ABSTRACT

Objectives. This study builds on previous observations about a suspected causal association linking tobacco smoking with depression. With prospective data, the study sheds new light on the temporal sequencing of tobacco smoking and depressed mood in late childhood and early adolescence.

Methods. The epidemiologic sample that was studied consisted of 1731 youths (aged 8–9 to 13–14 years) attending public schools in a mid-Atlantic metropolitan area, who were assessed at least twice from 1989 to 1994. A survival analysis was used to examine the temporal relationship from antecedent tobacco smoking to subsequent onset of depressed mood, as well as from antecedent depressed mood to subsequent initiation of tobacco use.

Results. Tobacco smoking signaled a modestly increased risk for the subsequent onset of depressed mood, but antecedent depressed mood was not associated with a later risk of starting to smoke tobacco cigarettes.

Conclusions. This evidence is consistent with a possible causal link from tobacco smoking to later depressed mood in late childhood and early adolescence, but not vice versa. (Am J Public Health. 1999;89:1837–1840)

Li-Tzy Wu, ScD, and James C. Anthony, PhD

Building on a large and growing body of evidence on tobacco smoking and depressed mood from mid-adolescence to adulthood, Patton and colleagues in 1996 authored a Journal article on the cross-sectional association between tobacco use and depression in teenagers. In this report, we seek to add new prospectively gathered evidence on this topic. Using survival analysis methods and data from late childhood to mid-adolescence, we estimate how much the risk of depressed mood might depend on tobacco smoking. Separately, we estimate how much the risk of starting to smoke might depend on depressed mood.

In preparing this work, we were mindful of past findings on associations between tobacco use and depression but were uncertain about whether these findings apply to late childhood and early adolescence. Of particular interest to us has been the issue of underlying shared vulnerability to both tobacco smoking and depressed mood, with some investigations of adults seeming to favor an inherited or genetic substrate and others seeming to favor a more social or psychological substrate. It is not possible to resolve this controversy with the present investigation. Nonetheless, the emergence of an association between tobacco smoking and depression in early adolescence might help us clarify whether early-life tobacco smoking promotes the onset of depressed mood, early-life depressed mood promotes the onset of tobacco smoking, or both. If both statements are true, then we may need to turn our investigation in the direction of some fairly simple explanatory conceptual models of underlying shared vulnerability. However, if the link from tobacco smoking to first-onset depression is observed without a link from depression to the initiation of tobacco smoking, then the argument of a shared vulnerability at this stage of life or this stage of smoking involvement must be elaborated to account for the asymmetry in the evidence. The possibility that the dynamics of tobacco–depression associations vary by stage of life or by stages of smoking involvement is not out of the question.

Methods

Data for this investigation come from a population-based prospective study conducted in the mid-Atlantic region of the United States between the mid-1980s and 1990s, reported in previous articles, one of which presented the results of a randomized trial of 2 preventive interventions, the Good Behavior Game and a Mastery Learning reading curriculum. In brief, 2 successive cohorts of first-graders from 43 classrooms within 19 elementary schools were recruited for study in 1985 and 1986 (n = 2311). Between 1989 and 1994, when the first yearly interview assessments were made to measure both tobacco smoking and sustained depressed mood, a total of 2150 student participants were assessed. The follow-up sample consisted of an almost equal proportion of males and females. Approximately 75% of youths were African Americans, about 1% were of Hispanic, American Indian, or Asian origin, and the rest were non-Hispanic Whites.

To estimate the temporal association between tobacco smoking and depressed mood, for the statistical analysis, we included only youths who were assessed on at least 2 consecutive occasions during the...
TABLE 1—Estimated Relative Hazard of Depressed Mood in Relation to Prior Tobacco Smoking From 8–9 to 13–14 Years of Age: Results Obtained From Survival Analyses

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted Relative Hazard (95% CI) (P)</th>
<th>Adjusted Relative Hazard (95% CI) (P)</th>
<th>Adjusted Relative Hazard (95% CI) (P)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antecedent tobacco smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.73 (1.35, 2.21) (.001)</td>
<td>1.64 (1.26, 2.12) (.001)</td>
<td>1.66 (1.28, 2.16) (.001)</td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.88 (0.76, 1.04) (.146)</td>
<td>0.87 (0.74, 1.02) (.094)</td>
<td>0.86 (0.73, 1.02) (.060)</td>
</tr>
<tr>
<td>Female</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-White</td>
<td>1.35 (1.10, 1.66) (.004)</td>
<td>1.39 (1.13, 1.71) (.002)</td>
<td>1.39 (1.12, 1.71) (.002)</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Prior alcohol use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.26 (1.07, 1.49) (.006)</td>
<td>1.21 (1.01, 1.44) (.035)</td>
<td>1.19 (0.99, 1.42) (.059)</td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Note. CI = confidence interval; 1.00 indicates the reference category.

*Data from 1731 youths attending public schools assessed between 1989 and 1994.

This model was adjusted for prevention trial characteristics (i.e., assignment to Good Behavior Game vs Master Learning interventions), in addition to sex, race/ethnicity, and prior alcohol use.

period 1989 to 1994. We observed no statistically significant difference in sex, age, or race/ethnicity between those assessed at least twice and those assessed once. We used data covering an age range from 8 to 9 years through 13 to 14 years to estimate the association between smoking (first assessed at 8–9 years) and later depressed mood (first assessed at 9–10 years). We used data covering an age range from 9 to 10 years through 13 to 14 years to estimate the association between depressed mood and subsequent initiation of tobacco smoking.

Data Collection and Variables

Data were collected by standardized face-to-face, private interviews with each student. Interviewers were aged 20 to 35 years and had completed a 1-week training program before conducting the interviews. Before each interview, verbal assent was obtained from each participating student. It was explained to each child that all of his or her answers would be kept confidential and that he or she could decide whether to answer any question or to end the interview at any time. Parental consent had been previously obtained.

Consistent with prior research, depressed mood was defined as being in a bad mood, feeling sad, feeling crabby, or feeling like crying all the time or almost all of the time and having one or more of these feelings for at least 2 weeks. We used depression-screening questions to assess the presence of depressed mood; the presence of depressive disorder was not assessed. Initiation of smoking refers to the first time that the youth smoked a tobacco cigarette, as determined by an interview question. Alcohol use included any use of beer, wine, or other alcoholic drink.

Statistical Analysis

The survival analysis was organized to estimate the association of tobacco smoking with depressed mood in both temporal sequences. First, the occurrence of depressed mood (at time \( t \)) was treated as the outcome, and antecedent tobacco smoking status (at time \( t - 1 \)) was the covariate. Next, initiation of tobacco use (at time \( t \)) was treated as the outcome, and antecedent depressed mood status (at time \( t - 1 \)) was the covariate. An analytic strategy that applied the case–base concept with elements of the nested case–control study design and the case–cohort design was used. Briefly, to test for a temporal sequencing from antecedent tobacco smoking to later occurrence of depressed mood, all prevalent cases of depressed mood up to the year of observation were excluded from the sample; the remaining at-risk youths were followed up to identify new cases of depressed mood. In this analysis, the "exposure" of interest is tobacco smoking in the 1-year interval before the onset of depressed mood (or in the comparable 1-year interval for noncases who remained at risk for depressed mood). During the interval of observation, a total of 598 students developed depressed mood, as defined and measured in this study.

Likewise, for the analysis of depressed mood to subsequent initiation of tobacco use, prevalent cases of tobacco smoking up to the year of observation were excluded from the sample. The remaining at-risk youths were followed to identify new cases of tobacco smoking. The risk of initiation of smoking among at-risk youths was then studied in relation to depressed mood in the 1-year interval before the initiation of smoking (or in the comparable 1-year interval for at-risk noncases). A total of 206 students started smoking tobacco during the observation interval.

SPSS survival analysis procedures were used for maximum likelihood estimation of regression coefficients under the Cox proportional hazards model. This model takes into account the prospective nature of the study—youths were passing from 8 years to 13 to 14 years of age—and accommodates change over time in the explanatory variables of interest (specifically, antecedent depressed mood and antecedent tobacco smoking). Sex, race/ethnicity, prior alcohol use, and prevention trial characteristics were introduced as control variables to constrain possible confounding influences in relation to the estimated associations.

Results

Tobacco Smoking as a Risk Factor for Subsequent Depressed Mood

Table 1 summarizes estimated relative hazards for occurrence of depressed mood from 8 to 9 years of age through 13 to 14 years of age. Tobacco smoking was associated with a modestly increased risk for first occurrence of depressed mood (unadjusted relative hazard = 1.73; 95% confidence interval [95% CI] = 1.35, 2.11; \( P < .001 \)). Relative to being female, being male was not associated with an increased risk for experiencing depressed mood, whereas being non-White relative to being non-Hispanic White was modestly associated with an excess risk for depressed mood (unadjusted relative hazard = 1.35; 95% CI = 1.10, 1.66; \( P = .004 \)). As indicated in the last column of Table 1, covariate adjustment had little influence on the estimates (e.g., adjusted relative hazard associated with tobacco smoking was 1.66; 95% CI = 1.28, 1.66; 95% CI = 1.00, 1.00).
TABLE 2—Estimated Relative Hazard of Tobacco Smoking in Relation to Prior Depressed Mood From 9–10 to 13–14 Years of Age: Results Obtained From Survival Analyses

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted Relative Hazard (95% CI) (P)</th>
<th>Adjusted Relative Hazard (95% CI) (P)</th>
<th>Adjusted Relative Hazard (95% CI) (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antecedent depressed mood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.07 (0.76, 1.52) (0.690)</td>
<td>1.01 (0.71, 1.44) (0.943)</td>
<td>1.06 (0.74, 1.51) (0.764)</td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.10 (0.84, 1.44) (0.497)</td>
<td>1.03 (0.78, 1.35) (0.845)</td>
<td>1.03 (0.78, 1.37) (0.840)</td>
</tr>
<tr>
<td>Female</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-White</td>
<td>0.68 (0.50, 0.94) (0.019)</td>
<td>0.76 (0.55, 1.05) (0.099)</td>
<td>0.83 (0.59, 1.17) (0.294)</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Prior alcohol use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2.60 (1.96, 3.47) (0.001)</td>
<td>2.54 (1.90, 3.39) (0.001)</td>
<td>2.75 (2.04, 3.70) (0.001)</td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Note. CI = confidence interval; 1.00 indicates the reference category.

aData from 1731 youths attending public schools assessed between 1989 and 1994.

This model was adjusted for prevention trial characteristics (i.e., assignment to Good Behavior Game vs Master Learning interventions), in addition to sex, race/ethnicity, and prior alcohol use.

2.16; P < .001). Prior use of alcohol was not associated with increased hazard of depressed mood (adjusted relative hazard = 1.19; 95% CI = 0.99, 1.42; P = .59).

To check the validity of statistical adjustments, we conducted an exploratory search for subgroup variation, but no product-term was found to improve the fit of the models.

Depressed Mood as a Risk Factor for Subsequent Tobacco Initiation

Table 2 indicates that antecedent depressed mood was not associated with subsequent initiation of tobacco smoking, or that the association was close to null, as indicated by the point estimate and confidence bounds (unadjusted relative hazard = 1.07; 95% CI = 0.76, 1.52; P = .690). In addition, sex was not associated with the initiation of tobacco smoking in this age group, but being non-White was associated with a lower risk of tobacco smoking when compared with being non-Hispanic White (unadjusted relative hazard = 0.68; 95% CI = 0.50, 0.94; P = .019).

Prior alcohol use was associated with an increased risk for initiation of tobacco smoking (unadjusted relative hazard = 2.60; 95% CI = 1.96, 3.47; P < .001), even with statistical adjustment for other covariates. Subgroup variation involving sex and prevention trial group assignment was found, consistent with intervention impact analyses reported in an earlier article.19

Discussion

The main finding of this study of youths aged 8 to 9 years through 13 to 14 years is that antecedent tobacco smoking signaled a modestly increased risk for subsequent occurrence of depressed mood, but antecedent depressed mood was not associated with an increased risk for starting to smoke tobacco cigarettes.

The evidence from this sample tends to support a 1-directional relationship from prior tobacco smoking to later depressed mood, but not from depressed mood to initiation of smoking, in the childhood–adolescent transition years.

Before we discuss this evidence in relation to its implications, 4 primary limitations deserve mention. First, this study sample came from the urban, mid-Atlantic region of the United States; hence, generalizability beyond this sample requires replication elsewhere. Second, the direct comparability between this study and studies with adult samples is restricted by our focus on early depressed mood and early initiation of tobacco smoking. In contrast, most adult studies have investigated major depression and nicotine dependence, or the progression to daily smoking. The etiologic relationships between depressed mood and initiation of tobacco smoking may be different from linkages between daily tobacco smoking, nicotine dependence, and major depression. Future research will be needed to investigate this possibility.

Tobacco Smoking and Depressed Mood

Third, the data used in this study are based on youths' self-reports. Self-reports are influenced by potential reporting errors and recall bias, but in a large epidemiologic sample with longitudinal assessments each year, alternative methods do not seem feasible. We also note that assessment of depressed mood among children remains controversial, but the nature of our research design is not such that it should bias the estimated tobacco–depression association.

Fourth, as described in prior reports,17–19 a great majority of eligible youths agreed to participate in the study at its inception. However, over the years there has been sample attrition (primarily as a result of students' out-migration from the public school system). Hence, the resulting estimates are for the residual cohort of youths who were growing up and going to school in this urban public school system. An investigation of the issue of differences between participants and nonparticipants with respect to histories of smoking and depression is under way as part of a follow-up at 19 to 20 years of age, but this data gathering will not be completed for 2 years.

Notwithstanding these limitations, this research has strengths that merit attention. First, the prospective nature of this study allowed us to go beyond a cross-sectional association to a consideration of temporal sequencing. Second, our focus on late childhood and early adolescence has some merits: in these life stages, there are limitations on the array of confounding variables that might explain observed relationships. In consequence, the study ruled out factors such as patterns of cessation and relapse that often characterize the natural history of adult tobacco smoking. For example, adults with a history of tobacco smoking or dependence are likely to have experienced the cycle of cessation and relapse that often includes depression as a symptom. Furthermore, many adult smokers have experienced chronic exposures of the central nervous system to nicotine or other components of tobacco use. Although this study cannot assess hypotheses about sustained smoking, it may be that the tobacco smoking–depression relationship is more dynamic than has been conceived thus far. Initiation, regular use, nicotine dependence, and cessation may all have different relationships with depression.12 Clearly, additional prospective epidemiologic studies as well as basic pharmacologic and neuroscience research are warranted in a continuing effort to unravel the observed relationship between tobacco smoking and depression.

Overall, our findings indicate a 1-directional relationship of antecedent tobacco use leading to later onset of depressed mood during early adolescence, but not vice versa.
These results do not support a simple "common factor" hypothesis as offered by other investigations that focused on adult daily smoking and nicotine dependence, unless the common factor model is elaborated to account for a sequence from tobacco smoking to depression but no sequence from depressed mood to tobacco smoking.2,6-9,11,14 The self-medication hypothesis,26 if meant to imply that depression leads to early-onset initiation of tobacco smoking, is not supported by these study data. Nonetheless, while self-medication may not lead to smoking the first cigarette, it might lead to smoking many cigarettes per day or to regular daily smoking.26

Our observations are more consistent with hypotheses in which nicotine exposure or other components of tobacco smoking are claimed to affect depressed mood (e.g., via central nervous system processes27-30 or thyroid function,31 which then play a role in the occurrence of depressed mood). Such a neuropharmacologic hypothesis is also consistent with the literature on smoking cessation and depression,13,30,32 In addition, we note that Breslau and colleagues, after studying adults, suggested that major depression predicts a progression to daily smoking among adult smokers but not to smoking initiation among adult nonsmokers.12

Although alcohol use was not the primary interest of the study, the relationship between alcohol use, tobacco smoking, and depressed mood was consistent with the literature and may have some implications for new research.30 New research efforts are needed to investigate the neuropharmacologic effects of nicotine and alcohol on psychiatric illnesses. As suggested by Glassman,30 studies on tobacco smoking and its associated psychiatric illnesses offer an opportunity to increase our understanding both of normal brain function and of psychopathologic processes.

In conclusion, this study provides evidence that tobacco smoking in late childhood and early adolescence may constitute a causally important risk factor for later onset of depressed mood. Taking a step back from empirical results such as these, we now propose that conceptual models of the tobacco-depression relationship have not yet disentangled what is true for early-onset tobacco smoking from what is true for later-onset tobacco smoking, as well as what might be true for the different stages of tobacco involvement: the initiation stage, the progression or dependence stages, and the cessation stage.

Given the adverse consequences of tobacco smoking and adolescent depression, the association between the two deserves attention early in a child's life. Future research will be needed to identify effective interventions for preventing the initiation of tobacco smoking among youths. Future experimental research may help us shed new light on the association between tobacco and depression if we can gain experimental control over which youths start smoking and which do not. These future experiments may prove to be our only path to definitive evidence about tobacco as a cause of depressed mood in youths.

Contributors
J.C. Anthony was principal investigator for the longitudinal research described in the study. L.-T. Wu was responsible for analyses and scientific writing under J.C. Anthony's supervision as postdoctoral mentor.

Acknowledgments
Data for this study came from the Prevention Research Center (PRC) at Johns Hopkins University. The PRC study was approved by the Institutional Review Board. Consent for participation in the study was obtained from each participating student's parents, and verbal assent was obtained from each participating student.

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