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The Role of Psychiatric Disorders in the Relationship between Cigarette Smoking and DSM-IV Nicotine Dependence among Young Adults

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Abstract

This study set out to evaluate the association between cigarette smoking and DSM-IV nicotine dependence and to determine whether psychiatric disorders may signal greater sensitivity to nicotine dependence at similar levels of smoking exposure. Drawing on the young adult sample (age 18 to 25) from the National Epidemiologic Survey of Alcohol Related Conditions (NESARC), logistic regression analyses were conducted. Smokers with major depression, alcohol use disorders or specific phobia had a higher risk of meeting DSM criteria for nicotine dependence than those without these disorders. When examining smoking quantity, rates of nicotine dependence were similar for those with and without major depression among non-daily smokers, yet among daily smokers, rates of nicotine dependence were consistently higher among those with major depression compared to those without. Alcohol dependence elevated the risk of nicotine dependence at low to moderate levels of use. However, no difference in risk for nicotine dependence was seen between alcohol dependent and non-dependent individuals smoking more than a pack a day. Increased risk of nicotine dependence among those with a specific phobia was consistent across the range of current smoking levels. These findings add to the growing literature documenting dependence in non-daily smokers and demonstrate that while chronic smoking is often a key feature in dependence, psychiatric disorders may signal greater sensitivity to nicotine dependence symptoms at substantially lower levels of smoking exposure.

Keywords

smoking; nicotine dependence; sensitivity; major depression; alcohol dependence

Introduction

One of the most potent groups of risk factors consistently implicated in both the etiology of smoking behavior as well as the subsequent developmental course of nicotine dependence is the psychiatric disorders. Evidence for these associations comes from longitudinal investigations in which depression (Breslau et al., 1998, Dierker et al., 2001), anxiety (Patton et al., 1998), alcohol (Federman et al., 1997), and behavior disorders (Breslau, 1995), have each been shown to increase risk of later smoking. Discussion of the mechanism of association

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with nicotine dependence has often focused on the role of psychiatric disorders in elevating an individual's probability of smoking exposure (i.e. increasing the likelihood of initiation, promoting earlier onset, and/or influencing the number of cigarettes or persistence of smoking), suggestive that it is the increased exposure that then causes physiological adaptations that lead to dependence symptoms (Pomerleau, 1995). While it is true that smoking exposure is a necessary requirement for nicotine dependence, emerging evidence suggests that frequency and quantity of smoking are markedly imperfect indices for determining an individual's probability of developing nicotine dependence. For example, nicotine dependence has recently been reported among population subgroups reporting relatively low levels of daily (Kandel and Chen, 2000, DiFranza et al., 2000, O'Loughlin et al., 2003) and non daily (Dierker et al., In press) smoking..

A complementary or alternate role that psychiatric disorders may play is as a cause or signal of greater sensitivity to nicotine dependence at similar levels of exposure. That is, individuals with specific psychiatric disorders may experience symptoms of nicotine dependence at lower levels of use compared to individuals without the disorder. These early emerging dependence symptoms may in turn increase the likelihood of continued smoking and difficulty in quitting. To date, there has been relatively little epidemiologic research examining sensitivity for nicotine dependence (DiFranza et al., 2000, O'Loughlin et al., 2003) and available research has been largely based on an exploration of individual differences between demographic subgroups (i.e. age, gender and ethnicity) (Kandel and Chen, 2000).

The present study examined young adults from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) 1) to determine which psychiatric disorders are associated with nicotine dependence over and above exposure to smoking and 2) to evaluate whether the relationship between current smoking and nicotine dependence is similar for individuals with and without psychiatric disorders.

Method

Sample

The sample from the first wave of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), described in detail elsewhere (Grant et al., 2004), represents the civilian, non-institutionalized adult population of the United States and includes persons living in households, military personnel living off base, and persons residing in the following group quarters: boarding or rooming houses, non-transient hotels and motels, shelters, facilities for housing workers, college quarters and group homes. The housing unit sampling frame of the NESARC was the U.S. Bureau of Census Supplementary Survey and the Census 2000 Group Quarters Inventory. One adult was selected for interview in each household and face-to-face computer assisted interviews were conducted in respondents' homes following informed consent in which the procedure was fully explained. The sampling frame response rate was 99%, the household response rate was 89%, and the individual response rate was 93% (overall survey response rate 81%). In order to 1) focus on a period of risk for the onset of established smoking behavior (i.e. young adulthood); 2) reduce the length of retrospective recall and 3) limit exposure to smoking to years rather than decades, the present analyses are based on participants age 18 to 25 reporting any smoking in the past year (N=1706).

Measures

Lifetime psychiatric disorders were assessed using the NIAAA, Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV (AUDADIS-IV) (Grant et al., 2003, Grant et al., 1995). Reliability and validity estimates have been previously reported for both mood and anxiety disorder modules (Canino et al., 1999, Grant et al., 2003) and substance use

modules (Grant et al., 2003, Grant et al., 1995) and have been consistently found to meet or surpass acceptable levels. The following non-hierarchical disorders were examined: major depression, dysthymia, generalized anxiety disorder, panic disorder with or without agoraphobia, social phobia, specific phobia, alcohol dependence, other drug dependence (i.e. amphetamine, opioid, sedative, tranquilizer, cocaine, inhalant, hallucinogen, cannabis, or heroin), and antisocial personality disorder.

The tobacco module of the AUDADIS-IV contains detailed questions on the frequency, quantity and patterning of tobacco use as well as symptom criteria for DSM-IV nicotine dependence. Smoking questions examined in the present analyses included age of smoking onset ("About how old were you when you smoked your first full cigarette?"), age of daily smoking onset ("About how old were you when you first started smoking everyday?"), and age of onset for nicotine dependence ("About how old were you the first time some of these [nicotine dependence symptoms] began to happen to you around the same time?"). Current smoking was evaluated through frequency ("About how often did you usually smoke in the past year?") coded dichotomously in terms of the presence or absence of daily smoking and quantity ("On the days that you smoked in the last year, about how many cigarettes did you usually smoke?"). A variable reflecting number of years since smoking initiation was created by subtracting smoking onset age from current age. Algorithms developed for the AUDADIS-IV variables operationalize the diagnostic criteria for DSM-IV nicotine dependence experienced in the past 12 months (current) and prior to the past 12 months (past).

Statistical Analyses

Logistic regression models were estimated to test the association between individual psychiatric disorders and nicotine dependence, with control for comorbid psychiatric disorders, current smoking, number of years since smoking initiation, age of smoking onset, ever daily smoking, other tobacco use in the past year (i.e. cigars, snuff, pipe or chewing tobacco), age, ethnicity and gender. Current smoking quantity was grouped according to the following criteria: Nondaily smoking, 1–5 cigarettes per day, 6 to 10 cigarettes per day, 11 to 15 cigarettes per day, 16 to 20 cigarettes per day, and >20 cigarettes per day. The midpoint of each category was used in the logistic regression analysis. Next, two-way interactions between psychiatric disorders and current smoking were included in the full models to evaluate whether the relationship between nicotine dependence and current smoking was similar for individuals with and without psychiatric disorders. Sample weights were used in each individual analysis to correct for differences in the probability of selection and to adjust for non-response. Adjustments for the design effects were incorporated into the estimation process implemented by SAS (Version 9.1) survey procedures to generate accurate standard errors.

Results

Prevalence of Smoking and Nicotine Dependence

More than a third (35.8%, SE 0.77) of young adults reported smoking 100 or more cigarettes in their lifetime, the majority of whom smoked during the year prior to involvement in the survey (88.8%, SE 0.83). There were a total of 1706 young adults reporting any smoking within the past 12 months. Three hundred eighty six (22.5% SE 1.21) reported their current smoking at non daily levels, 249 (12.9% SE .90) smoked between 1 and 5 cigarettes per day, 471 (27.0% SE 1.28) smoked between 6 and 10 cigarettes per day, 134 (7.8% SE .70) smoked between 11 and 15 cigarettes per day, 368 (23.5% SE 1.23) smoked between 16 and 20 cigarettes per day and 87 (6.2% SE .71) smoked more than 20 cigarettes. Among non-daily smokers, over a third (35.6% SE 2.54) smoked less than once per week, 22.3% (SE 2.19) smoked 1 to 2 days per week, 24.4% (SE 2.24) smoked 3 to 4 days per week, and the remaining 18.7% (SE 1.87) smoked 5 to 6 days. There was an average of 6.8 years since smoking initiation among past

year smokers (SE=.09): Only 16.4% (SE 1.05) of past year smokers reported use of any other tobacco products (i.e. cigars, snuff, pipe or chewing tobacco) during the preceding 12 months. A total of 896 past year smokers also met criteria for nicotine dependence during the past 12 months. The majority of these individuals reported the onset of nicotine dependence prior to the past year (n=723, 82.3% SE 1.42). The average number of years since the onset of nicotine dependence was 2.2 years (SE.08).

Psychiatric Disorders, Smoking Exposure and Nicotine Dependence

Table 1 presents both the univariate and multivariate associations from logistic regression models. After statistical control for psychiatric comorbidity, smoking exposure, other tobacco use in the past year, and demographic characteristics, those individuals with a lifetime history of major depression were 2.6 times (CI 1.88–3.63) more likely to report current nicotine dependence compared to those without major depression. Further, young adults having met criteria for a specific phobia were 1.8 times (1.16–2.88) more likely to be nicotine dependent than those without a specific phobia. Finally, individuals who met criteria for alcohol dependence were 2.8 times (2.06–3.84) more likely to report current nicotine dependence.

Variability in the association between current smoking and nicotine dependence based on the presence or absence of major depression, specific phobia, and alcohol dependence was tested through the addition of two-way interactions between individual psychiatric disorders and current smoking included in the full model. The two-way interaction between major depression and current smoking was significant (Figure 1). While at non-daily levels of use, rates of nicotine dependence were similar for those with and without major depression, among daily smokers, rates of nicotine dependence were consistently higher among those with major depression compared to those without. At the highest level of use (i.e. > 1 pack per day), 100% of the individuals with major depression met criteria for nicotine dependence compared to only 65% of those without major depression. Notably, more than 65% of individuals with major depression met criteria for nicotine dependence when smoking only 1 to 5 cigarettes per day.

The two-way interaction between alcohol dependence and current smoking was also significant (Figure 2). An examination of rates of nicotine dependence among individuals without alcohol dependence revealed an increase in rates of nicotine dependence across levels of current smoking. Alcohol dependence elevated the risk of nicotine dependence at low to moderate levels of use. However, no difference in risk for nicotine dependence was seen between alcohol dependent and non-dependent individuals smoking more than a pack a day. The two-way interaction between specific phobia and current smoking did not reach statistical significance, suggesting that the increased risk of nicotine dependence among those with a specific phobia was consistent across the range of current smoking levels.

Discussion

The present study examined whether higher rates of nicotine dependence among those with psychiatric disorders might be explained by greater risk for nicotine dependence at similar levels of use within a nationally representative sample of young adults. Two major findings emerged. First, after statistical control for psychiatric comorbidity and smoking exposure (i.e. current smoking, years since smoking onset and ever daily smoking), major depression, specific phobia and alcohol dependence were each associated with increased risk of current nicotine dependence. Second, the association between smoking exposure and nicotine dependence was found to differ according to the presence or absence of major depression and alcohol dependence.

Psychiatric Disorders and Nicotine Dependence

Variations in the association between smoking and nicotine dependence were seen based on the presence or absence of major depression. While rates of nicotine dependence were similar for those with and without major depression at non-daily smoking levels, among daily smokers, prevalence of nicotine dependence was consistently higher at each level of daily smoking among those with major depression compared to those without. Further, 65% of individuals without major depression and smoking more than 1 pack of cigarettes per day met criteria for nicotine dependence, while more than 65% of those with major depression reported meeting criteria for nicotine dependence when smoking only 1 to 5 cigarettes per day. Taken together, these results suggest that major depression may signal a substantial increase in sensitivity to nicotine dependence even at relatively low levels of daily smoking behavior.

Similarly, we found that specific phobia was associated with nicotine dependence after controlling for psychiatric comorbidity and smoking exposure, with increased risk for nicotine dependence for those with specific phobia consistent across levels of smoking. While not statistically significant in the full multivariate model, odds ratios for the association between nicotine dependence and both panic (1.5 C.I. 0.79–2.96) and social phobia (1.5 C.I. 0.74–2.87) were comparable to that of specific phobia (1.8 C.I. 1.16–2.88).

The relationship between both depression and anxiety, and the emergence of smoking behavior has been hypothesized to result from increased exposure to cigarettes stemming from the need to medicate negative affective experiences common to these types of disorders (Miran and Weiss, 1991). While anxiety and depression have been most often evaluated in terms of their potential role in increasing smoking exposure, animal models of negative affect and nicotine administration have begun to suggest the possibility that stress and negative affect may influence response to nicotine (Kassel et al., 2003). To date, studies have shown both increases and decreases in responsiveness to nicotine as a function of stress in rats. For example, experimentally induced chronic stress (via twice daily injections or forced swim) was found to reduce the normal thermic (i.e. core temperature) response to nicotine (Flemmer and Dilsaver, 1989, Peck et al., 1991), while adolescent preexposure to stress enhanced sensitization to the locomotor effects of nicotine in female rats (McCormick et al., 2004). The present findings compliment this experimental work in demonstrating increased risk for nicotine dependence at similar levels of smoking exposure for those with major depression or specific phobia.

Variations in the association between smoking and nicotine dependence were also detected based on the presence or absence of alcohol dependence. That is, smokers without a lifetime history of alcohol dependence displayed an increase in rates of nicotine dependence across levels of current smoking, while those with alcohol dependence showed elevated and statistically similar rates of nicotine dependence across levels of smoking. Consequently, the prevalence of nicotine dependence among alcohol dependent daily smokers was high (~80%) regardless of the number of cigarettes smoked per day or years since smoking initiation, suggesting that even low levels of cigarettes use may convey substantial risk in this population.

Previously, the link between alcohol use and smoking behaviors has most often been discussed in terms of the role of each behavior in increasing exposure through common co-use. Research within adolescence and young adulthood has clearly demonstrated, for example, the predictive value of both smoking and drinking in mapping the initiation and escalation of the other (Duncan et al., 1998, Jensen et al., 2003). While alcohol use can increase smoking behavior, emerging evidence has begun to suggest the possibility of a complementary mechanism of association between smoking and drinking that may stem from the role of alcohol in sensitizing pathways that make nicotine more reinforcing, and vice versa. Several studies, for example, have demonstrated changes in the effects of alcohol or nicotine as a consequence of exposure

to the other, that aversive effects of one drug may be counteracted by the other, that increasing tolerance for one substance may have cross-over effects in terms of tolerance for the other substance and that levels of sensitivity for one substance which can be selectively bred within mouse lines is related to differential sensitivity to the other substance (Bien and Burge, 1990, Collins, 1990, Littleton and Little, 2002, Prendergast et al., 2002). The present findings seem to confirm, through epidemiologic data focused on level of smoking, the likely role that alcohol use may play in the experience of nicotine dependence symptoms.

Strengths and Limitations

The current findings should be interpreted within the context of study limitations. First, “usual” smoking may be an incomplete measure of current smoking exposure. For example, studies of smoking topography, comprised of variables such as maximum puff velocity, puff volume, and number of puffs, reveal that smokers vary considerably in the amount of smoke they inhale when they smoke a cigarette (Kozlowski et al., 2001). Consequently, the number of cigarettes smoked over a given period is not strongly related to total nicotine exposure for that same period. Additionally, the assessment of usual consumption does not operationalize different patterns of smoking throughout the day (e.g binge experiences) or differences in nicotine exposure that are related to individual differences in nicotine metabolism (Malaiyandi et al., 2005). Thus, it is also possible that variability in nicotine dependence at similar levels of smoking between those with or without specific psychiatric disorders may still be based on variability in levels of nicotine exposure not captured by the present measure of the construct. Alternately, differences in rates of nicotine dependence may be driven by systematic differences in subjective evaluations of nicotine dependence symptoms rather than physiologic differences in sensitivity. That is, there may be biases in the way those with certain disorders respond to questions about nicotine dependence. For example, those with MDD may be more likely to answer questions more negatively and see themselves as more addicted. Future research utilizing both experimental and epidemiologic methods is needed to support or reject these alternative explanations.

Given the cross-sectional nature of the data, it is important to note that the present findings have limited implications for understanding the relationship between cigarette use and the emergence of dependence. That is, when examining smoking history among participants who reported nicotine dependence at non daily levels of use, half reported smoking at daily levels in the past suggesting that their dependence may in fact have been established at higher levels of use. Research on the emergence of dependence symptoms among novice adolescent smokers has been previously reported and has supported the emergence of some features of nicotine dependence well before the onset of daily smoking for a subgroup of smokers (DiFranza et al., 2000, Karp et al., 2005). Similar longitudinal work will be needed to begin to establish the role of psychiatric disorders in the emergence of nicotine dependence symptoms. Given the relatively low base rates of both nicotine dependence and specific psychiatric disorders as well as the variability in age of onset and period of risk for established smoking behaviors, this work may need to be targeted at high risk samples that maximize the number of informative cases.

With the goal of focusing on informative cases, we chose to examine young adults between the ages of 18 to 25 as this has been shown to be a period during which those who will try smoking have already initiated yet remain at particular risk for more established smoking behavior and the onset of nicotine dependence (Breslau et al., 2001). When examining the association between smoking exposure and nicotine dependence in the larger NESARC sample, patterns were generally consistent with those reported for young adults. A potentially more informative sample for examining individual differences in sensitivity to nicotine dependence at low levels of smoking exposure would include adolescents under age 18, given that sensitive individuals are hypothesized to meet criteria for nicotine dependence soon after

smoking initiation. In fact, data from the National Household Survey on Drug Abuse confirms higher rates of a proxy measure of nicotine dependence for adolescents compared to adults at the same level of use (Kandel and Chen, 2000). The relative dearth of nationally representative and up-to-date data on psychiatric disorders and nicotine dependence among adolescents, however, currently preclude adequate opportunities to pursue this question from an epidemiologic perspective.

It should also be noted that our findings are directly tied to the measurement of nicotine dependence according to DSM-IV, a conceptualization which was developed based on adult substance use patterns. It has been argued that the nicotine dependence among younger smokers is best measured by assessments developed to measure emergent smoking behavior (DiFranza et al., 2000). Perhaps with a more sensitive measure of early dependence such as the Hooked on Nicotine Checklist, differences in symptom levels would have been observed at the lowest levels of smoking in the comparison between depressed and non-depressed subjects.

Despite study limitations, the present investigation has practical implications that will guide future research. First, the major strength of the NESARC study is the large and representative sample as well as assessment of nicotine dependence across the continuum of smoking behavior, including non-daily use. Past research has shown that approximately 70% of all people try a cigarette sometime during their life (SAMHSA, 2002), yet only half of those who reach daily smoking levels continue smoking to the point of dependence (Breslau et al., 2001). Given that most smoking interventions target the prevention of the first smoking experiences within general population samples (Lantz et al., 2000) or the treatment of heavily dependent, chronic smokers among help seeking populations (Fiore, 2000), the present findings suggest needed attention to individuals with psychiatric disorders before daily smoking patterns are formed. Currently, the malleability of smoking behavior during this uptake process is unknown, but may represent appropriate timing for indicated intervention programming (Fiore, 2000, Okuyemi et al., 2002).

As the major dependence producing agent in cigarettes, nicotine is believed to play the pivotal role in keeping smoking rates stable. While chronic use is a key feature, the present study has shown substantial individual variability in nicotine dependence based on the presence or absence of specific psychiatric disorders even when controlling for smoking exposure. Thus, this study adds to the accumulating evidence that the expression of dependence can vary considerably across individuals with comparable exposure to smoking (DiFranza et al., 2000, O'Loughlin et al., 2003, Kandel and Chen, 2000, Dierker et al., In press). Understanding the different roles that psychiatric disorders may play during periods of risk for the establishment of smoking behavior and nicotine dependence will require sustained and integrated effort across epidemiology and experimental work, both animal and human. Reliance on rich and diverse measurement of nicotine exposure will further allow an identification of population subgroups more or less sensitive to nicotine dependence across the continuum of smoking behaviors.

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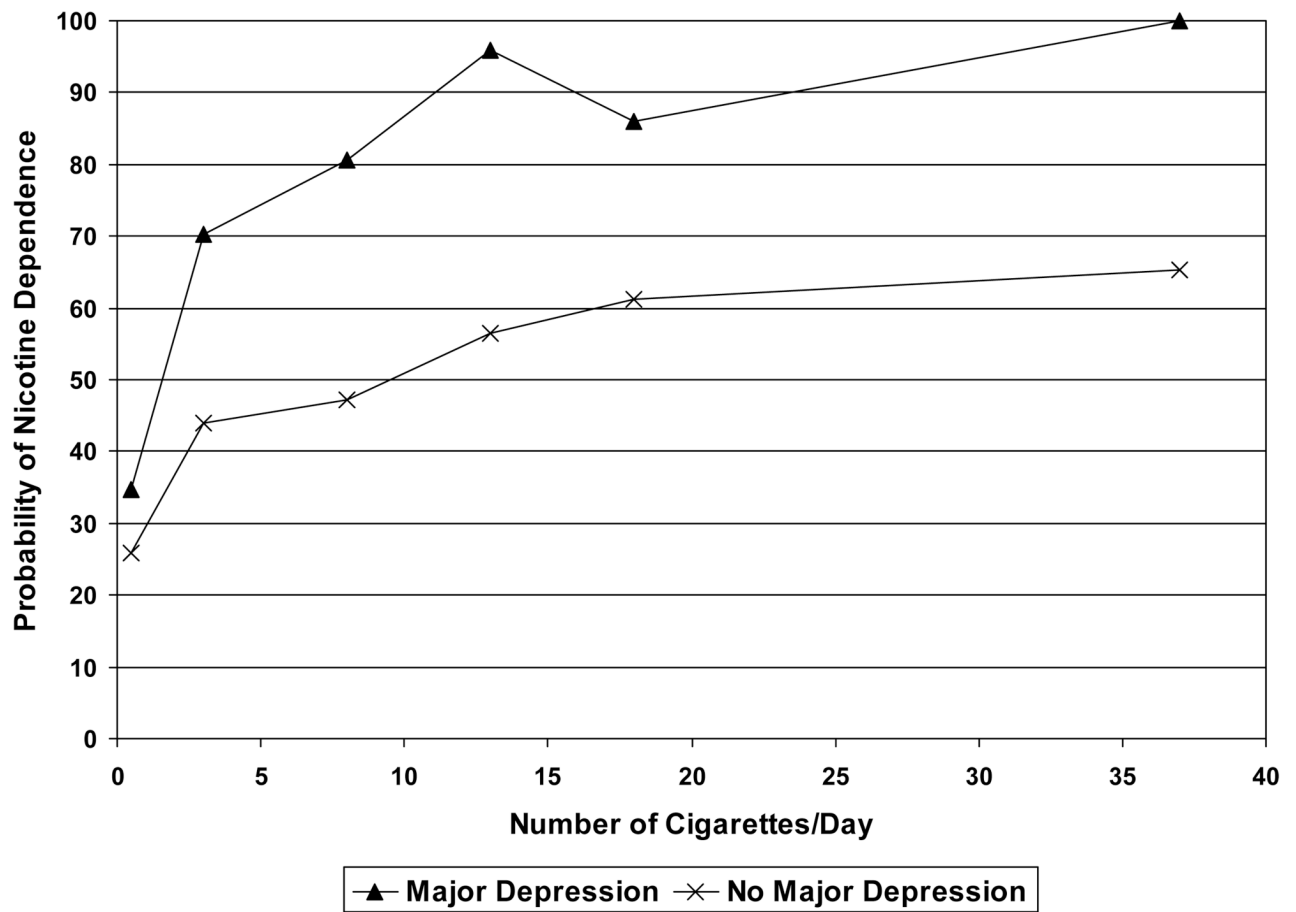


Figure 1.

Association between DSM-IV nicotine dependence and current smoking by lifetime history of major depression (N=1706).

First value (x-axis) represents less than daily smoking. Remaining values indicate number of cigarettes smoked/day.

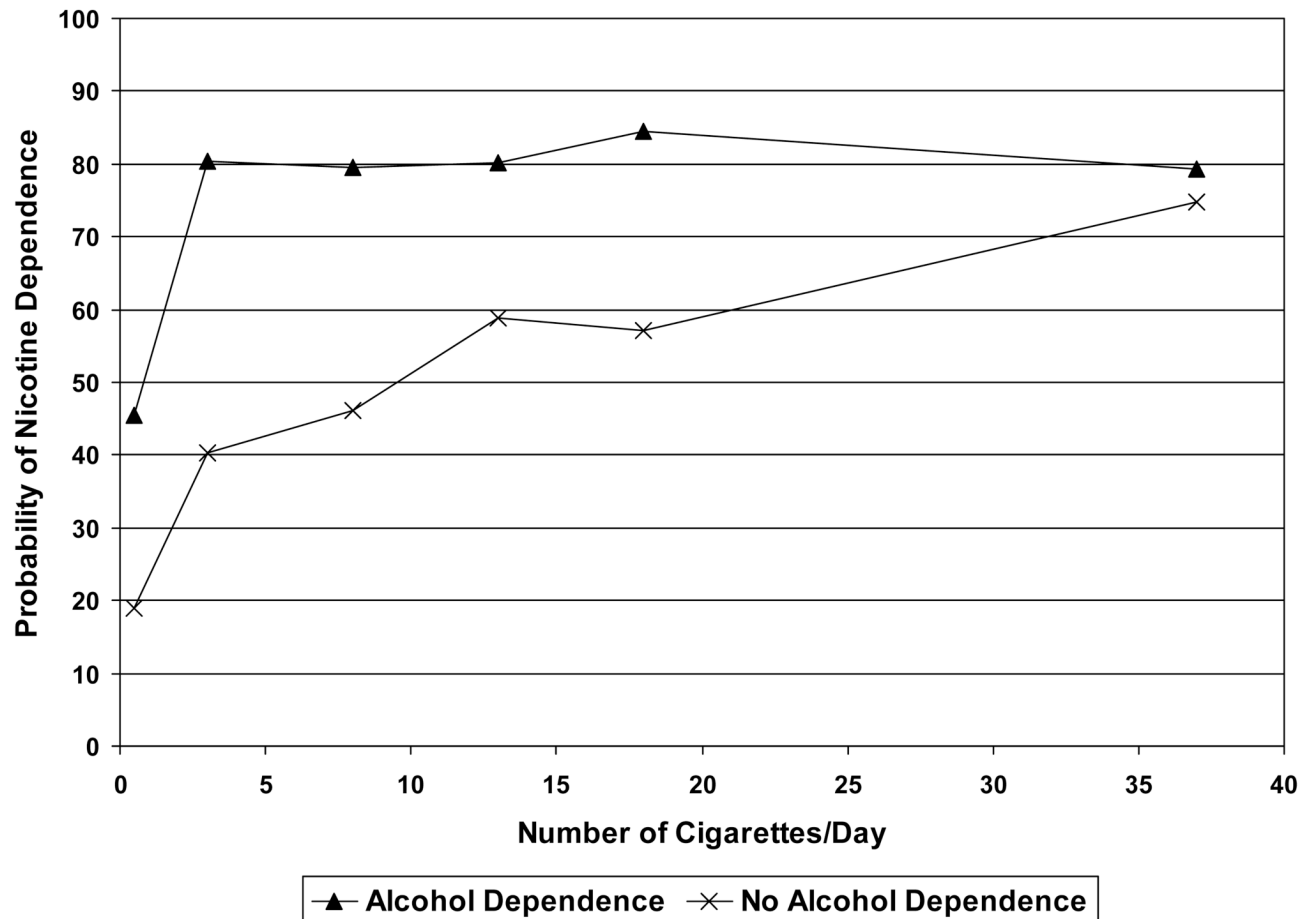


Figure 2.

Association between DSM-IV nicotine dependence and current smoking by lifetime history of alcohol dependence (N=1706).

First value (x-axis) represents less than daily smoking. Remaining values indicate number of cigarettes smoked/day.

Table 1

Odds ratios from univariate and multivariate models of psychiatric disorders, smoking exposure and other covariates on current (past 12 month) DSM-IV nicotine dependence among young adults (age 18 to 25) who report smoking in the past year (N=1706).

	<u>Univariate Model</u>		<u>Multivariate Model</u>	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Smoking				
Current smoking	1.1 **	1.05–1.08	1.1 **	1.03–1.07
Number of years since smoking initiation	1.1 **	1.04–1.10	1.0	0.93–1.11
Age of smoking initiation	0.9 **	0.84–.91	1.0	0.86–1.09
Ever smoked daily	5.1 **	3.22–8.09	3.3 **	1.89–5.72
Other tobacco use	1.5 **	1.11–2.03	1.2	0.81–1.78
Psychiatric Disorders (Lifetime)				
Major Depression	3.2 **	2.42–4.23	2.6 **	1.87–3.63
Dysthymia	2.3 **	1.31–3.93	0.6	0.34–1.12
Generalized Anxiety Disorder	2.8 **	1.55–5.02	1.3	0.57–2.77
Panic disorder with or without Agoraphobia	3.6 **	2.12–5.96	1.5	0.79–2.96
Social Phobia	3.4 **	1.94–6.07	1.5	0.74–2.87
Specific Phobia	3.4 **	2.37–4.93	1.8 **	1.16–2.88
Alcohol Dependence	3.5 **	2.67–4.46	2.8 **	2.06–3.84
Drug Dependence ^a	4.0 **	2.57–6.09	1.2	0.69–1.93
Antisocial Personality Disorder	2.8 **	1.92–4.03	1.3	0.81–1.99
Demographic Characteristics				
Ethnicity (vs. White)				
Black	0.8	0.53–1.06	1.3	0.84–1.91
Hispanic	0.5 **	0.39–0.74	0.8	0.56–1.10
Sex	0.9	0.71–1.10	0.8	0.59–1.04
Age	1.0	0.91–1.02	0.9	0.83–1.06

^a Includes dependence on amphetamines, opioids, sedatives, tranquilizers, cocaine, inhalants, hallucinogens, cannabis, or heroin.

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p<.01