. The baseline CO measure was taken immediately following arrival. Participants were seated in a comfortable recliner in a small room equipped with a smoke exhaust system and had the smoking topography equipment explained to them. They were asked to place their own cigarette in the mouthpiece of the smoking topography device and instructed to light their cigarette and smoke as usual. The investigator left the room while the participant smoked. When the participant had extinguished the cigarette, the investigator reentered the smoking room.

For the CO boost assessment, a research assistant explained the CO breath sample device and smoking topography equipment as well as the procedures for using both devices. To complete the pre-cigarette CO measurement, participants were instructed to take a large breath, hold it for 2 seconds, exhale, take another deep breath, and hold that breath for 10 seconds as per the recommendations of the American Thoracic Society (19). Then, when instructed to do so, participants exhaled as forcefully and as long as they were comfortably capable. The largest reading from the digital display of the CO breath device was recorded as the pre-cigarette CO level.

Two minutes after providing the pre-cigarette CO breath sample, participants were instructed to smoke while the researcher left the room. Participants were asked to repeat the CO breath sample procedure within 2 minutes after the cigarette had been extinguished. This CO measure was recorded as the post-cigarette CO level.

Participants were randomly assigned to receive either transdermal nicotine (TN; Nicoderm CQ) or nicotine NS (Nicotrol) treatment. NRT use was initiated on the target quit date (week 3) and continued for an 8-week period. NS participants were instructed to administer between 8 and 40 doses daily (with a maximum of five doses per hour) beginning on the target quit date. After the first 4 weeks of NS use, participants were instructed to taper the number of daily NS doses by one third for a 2-week period and then by another one third for the final 2 weeks of treatment. TN participants were instructed to apply their first patch on the morning of their target quit date (session 3). A 24-hour dose formulation was used. After 4 weeks of 21 mg, the TN was also tapered using 2 weeks of 14 mg and 2 weeks of 7 mg patches. In addition to NRT, all participants received seven sessions of standardized smoking cessation behavioral group counseling that included components of nicotine fading, identification and management of smoking triggers, stress management, problem solving, and relapse prevention. Each group had 10 to 15 participants. All counseling was delivered by two Master's level counselors who led an equal number of TN and NS groups and received weekly supervision to ensure protocol adherence.

Equipment. All cigarettes were smoked using the Clinical Research Support System smoking topography machine (Plowshare, Baltimore, MD) calibrated as per the manufacturer's instructions. This device is designed to collect smoking topography variables. This device works by placing a cigarette in a sterilized flow meter mouthpiece, which is connected to a pressure transducer. The pressure transducer measures pressure changes that occur during inhalation. The pressure changes are amplified, digitized, and sampled at 1,000 Hz. Clinical Research Support System software converts the signal to airflow (mL/s) in real time (seconds) and from this provides number of puffs taken on the cigarette, puff volume, puff duration, maximum flow, and interpuff interval (time between puffs). The equipment was calibrated as per the manufacturer's instructions.

CO measures were made using a Vitalograph Breath CO Analyzer (McNeil International, Inc., Lenexa, KS). The manufacturer had calibrated this device within the past year. A new, disposable cardboard mouthpiece was provided for each participant. The device has a digital screen, which reports CO levels in parts per million (ppm). The largest value displayed was recorded during all CO breath samples.

Measures

Demographic and Smoking History Measures. Age, sex, race, years smoking, cigarettes per day, and time since last cigarette were collected during the pretreatment baseline. The Fagerström Test for Nicotine Dependence (20) was used to measure nicotine dependence.

Cigarette Characteristics. Participants provided information on their own cigarette brand by completing a cigarette characteristics questionnaire. The items included cigarette size (king, regular, 100s, 120s, and other), filtered versus nonfiltered, soft/hard pack, tar-nicotine level, and menthol versus nonmenthol.

Topography Measures. The software for the Clinical Research Support System smoking topography system collects participant data for number of puffs, puff volume, time between puffs (interpuff interval), puff

duration, and maximum puff velocity. Maximum puff velocity captures the greatest velocity at any one instant during the puff. The mean maximum puff velocity (mean V_{max}) was defined as the sum of the maximum puff velocity for each puff divided by the total number of puffs. In addition, mean puff velocity was calculated by dividing each puff volume by the corresponding puff duration, summing these values for all puffs, and dividing by total number of puffs. Mean puff velocity may be more indicative of the typical rate of flow during the puff and not simply the maximum puff volume achieved at any one instant during the puff.

Outcome Measures. Abstinence from cigarettes at the end of the 8-week treatment phase was the primary outcome. Failure was defined as 7 consecutive days of smoking between target quit date and end of treatment and/or a CO >10 ppm at end of treatment (21, 22).

CO boost was a secondary outcome measure and is defined as the difference between post-cigarette CO level and pre-cigarette CO level reported in ppm. Only a subset of participants, from the July to August 2003 cohort, provided both pre-cigarette and post-cigarette CO breath samples (n = 50).

Statistical Analyses. Descriptive statistics were used to characterize the participants, their own cigarette brand, and smoking topography measures. χ^2 tests (for categorical measures) and t tests (for continuous measures) were used to determine the associations of covariate measures with abstinence. Variables significantly associated with abstinence were included in a backward stepwise logistic regression model. Nicotine dependence, cigarette type, and treatment group (patch versus spray) were selected a priori as controlling variables in the analyses. Topography variables were tested in a stepwise logistic regression model of abstinence, controlling for the potential confounder variables. Topography variables with $P > 0.2$ associations were dropped from the backward elimination model.

One-way ANOVA (for categorical measures) and Pearson correlations (for continuous measures) were used to determine the associations of covariates with CO boost. Variables significantly associated with CO boost were included in a multivariate model. Stepwise linear regression analysis was used for analysis of CO boost, with time since last cigarette and initial CO level selected a priori as controlling variables. Topography variables with $P > 0.2$ associations were dropped from the backward elimination model.

Results

Descriptive Data. Fifty-four percent of the participants were female, 66.1% were Caucasian, 29.7% were African American, and 3.3% were from other minority groups. Participants ranged in age from 21 to 71 years (mean, 45.8; SD, 10.7). Most participants had completed high school (93.4%) and many had at least some college education (76%). On average, participants reported smoking about a pack per day (mean, 21.2 cigarettes; SD, 7.8) and had been smoking for a mean (SD) of 29.3 (10.8) years. Mean (SD) Fagerström Test for Nicotine Dependence score was 5.5 (2.1). On average, self-reported abstinence from smoking was ~1 hour (mean, 64.6 minutes; SD, 38.5; range, 12-220 minutes), consistent with 1-hour abstinence requirements. Time since last cigarette did not significantly correlate with smoking topography measures (all Ps > 0.10). At end of treatment, 32.5% of participants were considered abstinent, 32.7% of TN versus 32.2% of NS. The CO boost subset group (n = 50) had significantly more females (62.7%) and fewer abstinent subjects (14.6%) than the overall study sample (n = 113).

Cigarette Characteristics. Sixty-five percent of participants smoked king size (85 mm) cigarettes, 33% smoked 100s (100 mm), 1% smoked regular size (65 mm) cigarettes, and 1% smoked 120s (120 mm). Most participants preferred full flavor cigarettes (47%) followed by light brands (40%), ultralight brands (8%), and mediums (3%). Sixty-four percent smoked nonmenthol brands. One participant reported smoking nonfiltered cigarettes. Based on Federal Trade Commission testing values (23), mean (SD) nicotine level of brand smoked was 0.93 mg (0.027; range, 0.2-1.7 mg). The CO boost subset group did not differ by any cigarette characteristics.

Topography measures are presented in Table 1. Topography results from our study participants are similar to those found elsewhere (e.g., ref. 24). The mean CO boost was 7.1 ± 4.1 ppm, similar to previous research (e.g., ref. 6).

Predictors of Abstinence. Abstinence rates did not differ significantly by categories of cigarette size, cigarette pack type, cigarette type, or menthol versus nonmenthol (all $P > 0.20$). When cigarette type was dichotomized to full flavor/mediums versus light/ultralight, the χ^2 analyses was significant ($\chi^2 = 4.28$; $P = 0.04$) such that smokers of full flavor/medium cigarettes were more likely to be abstinent at end of treatment. Abstinence did not differ significantly by sex, race, age, years smoking, cigarettes per day, nicotine dependence, or time since last cigarette (all Ps > 0.10).

Univariate analyses of the topography variables predicting abstinence indicated that mean V_{max} ($\chi^2 = 4.29$; $P = 0.04$) and mean time between puffs ($\chi^2 = 6.07$; $P = 0.01$) were significant predictors and that mean puff volume ($\chi^2 = 2.79$; $P = 0.09$), mean puff duration ($\chi^2 = 0.85$; $P = 0.36$), and mean puff velocity ($\chi^2 = 0.36$; $P = 0.55$) were not significant predictors of abstinence.

When all smoking topography variables, nicotine dependence, cigarette type, and treatment group were included in a logistic regression model, mean V_{max} [odds ratio (OR), 1.12; 95% confidence interval (95% CI),

Table 1. Descriptive data on smoking topography and CO boost (n = 113)

Variable	Mean	SD	Range
No. puffs	12.7	4.0	5-25
Puff volume (mL)	54.8	16.9	19.5-113.8
Total puff volume (mL)	675.7	244.7	214.1-1386.0
Interpuff interval (s)	24.8	11.9	8.0-60.3
Puff duration (s)	1.6	0.5	0.7-3.0
Puff velocity (mL/s)	34.3	8.2	18.4-60.2
Maximum puff velocity (mL/s)	51.7	14.7	24.5-93.8
Pre-cigarette CO (ppm)	22.6	9.6	8-53
Post-cigarette CO (ppm; n = 50)	29.8	11.5	12-68
CO boost (ppm; n = 50)	7.1	4.1	1-17

1.02-1.24; $P = 0.02$], mean puff volume (OR, 0.95; 95% CI, 0.91-0.98; $P = 0.01$), mean time between puffs (OR, 1.06; 95% CI, 1.00-1.11; $P = 0.03$), and cigarette type (OR, 0.35; 95% CI, 0.14-0.89; $P = 0.03$) were significant predictors of abstinence. Interactions of topography measures with treatment group were tested but were not statistically significant (Table 2).

Predictors of CO Boost. CO boost did not significantly differ by categories of cigarette size, cigarette type, menthol versus nonmenthol, sex, or race (all Ps > 0.10). Age, years smoking, cigarettes per day, nicotine dependence, and time since last cigarette were not significantly correlated with CO boost. Pre-cigarette CO was significantly correlated with CO boost ($r = 0.29$; $P = 0.04$).

Stepwise regression analyses showed that mean puff velocity ($\beta = 0.171$; $P = 0.01$) was the only significant predictor of CO boost in a model that included time since last cigarette ($\beta = 0.223$; $P = 0.13$), initial CO ($\beta = 0.101$; $P = 0.10$), and mean puff duration ($\beta = 2.31$; $P = 0.10$; Table 3).

Discussion

The current study is the first to report an association between smoking topography and abstinence. Participants who were abstinent had a greater mean V_{max}, had smaller mean puff volume, took a longer time between puffs, and were more likely to smoke full flavor cigarettes than those who were not abstinent. Smaller mean puff volume and longer time between puffs predicting abstinence is consistent with our hypothesis that topography measures resulting in greater consumption would be associated with relapse.

Our finding that a greater mean V_{max} predicted abstinence initially seems opposite to what one might predict. However, if those who smoke more intensely do so because they are more nicotine dependent and therefore are attempting to extract more nicotine relative to those who smoke less intensely, then it could be postulated that these smokers may be particularly responsive to NRT. Although there was no difference in measured nicotine dependence between abstainers and nonabstainers, the topography difference may be too subtle to be observed in the nicotine dependence measure (Fagerström Test for Nicotine Dependence) that categorizes cigarettes per day and does not assess how each cigarette is smoked. To test this nicotine replacement hypothesis, it would be necessary to have a placebo group for comparison. This large smoking cessation trial did not have a placebo group, as it was designed to compare individual differences in response to two alternate forms of NRT.

Table 2. Stepwise logistic regression model for smoking topography measures predicting abstinence, controlling for nicotine dependence, treatment group, and cigarette type ($n = 113$)

Predictors	Abstinence	
	OR (95% CI)	P
Nicotine dependence (Fagerström Test for Nicotine Dependence 0-10)	1.01 (0.81-1.26)	0.94
Treatment group (0 = patch, 1 = spray)	1.11 (0.45-2.75)	0.82
Cigarette type (full flavor/ medium = 0, light/ultralight = 1)	0.35 (0.14-0.89)	0.03
Mean time between puffs (interpuff interval)	1.06 (1.00-1.11)	0.03
Mean puff volume	0.95 (0.91-0.98)	0.01
Mean puff velocity	0.87 (0.74-1.02)	0.09
Mean V_{max}	1.12 (1.02-1.24)	0.02

NOTE: ORs are expressed as per unit change in the smoking topography measures.

Table 3. Stepwise regression model for smoking topography measures predicting CO boost, controlling for time since last cigarette and initial CO ($n = 50$)

Predictors	CO boost	
	β coefficient	P
Time since last cigarette	0.223	0.13
Initial CO	0.101	0.10
Mean puff duration	2.31	0.10
Mean puff velocity	0.171	0.01

The current study is also the first to identify an association between mean puff velocity and amount of smoke exposure as measured by exhaled CO. Mean puff velocity seems to be a better indicator of smoke exposure than maximum puff velocity. Mean puff velocity reflects the average velocity over the entire puff, whereas maximum puff velocity indicates how quickly the smoke enters the mouth during a discrete time during the puffing process. Our data also suggest that mean puff velocity is a better predictor of CO boost than puff volume. This is in contrast to previous research that has focused on the effect of puff volume on smoke exposure, CO boost, and carcinogenic exposure (17, 25). There was a trend in our data between puff volume and CO boost ($P = 0.09$) in a direction consistent with previous research. Therefore, we feel our data are similar to prior findings. Further, most previous research has not reported including puff velocity, which does not mean the measure was not significant in previous studies.

The present study has some limitations. The study population was composed of treatment seeking smokers and may not generalize to a non-treatment-seeking smoking population (26). Data were collected from a cohort that was predominantly female and included many menthol smokers. Puffing patterns differ by gender and mentholation (9, 10). However, the topography measurements from the subjects are similar to the results in a previous study using a non-treatment-seeking population (i.e., ref. 24). Another potential limitation is that the results are based on only one cigarette smoked using the topography mouthpiece. Although assessments across multiple sessions would be desirable, recent research has reported a significant within-subject correlation for several smoking topography measures in participants who were asked to smoke different cigarettes on multiple days (27).

Although preliminary, data from this study may have implications for smoking treatment and cancer control. The CO boost results may shed some light on how an individual's smoking topography could influence lung cancer risk. This topic has received little attention, although one study found that, as self-reported depth

of inhalation increased, lung cancer risk also increased (28). An increase in adenocarcinoma has been attributed to the deeper inhalation of smoke, promoted by milder-tasting smoke from low-tar, ventilated cigarettes (29, 30). Our findings suggest that increases in mean puff velocity may also regulate exposure to the toxic components of tobacco smoke. Additional research is needed to validate the new findings regarding smoking topography and abstinence. Smoking topography measures may provide useful information from identifying smokers most vulnerable to relapse and those most responsive to particular interventions.

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