Nicotine & Tobacco Research, Volume 11, Number 9 (September 2009) *1035–1041*

Original Investigation

Using MIMIC models to examine the relationship between current smoking and early smoking experiences

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Abstract

Introduction: The present study expands previous research on early experiences with tobacco by using a Multiple Indicator Multiple Causes (MIMIC) model, which permits combining indicators tapping into pleasant experiences into one latent construct and those indicators of unpleasant experiences into another latent construct.

Methods: A sample of 458 participants was recruited via newspaper advertisements. Response to early experimentation with cigarettes was assessed using the Early Smoking Experiences questionnaire, in which participants were asked the following question: "The first time you tried cigarettes, did you experience any of the following? (pleasurable and displeasurable sensations [overall], pleasurable rush or buzz, dizziness, relaxation, nausea, cough, difficulty inhaling)." These experiences were rated on a scale ranging from 1 = *none* to 4 = *intense*.

Results: The MIMIC model revealed that current smoking status and age of initial experimentation with cigarettes were significantly associated with both early pleasant and unpleasant experiences ($p < .05$). African Americans were less likely than Whites to have early unpleasant experiences ($p < .05$). No association was found between race and early pleasant experiences.

Discussion: Our findings are consistent with the inferences that pleasant experiences in response to early experimentation with smoking lead to regular smoking and that positive experiences play a stronger role than negative experiences in the transition to regular smoking. Our study also demonstrates that the MIMIC model is pertinent and practicable in nicotine and smoking research. We recommend it as a useful tool for identifying endophenotypes related to nicotine dependence and tobacco use latent constructs.

Introduction

Initial exposure to nicotine activates a series of biochemical events in the reward and craving areas of the brain (Littleton, 2001; Quick & Lester, 2002). Although models attempting to explain the neurological changes leading a person to become a smoker differ with respect to the relative contribution of subsequent exposure (DiFranza & Wellman, 2005; Gurling, Grant, & Dangl, 1985; Poulos & Cappell, 1991), all concur that early experiences with smoking may be critical in determining whether that individual goes on to become a smoker (Friedman, Lichtenstein, & Biglan, 1985).

Pomerleau, Collins, Shiffman, and Pomerleau (1993) have argued that individuals who persist in smoking, although they may experience unpleasant as well as pleasant sensations upon smoking their first cigarette, may be constitutionally sensitive to the reinforcing and/or rewarding effects of nicotine. The development of tolerance may be more rapid and self-administration more extensive in such individuals (Pomerleau, 1995). In addition, people who do not continue to smoke may be more sensitive to the aversive effects on initial cigarette use.

To date, efforts to explain the transition from first cigarette to eventual smoking status (e.g., DiFranza et al., 2004; Pomerleau, Pomerleau, & Namenek, 1998; Pomerleau, Pomerleau, Namenek, & Marks, 1999) have focused on single indicators of pleasant or unpleasant experiences (e.g., relaxation, dizziness, nausea). This approach has generated interesting new insights into the range of the initial responses to nicotine but is limited in its ability to provide a definitive characterization of the early experiences that drive or prevent the transition to smoking.

The present study was designed to extend previous research on early experiences with tobacco by using a Multiple Indicator Multiple Causes (MIMIC) model, which enables us to combine

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doi: 10.1093/ntr/ntp093
Advance Access publication on July 3, 2009
Received August 15, 2008; accepted March 11, 2009

indicators tapping into the pleasant experiences into one latent construct and those indicators of unpleasant experiences into a second latent construct. An additional advantage of this model is that it allows for simultaneous evaluation of correlations between the latent constructs and among the indicators and the explanatory variables. Moreover, estimates are adjusted for all the other covariates in the model. The resulting latent constructs served as outcome measures in determining what individual characteristics are associated with either pleasant or unpleasant early experiences upon initial experimentation with tobacco.

Methods

Participants were initially recruited as part of a laboratory investigation involving administration of nicotine to current smokers (Pomerleau, Pomerleau, Mehringer, Snedecor, & Ninowski et al., 2005). A subsequent supplement enabled recruitment of nicotine-exposed never-smokers (NENS) who did not participate in the laboratory study but were otherwise comparable to the smokers; additional current smokers were also recruited to augment the core sample of laboratory participants. The study protocol was approved by the University of Michigan Medical School Institutional Review Board.

Participants

A sample of 543 participants was recruited from Ann Arbor, MI, and environs via newspaper advertisements and public notices. Because of our interest in race differences, only the 458 participants who self-identified as either African American ($n = 78$) or White ($n = 380$) were included in our analyses. To ensure that they had achieved a stable smoking status, candidates had to be at least 25 years old, with a maximum age limit of 65 years old. The sample was designed to include approximately equal numbers of men and women and to overinclude individuals with depressive symptomatology. Exclusion criteria were as follows: currently pregnant or nursing; current or previous diagnosis of psychosis, bipolar disorder, mania, or suicide attempts; current (<6 months) use of psychoactive medication; recent consumption of alcohol beyond specified limits (15 drinks/week for women; 21 drinks/week for men) and current diagnosis of alcohol abuse; and current illegal drug use.

Participants were also stratified on smoking status, defined as follows: Current daily smokers ($n = 217$) were required to have smoked at least 5 cigarettes/day of ≥0.5 mg nicotine for at least 5 years and at their current rate for ≥6 months. NENS ($n = 241$) were defined as having smoked fewer than 100 cigarettes in their lifetime (a definition that has been in use by the CDC for many years; see Centers for Disease Control and Prevention [CDC], 1986), without having developed a pattern of regular smoking, and as not having used any form of tobacco within the past year. They were further required to have tried at least one cigarette, to establish that they had sufficient exposure to have persisted in smoking if they had the propensity to become a dependent smoker, rather than to have rejected it.

Demographic and smoking history assessments used in this study were developed in the University of Michigan Nicotine Research Laboratory. These were used to determine race, sex, current smoking status, and age at initial experimentation with cigarettes. The Early Smoking Experiences (ESE) questionnaire (Pomerleau et al., 1998) assessed subject's response to early experimentation with cigarettes. The ESE had been validated for the following items: "Buzz" or "buzzed" in both deprived smokers (Pomerleau, Pomerleau, Mehringer, Snedecor, & Cameron, 2005) and never-smokers (Perkins, Lerman, Coddington, & Karelitz, 2008) and "dizzy" in never-smokers (Perkins et al.). It was administered via scannable forms, in which participants were asked to respond to the following question: "The first time you tried cigarettes, did you experience any of the following? (pleasurable and displeasurable sensations [overall], pleasurable rush or buzz, dizziness, relaxation, nausea, cough, difficulty inhaling)." These experiences were rated on a scale ranging from 1 = *none*, 2 = *slight*, 3 = *moderate*, to 4 = *intense*. They were presented in a fixed sequence of standardized preworded and precoded survey questions.

Depression was assessed using the Center for Epidemiological Studies Depression Scale (CES-D; Weissman, Sholomakis, Pottenger, Prushoff, & Locke, 1977) and the Composite International Diagnostic Interview (CIDI; World Health Organization, 1997) module for major depression to determine any current or past history of major depression. To qualify as highly depressed smokers, candidates had to have a CES-D score of at least 16 (the standard cutoff for clinical depression) and/or a CIDI lifetime diagnosis of depression; to be categorized as low-depressed smokers, candidates had to have a CES-D score of less than 16 and no lifetime depression diagnosis via the CIDI.

Data analysis

Independent sample *t* tests were conducted to compare mean differences in age of initial experimentation with cigarettes between NENS and smokers. Fisher's exact test was used to test for differences when evaluating categorical variables. A MIMIC structural equation model (SEM), implemented in Mplus Software v5.1 (Muthén & Muthén, 2008), was used to determine the degree of association between current smoking status and pleasant and unpleasant early experiences. Briefly, SEMs consist of a system of simultaneous algebraic equations modeling relationships among observed and unobserved (latent) variables. In Figure 1, the latent trait in the MIMIC model is defined by the terms that constitute the ESE, and the observed variables are these ESE items. Furthermore, the ESE items are considered to be indicators of our latent variables—that is, pleasant and unpleasant experiences (the oval shapes). We introduced several covariates to the model to obtain adjusted estimates of their relationships with the latent variables. The MIMIC model basically consists of two parts:

1. A measurement model (two continuous latent variables underlie the categorical responses to the ESE items; on the right side of Figure 1, the measurement model relates the two unobserved latent constructs to the observed ESE items—arrows from the latent variables to the ESE items).
2. A regression model (analogous to simultaneous multiple regressions of the two continuous latent variables onto several covariates; on the left side of Figure 1 the regression model examines the association between the covariates of interest and the unobserved latent constructs—arrows from the covariates of interest to the latent variables).

MIMIC models allow the simultaneous estimation of two response latent factors—in our study, pleasant and unpleasant experiences—in relation to explanatory variables. It also permits the evaluation of each indicator variable as well as the correlation

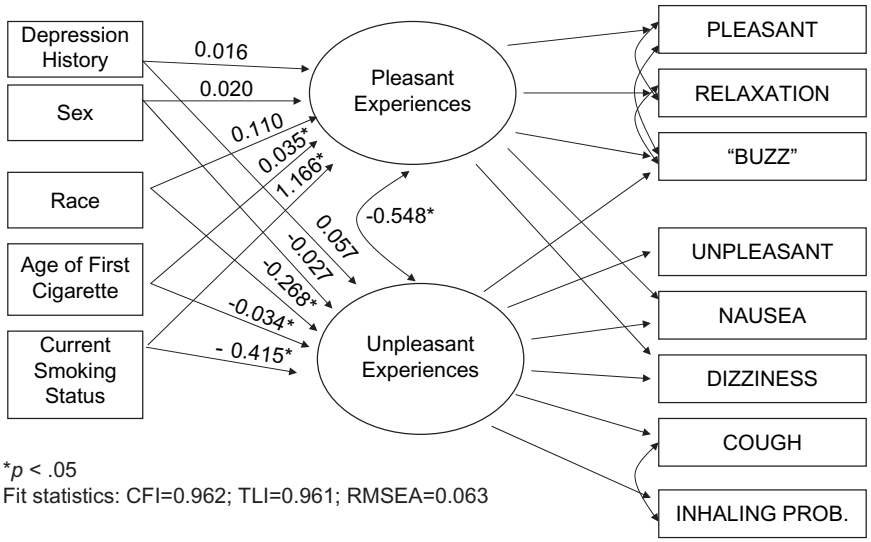

Figure 1. Path diagram for the Multiple Indicator Multiple Causes model examining the relationship between early smoking experiences and current smoking status. The ESE items on the right are assumed to measure a latent construct (i.e., unpleasant and pleasant experiences). On the left side are the covariates and their respective coefficients for the regression on the latent constructs. The double-headed arrow represents the correlation between the two latent constructs. Depression history was coded 0 = *negative* and 1 = *positive*, sex was coded 0 = *females* and 1 = *males*, race was coded 0 = *Whites* and 1 = *African Americans*, age of first cigarette is a continuous variable measured in years, and current smoking status coding was 0 = *nicotine-exposed never-smoker* and 1 = *current smoker*.

between factors, while controlling for all the covariates in the model. We analyzed several MIMIC models. The findings reported here are based on a model that contains the following covariates: history of depression, sex, current smoking status, race, and age of initial smoking experimentation.

Several criteria can be used to assess the fit of MIMIC models. The chi-square distribution for goodness of fit to evaluate differences between the observed data and model prediction is the classical test. This test is sensitive to samples larger than 200, as in our study, and will tend to reject the model even when the fit is adequate (Barrett, 2007). In other words, large samples will increase the chance of observing p values lower than .05. We used three model fit indices: the comparative fit index (CFI), where values of .95 or greater suggest adequate fit (Hu & Bentler, 1999); the Tucker-Lewis Index (TLI), which shares the same cutoff values as the CFI (Schumacker & Lomax, 2004); and the root mean squared error of approximation (RMSEA), where values of less than 0.08 indicate adequate fit and values under 0.05 suggest excellent fit (Browne & Cudeck, 1992).

Results

Sample characteristics

NENS comprised 52.6% of the study population. Sample characteristics for the two groups are shown in Table 1. The smokers consume on average almost a pack of cigarettes per day (17.2 ± 9.1 *SD*) and included a significantly higher proportion of males, African Americans, and participants with either current or past depression as diagnosed using the CIDI than did the NENS group. The observed differences were presumably largely adventitious since the same recruitment methods were used for all groups. The over-representation of African American smokers (that is, exceeding the proportion in the local population) also reflects our success in recruiting this group as a result of efforts to meet minority inclusion goals.

Group differences in early experiences with smoking

Early smoking experiences are shown in Table 2. The two groups did not differ significantly with respect to mean age of first experimentation with smoking. NENS differed significantly from smokers on all early experiences except for coughing and difficulty inhaling. For example, a significantly higher proportion of NENS rated their earlier experience as none or slight for pleasant sensations, relaxation, nausea, and dizziness. Unpleasant sensation was rated as either moderate or intense by a greater proportion of NENS.

Relationship of smoking status to pleasant or unpleasant latent factors

We performed an exploratory factor analysis (EFA) to examine the underlying dimensionality of our early-experience indicators. As expected, the EFA provided support for our two theoretically derived latent factors (i.e., pleasant experiences and unpleasant experiences). Only two eigenvalues were larger than one, 3.4 and 2.5, with a third factor producing an eigenvalue of 0.76. Moreover, the rotated and unrotated factor loadings for the indicators were all above 0.65, with pleasant indicators loading on the first factor and unpleasant indicators loading on the second. The RMSEA for the two-factor solution was 0.06 for an acceptable model fit (Browne & Cudeck, 1992).

The MIMIC model included race and age of initial experimentation and, due to our recruitment strategy, sex, current smoking status, and lifetime history of depression as observed covariates, some of which are not statistically robust but were kept in our model because of our recruitment strategy (see

Table 1. Selected characteristics of the study sample and by smoking status

	Total ($n = 458$), %	NENS ($n = 241$), %	Smokers ($n = 217$), %	p value
Sex				
Male	48.7	43.2	54.8	.015
Female	51.3	56.9	45.2	
Race				
White	83.0	89.6	75.6	<.001
African American	17.0	10.4	24.4	
History of depression				
No	62.2	69.7	53.9	<.001
Yes	37.8	30.3	46.1	
Age				
18–29	24.6	24.4	24.8	.392
30–39	30.6	29.1	32.4	
40–49	24.8	23.5	26.2	
50+	20.1	23.1	16.7	
Mean (±*SD*)	39.3 (10.8)	39.7 (11.1)	38.8 (10.5)	.382
Education				
Less than high school	2.0	0.4	3.8	<.001
High school	13.1	5.0	22.4	
More than high school	84.9	94.6	73.8	
Mean (±*SD*)	15.2 (2.2)	16.2 (2.0)	14.1 (2.0)	<.001

Note. NENS = nicotine-exposed never-smokers. Percentages may not add up to 100 because of rounding.

Methods section). Figure 1 displays the path diagram that forms the basis for our analysis of the relationship between early smoking experiences and current smoking status. In path diagrams, it is traditional to indicate observed variables by rectangles and latent variables by ovals. The association of one variable with another is represented by an arrow from the first to the second, with the arrows representing parameters to be estimated. Figure 1 indicates that the two latent factors are influenced by the observed variables (left side of Figure 1), and the ESE items (right side of Figure 1) are related to the "pleasant" and "unpleasant" latent variables. For example, in Figure 1, depression history, sex, race, age of initial experimentation with cigarettes, and current smoking status are considered to be formative—that is, they give rise to the latent variables. The observed ESE variables are referred to as reflective variables in that they "reflect" the latent variables. Therefore, we see that in the MIMIC models, one or more latent variables intervene between two sets of observed variables, one set of covariates and a second set of indicator variables.

We also tested for a correlation between the two latent factors. Evaluation of modification indices suggested the addition of two paths that allow two unpleasant indicators—"nausea" and "dizziness"—to load on the pleasant latent factor as well, based on the negative covariation or correlation of pleasurable sensations with dizziness and nausea (data not shown). Allowing the residuals of five indicators to be correlated improved the fit of the model (e.g., overall pleasurable sensations with relaxation, overall pleasurable sensations with buzz, relaxation with buzz, cough with difficulty inhaling). Fit indices for the final model were CFI = 0.962, TLI = 0.961, and RMSEA = 0.063.

Our MIMIC model confirms that current smokers were more likely to have early pleasant experience and less likely to have unpleasant ones while controlling for the other covariates in the model. Regarding race, Figure 1 also shows that African Americans were less likely than Whites to report early unpleasant experiences. No association was found between race and early pleasant experiences.

Discussion

Our use of the MIMIC model represents a novel approach to elucidating the contribution of early smoking experiences to current smoking status. Consistent with other reports in the literature (Chen et al., 2003; DiFranza et al., 2004; Hahn et al., 1990; Pomerleau et al., 1998, 1999; Wang, Fitzhugh, Trucks, Cowdery, & Perko, 1995), pleasurable sensations upon early experiences with smoking were identified as an important factor in the transition from experimentation to regular cigarette use. These early pleasant experiences do not exclude the concomitant experience of unpleasant sensations, but our findings suggest that the absence of unpleasant sensations cannot be ruled out as an additional contributing factor that facilitates the transition to smoking in vulnerable individuals. An advantage of our analytical approach is that our estimates were derived taking this fact into account.

The reduced likelihood of unpleasant sensations upon early smoking among African Americans may be related to the preference for menthol cigarettes (Giovino et al., 2004). Mentholated cigarettes provide cooling, smoothing, and anesthetic effects (Wayne & Connolly, 2004) and are described by users as refreshing, minty, and having more taste (Wiseman & McMillan, 1998). Thus, menthol, by masking the initial unpleasant taste of tobacco, may facilitate continued experimentation and the transition to regular smoking among African Americans. It may also be that physiological responses to the first cigarette are less pronounced and/or less potent than social determinants

Table 2. Early smoking experiences in the total study sample and by smoking status

	Total ($n = 458$), %	NENS ($n = 241$), %	Smokers ($n = 217$), %	p value
Age first tried cigarettes (mean ± *SD*)	15.6 (5.1)	15.9 (5.2)	15.2 (4.9)	.146
Pleasant sensation				
None	50.4	70.9	26.2	<.001
Slight	29.9	22.2	39.0	
Moderate	14.1	5.9	23.8	
Intense	5.6	1.0	11.1	
Missing	83	38	45	
Relaxation				
None	65.2	80.8	46.8	<.001
Slight	17.9	15.8	20.5	
Moderate	13.9	2.5	27.5	
Intense	2.9	1.0	5.3	
Missing	84	38	46	
Buzz				
None	53.9	78.1	25.9	<.001
Slight	19.5	12.4	27.6	
Moderate	15.7	7.0	25.9	
Intense	10.9	2.5	20.7	
Missing	83	40	43	
Unpleasant sensations				
None	25.1	18.8	32.4	<.001
Slight	25.1	19.8	31.2	
Moderate	26.4	25.7	27.2	
Intense	23.5	35.6	9.3	
Missing	83	39	44	
Nausea				
None	58.8	68.0	48.6	<.001
Slight	19.5	14.5	25.1	
Moderate	14.8	10.5	19.6	
Intense	6.9	7.0	6.7	
Missing	79	41	38	
Dizziness				
None	42.4	61.9	21.6	<.001
Slight	22.0	20.8	23.2	
Moderate	20.7	11.2	30.8	
Intense	14.9	6.1	24.3	
Missing	76	44	32	
Cough				
None	21.1	20.6	21.6	.410
Slight	32.9	30.7	35.4	
Moderate	24.7	24.1	25.4	
Intense	21.3	24.6	17.7	
Missing	78	42	36	
Difficulty inhaling				
None	20.6	20.6	20.5	.082
Slight	28.8	23.8	34.1	
Moderate	25.2	25.4	25.0	
Intense	25.5	30.2	20.5	
Missing	93	52	41	

Note. NENS = nicotine-exposed never-smokers. Percentages may not add up to 100 because of rounding.

(e.g., peer smoking, parental smoking) in driving the transition to smoking among African Americans.

We found that age at initial experimentation with cigarettes was positively related to pleasant experiences and negatively related to unpleasant ones after controlling for depression history, sex, race, and current smoking status. Thus, the older the individual is at the time of initial experimentation with cigarettes, the more likely she/he is to have pleasant experiences and the less likely to have unpleasant ones. This result may seem paradoxical, given that most research in this area supports the view that smoking onset early in adolescence

increases the probability of becoming a regular smoker or nicotine dependent (Breslau & Peterson, 1996; D'Avanzo, La Vecchia, & Negri, 1994; Hu, Davies, & Kandel, 2006; Taioli & Wynder, 1991). Since relatively few smokers start smoking after adolescence (Breslau & Peterson; Chen & Kandel, 1995), a possible explanation of our findings is that after controlling for current smoking status, positive experiences in combination with reduced negative ones may help overcome other maturational factors that militate against late-onset smoking. Alternatively, the frequent association of alcohol use with smoking experimentation in older individuals may complicate response to nicotine (McKee, Hinson, Rounsaville, & Petrelli, 2004). Further research is needed to replicate our observation and determine the extent to which it predicts later smoking.

Some limitations of our study should be noted. First, the fact that our sample was not representative of all smokers and NENS (e.g., very light or non-daily smokers, pregnant women, and individuals with serious psychopathology were excluded) restricts the generalizability of our conclusions. Second, only a few measures of possible social determinants for smoking were available (e.g., smoking peers, parental smoking).

Retrospective reports of early smoking experiences, though theoretically a source of bias and not universally validated (see, e.g., Riedel, Blitstein, Robinson, Murray, & Klesges, 2003), have been well supported in the literature, with repeated demonstrations of enhanced sensitivity in young smokers in the United States and elsewhere, indicating that the early-experience reports do not simply reflect selective recall of positive experiences by current smokers (Chen et al., 2003; DiFranza et al., 2004; Pomerleau et al., 1999). Studies of early experiences as well as other aspects of smoking behavior suggest that self-report of tobacco use is generally reliable (Brigham et al., 2008; Hudmon, Pomerleau, Brigham, Javitz, & Swan, 2005). Additional support is provided by our demonstration, using a period of abstinence to allow for dissipation of tolerance as a model for initial sensitivity, that retrospective reports of buzz during early experimentation with smoking significantly predicted which individuals rated re-exposure to nicotine administered via nasal spray as more pleasurable (Pomerleau et al., 2005) and by a study by Perkins et al. (2008) showing that *dizzy* and *buzzed* predicted prospectively assessed responses to nicotine via nasal spray in adult never-smokers. In addition to the above considerations, note that current smoking status was included in the MIMIC model to provide statistical control for retrospective reports on early smoking experiences.

Our findings are consistent with the inference that pleasant experiences in response to early experimentation with smoking lead to regular smoking and that positive experiences play a stronger role than negative experiences in the transition to regular smoking, providing support for the "sensitivity model" (Pomerleau, 1995). Longitudinal research in larger, randomly recruited samples, including both sociodemographic and genetic data, will be needed to determine conclusively the relative contribution of genetic factors (e.g., differential pharmacological effects of nicotine on neurobehavioral systems) and environmental factors (e.g., smoking peers, parental smoking) in determining ultimate smoking status in individuals of differing race and ethnicity.

Our study also demonstrates that the MIMIC model is pertinent and practicable in nicotine and smoking research. We recommend it as a useful tool for identifying endophenotypes related to nicotine dependence latent constructs and tobacco use.

Funding

This research was supported by the National Institutes of Health (R01 DA017640 and R01 DA006529 to OFP).

Declaration of Interests

None declared.

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