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Nicotine dependence and mental disorders among adults in the USA: evaluating the role of the mode of administration

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Abstract

Background.—To investigate the association between nicotine dependence (ND), by cigarette smoking and use of smokeless tobacco (UST), and mental disorders.

Method.—Face-to-face surveys ($n=43\ 093$) were conducted in the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Nicotine use, ND, and mental disorders were assessed using DSM-IV criteria.

Results.—UST-ND was associated with a significantly increased likelihood of any anxiety disorder, specific phobia, alcohol abuse and dependence. Consistent with previous findings, cigarette smoking-ND was associated with an increased likelihood of all mental disorders examined. Among those without ND, cigarette smoking was specifically associated with panic attacks and panic disorder ; non-dependent UST was not associated with mental disorders.

Conclusions.—Our findings suggest that the association between ND and mental disorders is relatively specific to the mode of nicotine administration. Among those who are nicotine dependent, cigarette use is associated with most major psychiatric disorders, whereas UST is associated with dysthymia and specific phobia. Among those who use tobacco but are not nicotine dependent, cigarette use is associated with dysthymia and panic disorder ; UST is not associated with any major mood or anxiety disorders. The link between mental disorders and nicotine is complex, and is associated primarily with dependence, and not with non-dependent use.

Keywords

Anxiety; depression; epidemiology; mental disorders; nicotine dependence

Introduction

In recent years, there has been growing interest in the relationship between nicotine dependence (ND) and mental disorders. Studies from three main areas have found a strong

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Declaration of Interest
None.

link between ND and mental disorders. First, several studies among adults in the community (Goodwin & Hamilton, 2002; Grant et al. 2004b; Breslau et al. 2004; Doescher et al. 2006) have shown links between mental disorders and ND. Second, data from clinical settings also show high rates of cigarette use and ND among patients seeking treatment for anxiety, depression, and other serious mental disorders (Glassman et al. 1990, 2001; Covey, 1999; Williams & Ziedonis, 2004; Covey et al. 2006). Third, results from previous clinical studies have further suggested that co-morbid depression and anxiety disorders may be uniquely linked with ND by hindering smoking cessation efforts (Williams & Ziedonis, 2004) and associated with increased symptoms of nicotine withdrawal, compared with those without depression and anxiety disorders (Covey, 1999; Glassman et al. 2001). In addition, some studies have shown evidence of specificity in the link between ND and mental disorders.

Specifically, studies to date have consistently shown that among anxiety disorders, the strongest links exist between ND and panic attacks and panic disorder (Breslau & Klein, 1999; Isensee et al. 2003), although the reason for these associations is not clear. One hypothesis is that the co-morbidity arises because of respiratory abnormalities involved in both cigarette smoking (i.e. damage to the respiratory system that results from cigarette use) and panic (i.e. dyspnea and other respiratory symptoms associated with panic attacks). Another hypothesis is that smoking contributes to maladaptive emotionally salient experiences (i.e. nicotine withdrawal) and emotion regulation strategies (i.e. smoking to cope reflexively with emotional distress) ; both of these factors are associated with increased risk of panic above and beyond the variance attributed to ND, smoking rate and medical illness (Zvolensky & Bernstein, 2005; Gregor et al. 2007). However, although studies have examined a range of mental disorders in terms of specificity in relation to ND, the mode of administration, or type of ND, has not yet been examined. Furthermore, while a number of studies have examined links between use of smokeless tobacco (UST) and mental health problems among adolescents (Rouse, 1989; Coogan et al. 2000; Tercyak & Audrain, 2002), the relationship between UST or UST-ND and mental disorders has remained largely unexamined in adults.

Although the prevalence of UST has increased in recent years (Burns et al. 1998; Baker et al. 2000) and evidence to date consistently suggests a link between UST and mental health problems, little is known about this link in the community relative to available knowledge on cigarette smoking and co-morbid mental disorders. In particular, although studies have shown relationships between cigarette smoking and a wide range of mental disorders (e.g. Grant et al. 2004b), with the exception of substance use disorders the association between UST and the full range of mental disorders has not been examined (Rouse, 1989). In addition, the relative strength of the associations between non-dependent UST and mental disorders and non-dependent cigarette use and mental disorders has not been investigated. If the link between ND and mental disorders is due purely to the neurotoxic effects of nicotine on the brain, then the link between ND and mental disorders among those with UST-ND should be largely equivalent to the link between mental disorders and cigarette smoking-ND. Understanding the prevalence of mental health problems among these smokers has considerable public health significance in terms of identifying the public health parameters of this problem. In addition, given previous studies showing that both mental disorders (Eaton & Keyl, 1990; Lorant et al. 2003) and cigarette smoking (Barbeau et al. 2004) are

more common among various demographic segments of the population, and most commonly concentrated among vulnerable populations (e.g. lower socio-economic status, younger), it is important to understand whether and to what degree demographic differences may play a role in the relationships between mental disorders and various types of tobacco use on a population level.

The current study attempted to fill these gaps by answering four main questions in a representative sample of adults in the USA. First, the study examined whether there is an association between mode of administration of tobacco and odds of major mood, anxiety, and substance disorders among adults with ND. Second, the study investigated whether there is an association between mode of administration of tobacco and odds of mental disorders among adults without a diagnosis of ND. Third, the study examined whether the association between mode of administration of nicotine and mental disorders is specific to some mental disorders and not others. Fourth, the study investigated whether the link between mental disorders and ND, through either mode of administration, is explained by differences in demographic characteristics. We hypothesized that ND would be associated with an increased likelihood of mental disorders, regardless of the mode of administration. We also predicted that demographic characteristics would explain much of this relationship as previous studies have identified factors such as low school achievement, poor relationships with family, and low household income to be associated with an increased likelihood of nicotine use and dependence and with mental disorders (Rouse, 1989; Eaton & Keyl, 1990; Wells et al. 1994; Ellickson et al. 2001; Juon et al. 2002; Conwell et al. 2003; Lorant et al. 2003; Barbeau et al. 2004).

Method

Sample

The sample was drawn from participants in the 2001–2002 National Epidemiologic Survey of Alcohol and Related Conditions (NESARC), a nationally representative US survey of 43093 civilian non-institutionalized participants aged ≥ 18 years, sampled cross-sectionally. Details of the sampling frame are described elsewhere (Compton et al. 2004; Grant et al. 2004b, c). The National Institute on Alcohol Abuse and Alcoholism (NIAAA) sponsored the study and supervised the fieldwork, conducted by the US Bureau of the Census. Young adults, Hispanics, and African-Americans were oversampled, and the study achieved an overall response rate of 81%. To adjust for non-response and selection probability, the sample was weighted and adjusted to reflect the US population from the 2000 Decennial Census in terms of age, race, sex and ethnicity. The research protocol, including informed consent procedures, received full ethical review and approval from the US Census Bureau and the US Office of Management and Budget. Detailed descriptions of the demographics of this sample can be found elsewhere (Grant et al. 2003b; Hasin & Grant, 2005; Hasin et al. 2005).

Interviewers, training, and field quality control

Interviewing was conducted by 1800 professional interviewers from the Census Bureau using computer-assisted software with built-in skip, logic and consistency checks. All

interviewers had experience with other national health-related surveys with an average of 5 years' experience, and were further trained for 10 days under the direction of NIAAA. Verification of the interviewers was conducted by regional supervisors who recontacted a random 10% of all respondents for quality control purposes. In addition, a randomly selected subset of respondents was reinterviewed with one to three complete sections of the Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV (AUDADIS-IV). This served as a test–retest reliability study of NESARC measures (Grant et al. 2001). In the few cases when accuracy was uncertain, the data were discarded and a supervising interviewer repeated the interview.

Measures

Diagnoses were assessed with the NIAAA AUDADIS-IV (Grant et al. 2001). This instrument was specifically designed for experienced lay interviewers and was developed to advance measurement of substance use and mental disorders in large-scale surveys.

Tobacco use

Respondents were considered to have ever used cigarettes if they had smoked ≥ 100 cigarettes during their lifetime, and included in these analyses were those who had additionally used cigarettes at least once in the past year ($n = 9913$). Respondents were considered to have ever used smokeless tobacco if they had used chewing tobacco products or snuff products at least 20 times, and included in these analyses were those who had additionally used smokeless tobacco at least once in the past year ($n = 1058$). To examine only the effect of UST and cigarettes, past-year pipe users ($n = 215$), past-year cigar users ($n = 1119$) and those who had used both cigarettes and smokeless tobacco in the past year ($n = 377$) were removed from the analysis (total $n = 1542$ due to overlap among those categories), leaving a final sample size of 41551. The test–retest reliability of the nicotine use variables and other AUDADIS-IV nicotine use measures (e.g. frequency and duration of use) were excellent, with interclass correlation coefficients of 0.83–0.84 (Grant et al. 2003a).

Nicotine dependence (ND)

Assessment of problem use is based on the unique characteristics of ND as distinct from other substances. To that end, the AUDADIS-IV used an extensive list of over 40 questions to assess ND, and obtains extensive information on time-frames of nicotine use and dependence. Diagnoses were indicated according to the DSM-IV. A respondent needed at least three out of seven criteria indicated to be diagnosed with ND (APA, 1994). Criteria for ND include: (1) need more nicotine to achieve desired effect; (2) meets criteria for nicotine withdrawal syndromes; (3) using tobacco more than intended; (4) persistent desire or unsuccessful efforts to cut down on nicotine use; (5) great deal of time spent using tobacco (e.g. chain smoking); (6) giving up activities in favor of nicotine use; (7) continued use despite recurrent physical or psychological problems likely to have been caused by nicotine use. Nicotine withdrawal was assessed as a syndrome as described by the DSM-IV based on daily use of nicotine as well as meeting at least four of eight symptoms upon cessation of nicotine use, including depressed mood, insomnia, irritability, anxiety, difficulty concentrating, restlessness, decreased heart rate, and increased appetite. Time-frames for diagnosis included the previous 12-month period and prior to the previous 12-month period.

The reliability and validity of the ND diagnosis was assessed by a random subsample of 347 respondents who were reinterviewed with the ND module up to 10 weeks after the initial appraisal (Grant et al. 2003b). The procedures used were similar to those used in the German National Health Interview and Examination Survey (Schmitz et al. 2003). The reliability of the previous 12-month (i.e. current) diagnosis was good ($\kappa = 0.63$). A series of linear regression analyses was also used to validate the diagnoses by examining the association between ND and Short-Form 12v2 (an often used measure of generic quality of life that generates 10 component and profile scores assessing various dimensions of physical and mental disability) physical disability scores (Ware et al. 2002).

Mental disorders

Seven Axis I psychiatric disorders were assessed in the AUDADIS-IV using DSM-IV criteria. Diagnoses are made in two time-frames: the past 12 months and prior to the past 12 months. For the present analyses, current diagnoses (past 12-month) were used. Two mood disorders (major depression, and bipolar disorder) and four anxiety disorders [social phobia, specific phobia, generalized anxiety disorder (GAD), and panic disorder] were diagnosed. Dysthymia was excluded because cell sizes for specific analyses were too small. The reliability and validity of the psychiatric disorder diagnoses have been well documented, and more detailed information can be found elsewhere (Grant et al. 2004a, b; Hasin et al. 2005).

Statistical analyses

Analyses were conducted using SUDAAN Version 9.01 to derive standard errors that account for the complex sampling scheme of the dataset (SUDAAN, 2002). Weighted percentages were obtained to describe the prevalence of mental disorders among UST and cigarette users with and without ND. Odds ratios (ORs) were derived from logistic regressions to establish the association between current tobacco status (predictor) and current (past 12-month) mental disorders. Demographic control variables included age (defined categorically as 18–29, 30–44, 45–64, and ≥ 65 years), sex, ethnicity (defined as White, Black, American Indian/Alaska Native, Asian/Native Hawaiian/Pacific Islander, Hispanic), marital status (defined as married, widowed/separated/divorced), education (defined as less than high school/high school diploma/GED, above high school), and income [defined as personal income (in US\$) $< 19\,999$, $20\,000$ – $34\,999$, $35\,000$ – $69\,999$, and $\geq 70\,000$]. Clinical control variables included any mood disorder, any anxiety disorder, any personality disorder, or any non-nicotine substance disorder and were included in the model based on the outcome variable of interest. Quantity of tobacco used was also controlled in statistical models, as individuals with ND are more likely to use more nicotine products compared to tobacco users without ND. For comparison across substance, the quartiles of tobacco use quantities was calculated among users of cigarettes and UST separately. Users of cigarettes were categorized based on quartile of use compared to other cigarette users, and users of UST were categorized similarly compared to other UST users.

Results

Table 1 shows the prevalence of mental disorders among those without any cigarette or UST in the past year, and among those in each group with and without ND. In general, those with

ND (either smokers or UST) had a higher prevalence of mental disorders than those without ND or those without any tobacco use. UST without ND had a lower prevalence of all mood and anxiety disorders compared to those without any tobacco use, but a higher prevalence of alcohol disorders, drug abuse, and antisocial personality disorder. We used multivariable logistic models to test these associations statistically.

Association between UST, cigarette use, and mood disorders (past 12 months)

Among adults without current ND (past 12 months), UST was associated with a decreased likelihood of any mood disorder and cigarette use was associated with decreased odds of mania/hypomania. After adjusting for demographics, co-morbid mental disorders and quantity of tobacco used, there were no significant associations between UST or cigarette use and mood disorders (Table 2). There was no significant association between UST and mood disorders. Among those with ND, there was no significant association between UST and any mental disorders. Use of cigarettes was significantly associated with all mood disorders among adults with ND. These associations remained significant albeit attenuated after adjusting for demographics, mental disorders, and quantity of cigarettes consumed.

Association between UST, cigarette use, and anxiety disorders (past 12 months)

Among those with ND, UST was associated with a significantly increased likelihood of any anxiety disorder and specific phobia, compared with no UST or cigarettes (Table 3). These associations remained statistically significant after adjusting for differences in demographic characteristics, co-morbid mental disorders, and quantity used. Nicotine-dependent cigarette use was associated with all anxiety disorders in the unadjusted models, although after adjustment for demographics and co-morbid mental disorders only, the association between nicotine-dependent cigarette use and social phobia and GAD were no longer statistically significant. After further adjustment for quantity, the association between cigarette use and panic attacks was no longer significant.

Among adults without current ND, UST was not significantly associated with any mental disorders after adjustment (Table 3). Cigarette use was associated with panic disorder in unadjusted and adjusted models. Cigarette use was associated with increased odds of panic attacks, but this link was no longer significant after adjusting for quantity.

Discussion

First, our findings suggest that nicotine-dependent UST is associated with a subset of mental disorders, specifically any anxiety disorder and with current specific phobia, whereas nicotine-dependent cigarette use appears to be strongly linked with a wide range of both mood and anxiety disorders. Second, the study suggests that cigarette use, in the absence of ND, is associated with increased likelihood of panic disorder, and that UST in the absence of ND is not associated with any mental disorders. Third, the links between UST, cigarette use and mental disorders do not seem to be strongly influenced by differences in demographic characteristics. To our knowledge, this is the first study to demonstrate a distinction in mode of administration of nicotine in association with mental disorders. As such, our results suggest that it is not necessarily ND *per se* that is associated with mental disorders, but ND

through cigarette smoking. These data also importantly suggest that, even in the absence of ND, cigarette smoking is associated with some, but not all, mental disorders ; specifically panic disorder.

These data provide new information on the link between nicotine use, ND, and mental disorders among adults in the community by examining the role of mode of administration in this link. Previous results showing an association between cigarette use and mood disorders have examined this relationship using measures of cigarette smoking that have not distinguished between the presence or absence of ND (Goodwin & Hamilton, 2002; Grant et al. 2004a). These previous studies have shown associations between cigarette smoking and most mental disorders, yet our results suggest that this association is driven primarily by cigarette smoking among those with ND, and is far more limited in terms of links with non-dependent cigarette use and dependent and non-dependent UST.

The discrepancy in the link between ND, cigarette smoking, UST and mood disorders suggests that the specific chemical effects of nicotine consumption is not the mechanism through which mood disorders are linked. Our finding that adjustment for quantity of tobacco use had little impact on the majority of these relationships further strengthens this point. Previous studies have suggested that it is conceivable that neurobiological effects of nicotine on the brain, particularly desensitization of the reward pathway by overstimulation of nicotinic receptors, may lead to the onset of mood disorders and major depression in particular (Goldstein & Volkow, 2002 ; Weinberger et al. 2006). Nicotinic receptors are members of the cholinergic receptor family, such as dopamine and serotonin (Salin-Pascual et al. 2003). This overstimulation has major effects at a cellular level because the body compensates by reducing the number of receptors available ; in particular, dopamine receptors (Czermak et al. 2004). It has been hypothesized that the high rate of depression among smokers is due to the reduction in these dopamine receptors, as it has been suggested that nicotine has an antidepressant effect (Cardenas et al. 2002). Nicotine addiction occurs because nicotine is needed to maintain the normal stimulation of the postsynaptic cells. It remains unclear whether smokers with depression smoke to avoid mood worsening or to avoid adverse mood changes brought on by nicotine abstinence; however, our data do not provide support for either of these theories (Cardenas et al. 2002). If it were the case that the neurotoxic effects of nicotine led to mood disorders, then the strength of the links between UST and mood disorders, and cigarette smoking and mood disorders among those with ND should be closer in magnitude, and adjustment for quantity used in each domain should have an impact. The data are not able to explain the mechanism of this link, but the association appears to be specifically related to dependent cigarette smoking. This association could be due to biological/physical reasons, such as decreased dopamine receptors or the desire to curb withdrawal symptoms (Jain, 2003; Khurana et al. 2003; Czermak et al. 2004), or social reasons, such as having peers who smoke or a socio-economic disadvantage (West & Sweeting, 1994; Mitchell & West, 1996; Tucker et al. 2002; Barbeau et al. 2004), but, at this point, it is only possible to speculate on why this might be the case. One additional possibility is that there is a dose-dependent relationship between exposure to nicotine and mental disorders and that this explains the discrepancy in the association between non-dependent and dependent cigarette smoking and mental disorders, although this explanation would not account for the discrepancy in results for nicotine-dependent cigarette smoking

versus nicotine-dependent UST. However, the only relationship significantly affected by the quantity of tobacco consumed was the association between dependent and non-dependent cigarette use and panic attacks (in the absence of panic disorder), which was no longer significant after adjusting for quantity. As such, there may be exposure to other toxins that occurs through cigarette smoking, and is dose related, that increases the risk of mental disorders. The potential toxins involved here may include ammonia, nitrogen oxides, formaldehyde, acetone, hydrogen cyanide, mercury, and trace metals (Baker et al. 2004), among others, and these need to be studied further for their potential impact on mental health. These toxins may be specific to cigarette use, not to any use of tobacco. It is also possible that the impact of heavy, chronic cigarette smoking (e.g. in dependence) on specific physical functions/aspects of health may help to explain the discrepancy between UST dependence and cigarette dependence and mental disorders. For instance, it may be that decreased respiratory function is associated with mental health problems, independent of the cause of respiratory impairment, as has been shown in a previous population-based study (Goodwin et al. 2006). If this were the case, it could partially explain the specificity found here, suggesting that other potential physical consequences of dependent cigarette smoking may underlie the observed association between cigarette smoking and mental disorders. There are data to suggest that respiratory abnormalities may reflect vulnerability to panic attacks and panic disorder (Dilsaver, 1987; Pohl et al. 1992; Breslau & Klein, 1999; Johnson et al. 2000). This possibility that suboptimal respiratory function may be associated with greater anxiety and poorer mental health is consistent with the suffocation alarm hypothesis linking panic with breathing/respiratory issues. The finding that quantity of cigarettes smoked seemed to be specific to panic attacks adds further weight to the potential importance of this area. Future work in this domain may benefit from testing hypotheses from contemporary perspectives of ND that have begun to explicitly recognize the motivational bases for use (Baker et al. 2006). Here, emerging work suggests that the specific motives for use may hold promise in terms of better understanding associations with psychological functioning (Gregor et al. 2007).

Limitations and directions for future investigations should be noted. First, the cross-sectional design of this study does not permit causal conclusions regarding the direction of the observed associations. Future prospective work using longitudinal data and laboratory studies could be useful next steps for work directed at isolating the role of the method of nicotine administration in terms of its association with mental disorders. Second, the use of the AUDADIS-IV excludes psychotic disorders such as schizophrenia and post-traumatic stress disorder (PTSD), both of which are linked with high rates of tobacco use, other substance use and other mental disorders (Hughes et al. 1986; Reiger et al. 1990; Kessler et al. 1995; Cosoff & Hafner 1998; Lasser et al. 2000; Creamer et al. 2001; Breslau et al. 2004; Feldner et al. 2007). As such, further investigation of these associations within studies that include data on PTSD, and have assessed life events and exposure to trauma and adverse life events, may be useful in adding to our understanding. Third, although these results are generalizable to the adult US population, it is not clear whether they are applicable internationally, especially because various cultural and economic factors affecting tobacco use can vary substantially by region. Future studies in various countries examining this issue are necessary, especially in regions where tobacco use is growing rapidly, as in China (Yang

et al. 2001) and developing countries (Tominaga, 1986; Gajalakshmi et al. 2000). Fourth, the small cell sizes in some of the UST analyses may have limited statistical power and therefore confidence in the results of a number of specific analyses. As such, replication of these results in future studies would be useful.

The present findings highlight the relationships that exist between tobacco use and mental health problems, but show that these may be influenced by mode of administration. To date, work has focused largely on examining the main effects between tobacco use and psychopathology without regard to administration. Future investigations could usefully build upon such work by attempting more advanced tests focused on mediating and moderating processes in such linkages. For instance, variation in the effect of tobacco mode of administration on mental disorders over time by birth cohort would provide useful information as the shifting prevalence of cigarette smoking and UST by age group may reflect better public understanding of the dangers of tobacco use. A particular area of previously neglected consideration is the role of other toxins in cigarettes and their potential impact on mental, as well as physical, health. And finally, given the observed associations in this and other related studies (Goodwin & Hamilton, 2002; Grant et al. 2003b; Breslau et al. 2004; McClernon et al. 2006), greater degrees of clinical attention could be directed at addressing tobacco use in the context of treatment for anxiety and mood disorders.

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References

- APA (1994). *Diagnostic and Statistical Manual of Mental Disorders*, 4th edn. American Psychiatric Association : Washington, DC.
- Baker F, Ainsworth SR, Dye JT, Crammer C, Thun MJ, Hoffmann D, Repace JL, Henningfield JE, Slade J, Pinney J, Shanks T, Burns DM, Connolly GN, Shopland DR (2000). Health risks associated with cigar smoking. *Journal of the American Medical Association* 284, 735–740. [PubMed: 10927783]
- Baker RR, Pereira da Silva JR, Smith G (2004). The effect of tobacco ingredients on smoke chemistry. Part I : Flavourings and additives. *Food and Chemical Toxicology* 42, 3–37.
- Baker TB, Japuntich SJ, Hogle JM, McCarthy DE, Curtin JJ (2006). Pharmacologic and behavioral withdrawal from addictive drugs. *Current Directions in Psychological Science* 15, 232–236.
- Barbeau EM, Krieger N, Soobader M (2004). Working class matters : socioeconomic disadvantage, race/ethnicity, gender, and smoking in NHIS 2000. *American Journal of Public Health* 94, 269–278. [PubMed: 14759942]
- Breslau N, Klein DF (1999). Smoking and panic attacks : an epidemiologic investigation. *Archives of General Psychiatry* 56, 1141–1147. [PubMed: 10591292]
- Breslau N, Novak SP, Kessler RC (2004). Psychiatric disorders and stages of smoking. *Biological Psychiatry* 55, 69–76. [PubMed: 14706427]
- Burns DM, Cummings KM, Hoffman D (1998). *Cigars : Health Effects and Trends Smoking and Tobacco Control*. Monograph No. 9 U.S. Department of Health and Human Services, NIH: Bethesda, MD.
- Cardenas L, Tremblay LK, Naranjo CA, Herrmann N, Zack M, Busto UE (2002). Brain reward system activity in major depression and comorbid nicotine dependence. *Journal of Pharmacology and Experimental Therapeutics* 302, 1265–1271.

- Compton WM, Grant BF, Colliver JD, Glantz MD, Stinson FS (2004). Prevalence of marijuana use disorders in the United States : 1991–1992 and 2001–2002. *Journal of the American Medical Association* 291, 2114–2121. [PubMed: 15126440]
- Conwell LS, O’Callaghan MJ, Andersen MJ, Bor W, Najman JM, Williams GM (2003). Early adolescent smoking and a web of personal and social disadvantage. *Journal of Paediatrics and Child Health* 39, 580–585. [PubMed: 14629522]
- Coogan PF, Geller A, Adams M (2000). Prevalence and correlates of smokeless tobacco use in a sample of Connecticut students. *Journal of Adolescence* 23, 129–135. [PubMed: 10831138]
- Cosoff SJ, Hafner RJ (1998). The prevalence of comorbid anxiety in schizophrenia, schizoaffective disorder and bipolar disorder. *Australian and New Zealand Journal of Psychiatry* 32, 67–72.
- Covey LS (1999). Tobacco cessation among patients with depression. *Primary Care* 26, 691–706. [PubMed: 10436294]
- Covey LS, Bomback A, Yan GW (2006). History of depression and smoking cessation : a rejoinder. *Nicotine and Tobacco Research* 8, 315–319. [PubMed: 16766424]
- Creamer M, Burgess P, McFarlane AC (2001). Post-traumatic stress disorder : findings from the Australian National Survey of Mental Health and Well-Being. *Psychological Medicine* 31, 1237–1247. [PubMed: 11681550]
- Czermak C, Lehofer M, Wagner E, Prietl B, Gorkiewicz G, Lemonis L, Rohrhofer A, Legl T, Schauenstein K, Liebmann P (2004). Reduced dopamine D₃ receptor expression in blood lymphocytes of smokers is negatively correlated with daily number of smoked cigarettes : a peripheral correlate of dopaminergic alterations in smokers. *Nicotine and Tobacco Research* 6, 49–54. [PubMed: 14982687]
- Dilsaver SC (1987). Nicotine and panic attacks. *American Journal of Psychiatry* 144, 1245–1246.
- Doescher MP, Jackson JE, Jerant AF, Hart LG (2006). Tobacco prevalence and trends in smoking: a national rural study. *Journal of Rural Health* 22, 112–118.
- Eaton W, Keyl PM (1990). Risk factors for the onset of DIS/DSM-III agoraphobia in a prospective, population-based study. *Archives of General Psychiatry* 47, 819–824. [PubMed: 2393340]
- Ellickson PL, McGuigan KA, Klein DJ (2001). Predictors of late-onset smoking and cessation over 10 years. *Journal of Adolescent Health* 29, 101–108.
- Feldner MT, Babson KA, Zvolensky MJ (2007). Smoking, traumatic event exposure, and post-traumatic stress : a critical review of the empirical literature. *Clinical Psychology Review* 27, 14–45. [PubMed: 17034916]
- Gajalakshmi CK, Jha P, Ranson K, Nguyen S (2000). Global patterns of smoking and smoking-attributable mortality In *Tobacco Control in Developing Countries* (ed. Jha P and Chaloupka F), pp. 11–39. Oxford University Press : New York.
- Glassman AH, Covey LS, Stetner F, Rivelli S (2001). Smoking cessation and the course of major depression: a follow-up study. *Lancet* 357, 1929–1932. [PubMed: 11425414]
- Glassman AH, Helzer JE, Covey LS, Cottler LB, Stetner F, Tipp JE, Johnson J (1990). Smoking, smoking cessation, and major depression. *Journal of the American Medical Association* 264, 1546–1549. [PubMed: 2395194]
- Goldstein RZ, Volkow ND (2002). Drug addiction and its underlying neurobiological basis : neuroimaging evidence for the involvement of the frontal cortex. *American Journal of Psychiatry* 159, 1642–1652.
- Goodwin RD, Chuang S, Simuro N, Davies M, Pine DS (2006). Association between lung function and mental health problems among adults in the United States : findings from the First National Health and Nutrition Examination Survey. *American Journal of Epidemiology* 165, 383–388. [PubMed: 17158187]
- Goodwin RD, Hamilton SP (2002). Cigarette smoking and panic : the role of neuroticism. *American Journal of Psychiatry* 159, 1208–1213.
- Grant BF, Dawson DA, Hasin DS (2001). The Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV version (AUDADIS-IV). National Institute on Alcohol Abuse and Alcoholism: Bethesda, MD.
- Grant BF, Dawson DA, Stinson FS, Chou PS, Kay W, Pickering R (2003a). The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV) : reliability of alcohol

- consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. *Drug and Alcohol Dependence* 71, 7–16. [PubMed: 12821201]
- Grant BF, Hasin DS, Chou SP, Stinson FS, Dawson DA (2004a). Nicotine dependence and psychiatric disorders in the United States : results from the national epidemiologic survey on alcohol and related conditions. *Archives of General Psychiatry* 61, 1107–1115. [PubMed: 15520358]
- Grant BF, Moore TC, Kaplan K (2003b). Source and Accuracy Statement : Wave 1 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). National Institute on Alcohol Abuse and Alcoholism: Bethesda, MD.
- Grant BF, Stinson FS, Dawson DA, Chou SP, Dufour MC, Compton W, Pickering RP, Kaplan K (2004b). Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders : results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Archives of General Psychiatry* 61, 807–816. [PubMed: 15289279]
- Grant BF, Stinson FS, Dawson DA, Chou SP, Ruan J, Pickering RP (2004c). Co-occurrence of 12-month alcohol and drug use disorders and personality disorders in the U.S. : results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Archives of General Psychiatry* 61, 361–368. [PubMed: 15066894]
- Gregor K, Zvolensky MJ, Bernstein A, Marshall EC, Yartz AR (2007). Smoking motives in the prediction of affective vulnerability among young adult daily smokers. *Behaviour Research and Therapy* 45, 471–482. [PubMed: 16712784]
- Hasin DS, Goodwin RD, Stinson FS, Grant BF (2005). Epidemiology of major depressive disorder : results from the National Epidemiologic Survey on Alcoholism and Related Conditions. *Archives of General Psychiatry* 62, 1097–1106. [PubMed: 16203955]
- Hasin DS, Grant BF (2004). The co-occurrence of DSM-IV alcohol abuse in DSM-IV alcohol dependence: results of the National Epidemiologic Survey on Alcohol and Related Conditions on heterogeneity that differ by population subgroup. *Archives of General Psychiatry* 61, 891–896. [PubMed: 15351767]
- Hughes JR, Hatsukami DK, Mitchell JE, Dahlgren LA (1986). Prevalence of smoking among psychiatric outpatients. *American Journal of Psychiatry* 143, 993–997.
- Isensee B, Wittchen HU, Stein MB, Hofler M, Lieb R (2003). Smoking increases the risk of panic : findings from a prospective community study. *Archives of General Psychiatry* 60, 692–700. [PubMed: 12860773]
- Jain A (2003). Treating nicotine addiction. *British Medical Journal* 327, 1394–1395. [PubMed: 14670889]
- Johnson JG, Cohen P, Pine DS, Klein DF, Kasen S, Brook JS (2000). Association between cigarette smoking and anxiety disorders during adolescence and early adulthood. *Journal of the American Medical Association* 284, 2348–2351. [PubMed: 11066185]
- Juon H, Ensminger ME, Sydnor KD (2002). A longitudinal study of developmental trajectories to young adult cigarette smoking. *Drug and Alcohol Dependence* 66, 303–314. [PubMed: 12062465]
- Kessler RC, Sonnega A, Bromet E, Nelson CB (1995). Posttraumatic stress disorder in the National Comorbidity Survey. *Archives of General Psychiatry* 52, 1048–1060. [PubMed: 7492257]
- Khurana S, Batra V, Patkar AA, Leone FT (2003). Twenty-first century tobacco use: it is not just a risk factor anymore. *Respiratory Medicine* 97, 295–301. [PubMed: 12693789]
- Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH (2000). Smoking and mental illness : a population-based prevalence study. *Journal of the American Medical Association* 284, 2606–2610. [PubMed: 11086367]
- Lorant V, Delière D, Eaton W, Robert A, Philippot P, Ansseau M (2003). Socioeconomic inequalities in depression: a meta-analysis. *American Journal of Epidemiology* 157, 98–112. [PubMed: 12522017]
- McClermon FJ, Hiott BF, Westman EC, Rose JE, Levin E (2006). Transdermal nicotine attenuates depression symptoms in nonsmokers: a double-blind, placebo-controlled trial. *Psychopharmacology* 189, 125–133. [PubMed: 16977477]
- Mitchell L, West P (1996). Peer pressure to smoke: the meaning depends on the method. *Health Education Research* 11, 39–49.

- Pohl P, Yeragani VK, Balon R, Lycaki H, McBride R (1992). Smoking in patients with panic disorder. *Psychiatry Research* 43, 253–262. [PubMed: 1438623]
- Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK (1990). Comorbidity of mental disorders with alcohol and other drug abuse. *Journal of the American Medical Association* 264, 2511–2518. [PubMed: 2232018]
- Rouse BA (1989). Epidemiology of smokeless tobacco use : a national study. *NCI Monographs* 8, 29–33.
- Salin-Pascual RJ, Alcocer-Castillejos NV, Alejo-Galarza G (2003). Nicotine dependence and psychiatric disorders. *Revista de Investigación Clínica* 55, 677–693.
- Schmitz N, Kruse J, Kugler J (2003). Disabilities, quality of life, and mental disorders associated with smoking and nicotine dependence. *American Journal of Psychiatry* 160, 1670–1676.
- SUDAAN (2002). Software for Survey Data Analysis (SUDAAN), Version 9.01 Research Triangle Institute : Research Triangle Park, NC.
- Tercyak KP, Audrain J (2002). Psychosocial correlates of alternate tobacco product use during early adolescence. *Preventive Medicine* 35, 193–198. [PubMed: 12200105]
- Tominaga S (1986). Spread of smoking to developing countries. *International Agency for Research on Cancer Scientific Publications* 74, 125–133.
- Tucker JS, Ellickson PL, Klein DJ (2002). Smoking cessation during the transition from adolescence to young adulthood. *Nicotine and Tobacco Research* 4, 321–332. [PubMed: 12215241]
- Ware JE, Kosinski M, Turner-Bowker DM, Gandek B (2002). *How to Score Version 2 of the SF-12 Health Survey Quality Metrics* : Lincoln, RI.
- Weinberger AH, Sacco KA, George TP (2006). Comorbid tobacco dependence and psychiatric disorders: towards the development of improved treatments. *Psychiatric Times* 23, 35–41.
- Wells JC, Tien AY, Garrison R, Eaton WW (1994). Risk factors for the incidence of social phobia as determined by the Diagnostic Interview Schedule in a population-based study. *Acta Psychiatrica Scandinavica* 90, 84–90.
- West P, Sweeting H (1994). *Family and Friends' Influences on Smoking in Mid to Late Adolescence : Cross-sectional and Longitudinal Perspectives* MRC Medical Sociology Unit: Glasgow, UK.
- Williams JM, Ziedonis D (2004). Addressing tobacco among individuals with a mental illness or an addiction. *Addictive Behaviors* 29, 1067–1083. [PubMed: 15236808]
- Yang GH, Ma J, Chen A, Zhang Y, Samet JM, Taylor CE, Becker K (2001). Smoking cessation in China: findings from the 1996 national prevalence study. *Tobacco Control* 10, 170–174. [PubMed: 11387539]
- Zvolensky MJ, Bernstein A (2005). Cigarette smoking and panic psychopathology. *Current Directions in Psychological Science* 14, 301–305.

Prevalence of past 12-month psychiatric disorders among those in distinct past 12-month smoking/use of smokeless tobacco groups^a

Table 1.

	No past year cigarette/use of smokeless tobacco (n=31975)		No past year nicotine dependence (n=4720)		Past year nicotine dependence (n=4252)	
	Use of smokeless tobacco (n=432)	Cigarettes (n=4720)	Use of smokeless tobacco (n=172)	Cigarettes (n=172)	Use of smokeless tobacco (n=172)	Cigarettes (n=4252)
Any mood disorder	7.4 (0.2)	4.1 (1.1)	8.2 (0.5)	9.4 (2.5)	21.5 (0.8)	
Depression	4.6 (0.2)	2.7 (0.9)	5.1 (0.4)	7.7 (2.5)	11.9 (0.6)	
Dysthymia	1.4 (0.1)	0.9 (0.5)	1.9 (0.2)	0.4 (0.4)	4.9 (0.4)	
Mania/hypomania	2.2 (0.1)	1.0 (0.5)	2.0 (0.3)	1.7 (1.0)	7.3 (0.5)	
Any anxiety disorder	9.7 (0.3)	5.0 (1.2)	9.2 (0.5)	16.1 (3.3)	22.8 (0.9)	
Panic with or without agoraphobia	1.5 (0.1)	0.6 (0.3)	2.2 (0.2)	1.9 (1.4)	6.7 (0.5)	
Panic attack (without disorder)	1.6 (0.1)	0.6 (0.3)	2.4 (0.3)	4.3 (2.6)	6.6 (0.5)	
Social phobia	2.4 (0.1)	0.7 (0.4)	1.5 (0.2)	4.2 (1.6)	5.9 (0.5)	
Specific phobia	6.2 (0.3)	3.4 (0.9)	5.9 (0.4)	11.7 (2.9)	14.5 (0.7)	
Generalized anxiety disorder	1.6 (0.1)	0.6 (0.4)	1.9 (0.3)	2.1 (1.3)	5.6 (0.5)	

All values are % (S.E.).

^a A total of 1542 respondents with past-year cigar or pipe use, or who both smoked cigarettes and chewed, were removed from analysis.

Table 2.

Odds of past 12-month mood disorder predicted by past 12-month smoking/use of smokeless tobacco status

		No past year nicotine dependence				Past year nicotine dependence			
		No past year cigarette/use of smokeless tobacco	Use of smokeless tobacco ^a	Use of smokeless tobacco controlled for quantity ^b	Cigarettes controlled for quantity ^b	Use of smokeless tobacco ^a	Use of smokeless tobacco controlled for quantity ^b	Cigarettes controlled for quantity ^b	Cigarettes controlled for quantity ^b
Any mood disorder	OR	1.00	0.53 (0.30-0.94)	0.53 (0.30-0.94)	1.11 (0.96-1.28)	1.29 (0.72-2.33)	1.11 (0.96-1.28)	3.42 (3.06-3.82)	3.42 (3.06-3.82)
	aOR	1.00	0.77 (0.44-1.34)	0.83 (0.50-1.37)	1.00 (0.86-1.16)	1.02 (0.51-2.02)	1.01 (0.87-1.18)	1.74 (1.52-1.99)	1.73 (1.48-2.02)
Depression	OR	1.00	0.58 (0.29-1.15)	0.58 (0.29-1.15)	1.12 (0.95-1.33)	1.73 (0.86-3.48)	1.12 (0.95-1.33)	2.80 (2.47-3.17)	2.80 (2.47-3.17)
	aOR	1.00	0.86 (0.42-1.78)	0.93 (0.48-1.80)	1.03 (0.85-1.24)	1.89 (0.86-4.14)	1.02 (0.84-1.25)	1.60 (1.36-1.88)	1.52 (1.25-1.85)
Mania/hypomania	OR	1.00	0.44 (0.15-1.29)	0.44 (0.15-1.29)	0.92 (0.70-1.23)	0.76 (0.23-2.55)	0.92 (0.70-1.23)	3.57 (3.00-4.24)	3.57 (3.00-4.24)
	aOR	1.00	0.53 (0.18-1.55)	0.62 (0.24-1.60)	0.71 (0.51-0.99)	0.47 (0.14-1.59)	0.80 (0.59-1.08)	1.54 (1.21-1.95)	1.69 (1.26-2.27)

OR, Odds ratio;aOR, adjusted odds ratio.

Bold values indicate $p < 0.05$. Values in parentheses are 95% confidence intervals.

^a Adjusted for age, sex, ethnicity, marital status, education, income, any substance disorder, any personality disorder, any anxiety disorder, and any other specific mood disorder other than that being tested in the model.

^b Adjusted for age, sex, ethnicity, marital status, education, income, any substance disorder, any personality disorder, any anxiety disorder, any other specific mood disorder and quantity (categorized by quartiles) other than that being tested in the model.

Odds of past 12-month anxiety disorder predicted by past 12-month smoking/use of smokeless tobacco status

Table 3.

		No past year nicotine dependence				Past year nicotine dependence				
		No past year cigarette/use of smokeless tobacco	Use of smokeless tobacco ^a	Use of smokeless tobacco controlled for quantity ^b	Cigarettes ^a	Cigarettes controlled for quantity ^b	Use of smokeless tobacco ^a	Use of smokeless tobacco controlled for quantity ^b	Cigarettes ^a	Cigarettes controlled for quantity ^b
Any anxiety disorder	OR	1.00	0.49 (0.29–0.81)	0.49 (0.29–0.81)	0.94 (0.83–1.07)	0.94 (0.83–1.07)	1.79 (1.10–2.91)	1.79 (1.10–2.91)	2.75 (2.46–3.06)	2.75 (2.46–3.06)
	aOR	1.00	0.73 (0.43–1.22)	0.72 (0.44–1.18)	0.92 (0.81–1.05)	0.86 (0.74–0.99)	1.97 (1.13–3.45)	1.89 (1.09–3.26)	1.60 (1.41–1.82)	1.41 (1.20–1.65)
Panic with or without agoraphobia	OR	1.00	0.38 (0.12–1.23)	0.38 (0.12–1.23)	1.51 (1.19–1.92)	1.51 (1.19–1.92)	1.29 (0.30–5.65)	1.29 (0.30–5.65)	4.80 (4.00–5.79)	4.80 (4.00–5.79)
	aOR	1.00	0.67 (0.21–2.16)	0.60 (0.18–2.01)	1.57 (1.23–2.02)	1.65 (1.28–2.12)	1.56 (0.33–7.43)	1.75 (0.45–6.83)	2.16 (1.75–2.67)	2.19 (1.68–2.85)
Panic attack (without disorder)	OR	1.00	0.36 (0.12–1.12)	0.36 (0.12–1.12)	1.47 (1.17–1.85)	1.47 (1.17–1.85)	2.75 (0.79–9.52)	2.75 (0.79–9.52)	4.29 (3.59–5.13)	4.29 (3.59–5.13)
	aOR	1.00	0.65 (0.21–1.98)	0.67 (0.27–1.64)	1.50 (1.18–1.91)	1.15 (0.79–1.67)	3.53 (0.89–14.08)	3.52 (0.44–28.03)	2.09 (1.70–2.56)	1.20 (0.78–1.85)
Social phobia	OR	1.00	0.29 (0.09–0.98)	0.29 (0.09–0.98)	0.59 (0.45–0.78)	0.59 (0.45–0.78)	1.75 (0.80–3.86)	1.75 (0.80–3.86)	2.51 (2.07–3.05)	2.51 (2.07–3.05)
	aOR	1.00	0.39 (0.11–1.31)	0.41 (0.14–1.19)	0.52 (0.39–0.70)	0.48 (0.35–0.67)	1.29 (0.56–2.94)	1.03 (0.44–2.39)	0.91 (0.72–1.17)	0.78 (0.58–1.05)
Specific phobia	OR	1.00	0.53 (0.30–0.95)	0.53 (0.30–0.95)	0.96 (0.83–1.11)	0.96 (0.83–1.11)	2.02 (1.15–3.55)	2.02 (1.15–3.55)	2.58 (2.29–2.90)	2.58 (2.29–2.90)
	aOR	1.00	0.91 (0.50–1.64)	0.93 (0.52–1.65)	0.99 (0.86–1.15)	0.95 (0.80–1.12)	2.53 (1.38–4.63)	2.34 (1.28–4.29)	1.63 (1.42–1.88)	1.52 (1.29–1.79)
Generalized anxiety disorder	OR	1.00	0.38 (0.11–1.31)	0.38 (0.11–1.31)	1.18 (0.87–1.59)	1.18 (0.87–1.59)	1.34 (0.39–4.62)	1.34 (0.39–4.62)	3.70 (3.01–4.55)	3.70 (3.01–4.55)
	aOR	1.00	0.72 (0.21–2.51)	0.57 (0.16–1.95)	1.16 (0.84–1.60)	0.96 (0.70–1.32)	1.60 (0.44–5.81)	1.53 (0.47–4.96)	1.27 (0.99–1.64)	1.02 (0.73–1.43)

OR, Odds ratio ; aOR, adjusted odds ratio.

Bold values indicate $p < 0.05$. Values in parentheses are 95% confidence intervals.

^a Adjusted for age, sex, ethnicity, marital status, education, income, any substance disorder, any personality disorder, any anxiety disorder, and any other specific mood disorder other than that being tested in the model.

^b Adjusted for age, sex, ethnicity, marital status, education, income, any substance disorder, any personality disorder, any anxiety disorder, any other specific mood disorder and quantity (categorized by quartiles) other than that being tested in the model.