

## Relationship of Nicotine Dependence, Subsyndromal and Pathological Gambling, and Other Psychiatric Disorders: Data From the National Epidemiologic Survey on Alcohol and Related Conditions

Jon E. Grant, J.D., M.D., M.P.H.; Rani A. Desai, Ph.D., M.P.H.; and Marc N. Potenza, M.D., Ph.D.

**Objective:** Nicotine dependence frequently co-occurs with subsyndromal and pathological levels of gambling. The relationship of nicotine dependence, levels of gambling pathology, and other psychiatric disorders, however, is incompletely understood.

*Method:* To use nationally representative data from the National Epidemiologic Survey on Alcohol and Related Conditions to examine the influence of DSM-IV nicotine dependence on the association between pathological gambling severities and other psychiatric disorders. Faceto-face interviews were conducted with 43,093 adults living in households and group-quarters in the United States. The main outcome measure was the co-occurrence of current nicotine dependence and Axis I and II disorders and severity of gambling based on the 10 inclusionary diagnostic criteria for pathological gambling. The study was conducted from 2001 to 2002.

**Results:** Among non–nicotine-dependent respondents, increasing gambling severity was associated with greater psychopathology for the majority of Axis I and II disorders. This pattern was not uniformly observed among nicotinedependent subjects. Significant nicotine-by– gambling-group interactions were observed for multiple Axis I and II disorders. All significant interactions involved stronger associations between gambling and psychopathology in the non–nicotine-dependent group.

*Conclusions:* In a large national sample, nicotine dependence influences the associations between gambling and multiple psychiatric disorders. Subsyndromal levels of gambling are associated with significant psychopathology. Nicotine dependence accounts for some of the elevated risks for psychopathology associated with subsyndromal and problem/pathological levels of gambling. Additional research is needed to examine specific prevention and treatment for individuals with problem/pathological gambling with and without nicotine dependence.

J Clin Psychiatry 2009;70(3):334–343 © Copyright 2009 Physicians Postgraduate Press, Inc. Received March 13, 2008; accepted May 15, 2008. From the Department of Psychiatry, University of Minnesota Medical School, Minneapolis (Dr. Grant); and the Department of Psychiatry, Yale University School of Medicine, New Haven, Conn. (Drs. Desai and Potenza).

Supported in part by (1) the National Institute on Drug Abuse (R01-DA019039), (2) the National Institute of Mental Health (K23 MH069754-01A1), (3) the Veterans Administration VISN1 MIRECC and REAP, and (4) Women's Health Research at Yale.

Dr. Grant is a consultant for Pfizer and Somaxon; has received grant/research support from Forest, GlaxoSmithKline, and Somaxon; and has consulted for law offices as an expert in pathological gambling. Dr. Potenza is a consultant for Boehringer Ingelheim and Somaxon; has received grant/research support from Mohegan Sun and Forest; is a member of the speakers/advisory boards for Boehringer Ingelheim; has received other financial or material support from Somaxon; and has consulted for law offices and the federal defender's office as an expert in pathological gambling and impulse control disorders. Dr. Desai has no personal affiliations or financial relationships with any commercial interest to disclose relative to the article.

Corresponding author and reprints: Jon E. Grant, J.D., M.D., M.P.H., Department of Psychiatry, University of Minnesota Medical School, 2450 Riverside Ave., Minneapolis, MN 55454 (e-mail: grant045@umn.edu).

**P** athological gambling is characterized by persistent and recurrent maladaptive patterns of gambling behavior that affects 0.4% to 1.6% of the U.S. population.<sup>1,2</sup> This classification typically refers to individuals who meet at least 5 of the DSM-IV criteria for pathological gambling.<sup>3</sup> When only 3 or 4 DSM-IV criteria are met, the individual is generally referred to as a problem gambler, indicating that the gambling behavior is problematic but not as severe as pathological gambling. In studies that have used screening instruments to identify problem gamblers, problem gambling has been found in approximately 2.5% of the U.S. population.<sup>4</sup>

Approximately two thirds of the U.S. adult population report gambling in the previous year,<sup>5</sup> and most people gamble without developing either problem or pathological gambling.<sup>4</sup> Although pathological gambling may have a low prevalence in the community (i.e., some studies suggest it is less than 1% of the population), when problem and pathological gambling are considered together as the extreme end of a behavioral continuum of gambling, up to approximately 4% of the adult population<sup>1</sup> report symptoms consistent with problematic gambling. Studies employing DSM-based instruments typically find lower

#### FOR CLINICAL USE

- Problem gambling is relatively common and often associated with nicotine dependence.
- Even low-risk gambling is positively associated with multiple psychiatric disorders in non-nicotine-dependent individuals.
- Clinicians should screen for and provide brief interventions around gambling, smoking, and other psychiatric disorders.

prevalence estimates than studies employing gambling screens.<sup>2,4</sup> Problem/pathological gambling (PPG) is associated with impaired functioning, reduced quality of life, and high rates of bankruptcy, divorce, and incarceration.<sup>6</sup> Increased availability and social acceptance of gambling has raised public health concerns about the potential dangers of less destructive patterns of gambling.<sup>7,8</sup> Because of the public health implications and data suggesting that problem gambling behaviors lie along a continuum,<sup>9–11</sup> it is important to examine the impact of varying severity levels of gambling.

Among U.S. adults, 12.8% report nicotine dependence, and nicotine dependence is highly associated with DSM-IV Axis I and II disorders.<sup>12–15</sup> Problem/pathological and recreational gambling are associated with elevated proportions of nicotine dependence (41%–55% and 30%, respectively),<sup>10,16</sup> and tobacco smoking in clinical samples of problem and pathological gamblers has been associated with increased gambling severity and more frequent psychiatric problems.<sup>17–19</sup> Although previous research suggests that multiple disorders are linked (gambling and psychiatric disorders,<sup>2</sup> nicotine use and psychiatric disorders, <sup>12–15</sup> and nicotine use and gambling<sup>17–19</sup>),<sup>20</sup> no study has systematically examined the interactions of gambling, nicotine, and psychiatric disorders.

We use data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a large national survey of non-institutionalized adults, to examine the relative influence of problem gambling behaviors and nicotine dependence on other psychiatric disorders. The NESARC included a DSM-IV-based assessment of pathological gambling, and these data have been used previously to examine co-occurrences between pathological gambling and other psychiatric disorders.<sup>2,21</sup> In these prior studies examining pathological gambling using the NESARC data, lifetime measures of pathological gambling were employed, likely because past-year estimates of pathological gambling in the sample (approximately 0.2%) yielded less power to examine co-occurring disorders. It has been argued that lifetime prevalence estimates are less relevant to public health, "less germane to clinicians and practitioners and subject to retrospective recall bias."12(p1108) In contrast to some prior studies that utilized lifetime measures of pathological gambling, we chose to examine past-year rates for these reasons.<sup>22,23</sup>

Prior studies have found elevated odds of co-occurrence between subsyndromal levels of gambling and nongambling psychopathology. For example, in the St. Louis, Mo. site of the Epidemiologic Catchment Area (ECA) survey, recreational gambling was associated with a broad range of mainly Axis I disorders.<sup>10</sup> Although informative, the gambling data from the ECA study were geographically limited to the St. Louis site, utilized earlier iterations of DSM criteria, and did not assess for a broad range of Axis II disorders. Given the incomplete data on the cooccurrence of different levels of gambling and nicotine use and a broad range of psychiatric disorders,<sup>2</sup> the purpose of this study was to fill these gaps in knowledge. Specifically, using the NESARC data, we sought to (1) examine the prevalence and sociodemographic correlates of varying levels of gambling pathology in nicotine-dependent and non-nicotine-dependent individuals, (2) compare prevalence estimates of psychiatric disorders in nicotine and non-nicotine-dependent individuals based on level of gambling pathology, and (3) investigate the influences of nicotine dependence and gambling pathology and their interaction on a range of psychiatric disorders. Recognizing the associations between gambling severity, nicotine status, and psychiatric disorders is important, as identifying and treating the co-occurring disorders may significantly improve the prognosis of the primary disorder. Additionally, to the extent that co-occurring disorders may potentially contribute to the development or maintenance of PPG, it is also important to recognize the possible associations with PPG, which is often under-recognized in clinical settings.

#### METHOD

#### Sample

Data from the 2001–2002 NESARC, described elsewhere,<sup>12,24</sup> were analyzed. Briefly, the NESARC, conducted by the National Institute on Alcohol Abuse and Alcoholism and the Bureau of the Census, surveyed a nationally representative sample of non-institutionalized U.S. residents (citizens and noncitizens) aged 18 years and over. Respondents were identified using a multi-stage stratified sample, and the sample was enhanced with members of group-living environments, such as dormitories, group homes, shelters, and facilities for housing workers.

335

Jails, prisons, and hospitals were not included. The study over-sampled black and Hispanic households, as well as young adults aged 18 to 24 years, in order to have sufficient power to perform meaningful analyses focusing on these populations. Weights have been calculated to adjust standard errors for these over-samples and nonresponse.<sup>24</sup> The final sample consisted of 43,093 respondents, representing an 81% response rate. After complete description of the study to the subjects, informed consent was obtained. The current investigation utilized publicly accessible, de-identified data and was thus exempted from formal institutional review board review.

#### Measures

The Alcohol Use Disorder and Associated Disabilities Interview Schedule–DSM-IV version (AUDADIS-IV),<sup>25</sup> a structured diagnostic assessment tool, was administered by trained lay interviewers in the NESARC study. The AUDADIS-IV has demonstrated good reliability and validity for detecting psychiatric disorders in a community sample.<sup>25</sup> The NESARC data set contains diagnostic variables derived from AUDADIS-IV

algorithms and based on DSM-IV criteria. The data contain diagnostic variables for major depression, dysthymia, mania and hypomania, panic disorder with and without agoraphobia, social phobia, simple phobia, generalized anxiety disorder, alcohol abuse and dependence, drug abuse and dependence, and nicotine dependence. We used past-year measures of these disorders. Lifetime measures were used of the 7 DSM-IV Axis II disorders assessed with the AUDADIS-IV: antisocial, avoidant, dependent, histrionic, obsessive-compulsive, paranoid, and schizoid personality disorders.

The primary independent variable in the present analyses was severity of problem gambling, based on the 10 DSM-IV diagnostic inclusionary criteria for pathological gambling. Consistent with previous population-based studies, including those using the NESARC data,<sup>7,23,26,27</sup> we divided the sample into 4 groups: nongamblers and low-frequency gamblers, who reported that they had never gambled > 5 times in a single year in their lifetime (referred to hereafter as "non/low-frequency gamblers"); low-risk gamblers, who reported gambling > 5 times in a year and no symptoms of pathological gambling in the previous year; at-risk gamblers, who reported gambling > 5 times in a year and 1–2 symptoms of pathological gambling in the previous year; and problem/pathological gamblers, who reported  $\geq 3$  DSM-IV criteria of pathological gambling in the previous year. The low frequency of pathological gambling (approximately 0.2% of the sample reported  $\geq$  5 symptoms) necessitated the combina-

Table 1. Sociodemographic	Characteristics	s of the NESARC Sample
by Nicotine Dependence <sup>a</sup>		

	Depe	otine endent 4962)	Depe	licotine ndent 8,131)		
Characteristic	Ν	%	Ν	%	$\chi^2$	р
Gender					34.53	<.0001
Female	2572	46.87	22,003	52.84		
Male	2390	53.13	16,128	47.16		
Education					127.12	< .0001
Less than high school	978	18.61	6871	15.22		
High school graduate	1689	35.15	10,858	28.47		
Some college	1709	34.63	10,954	29.48		
College or higher	586	11.60	9448	26.83		
Employment					20.73	.0001
Full-time	2697	56.52	19,570	53.04		
Part-time	530	11.17	3733	10.39		
Not working	1735	32.31	14,828	36.57		
Marital status					66.15	<.0001
Married	2134	53.63	19,947	62.79		
Previously married	1454	21.52	9663	16.86		
Never married	1374	24.84	8521	20.34		
Race/ethnicity <sup>b</sup>						
White race	3952	87.30	28,837	82.65	38.28	<.0001
Black race	872	9.36	7728	11.90	21.96	<.0001
Hispanic ethnicity	536	5.69	7772	12.42	28.54	< .0001

<sup>a</sup>Ns represent actual number of respondents in each category; %s indicate weighted percentages.

<sup>b</sup>Race and ethnicity categories are not mutually exclusive.

Abbreviation: NESARC = National Epidemiologic Survey on Alcohol and Related Conditions.

tion of the problem and pathological groups, a strategy employed in prior gambling studies.<sup>10,23,27</sup>

The following sociodemographic variables were included in the analyses: age, gender, race/ethnicity, education, marital status, and employment status. Dummy variables for 3 race/ethnicity groups (black, white, and Hispanic) were created. These groups were not mutually exclusive, as a respondent could have identified with more than 1 race or ethnicity. As previously cited,<sup>23</sup> we employed the approach of using non–mutually exclusive categories, consistent with current federal guidelines as described by the Office of Management and Budget.<sup>28</sup>

## **Data Analyses**

The primary research question concerned differences in the associations between gambling and psychiatric disorders based on DSM-IV past-year nicotine dependence (nicotine-dependent vs. non-nicotine-dependent). Using  $\chi^2$  analyses, we first examined associations between gambling severity and sociodemographic variables, stratified by nicotine dependence, in order to identify sociodemographic variables potentially influencing the relationship between nicotine dependence, gambling severity, and psychiatric disorders. Next, we examined unadjusted weighted rates of psychiatric disorders, stratified by both gambling severity and nicotine dependence. Finally, we fit a series of logistic regression models in which psychiatric disorders were the dependent variables of interest and the 4-level gambling variable, nicotine dependence,

		Nicotin	e Depender	N = 4962			Non–Nicotine Dependent ( $N = 38,131$ )						
Characteristic	Non/LF Gamblers $(N = 2961)^{c}$	Low-Risk Gamblers (N = 1568)	At-Risk Gamblers (N = 244)	Problem/ Pathological Gamblers (N = 96)	$\chi^2$	р	Non/LF Gamblers $(N = 27,924)^{c}$	Low-Risk Gamblers (N = 8396)	At-Risk Gamblers (N = 701)	Problem/ Pathological Gamblers (N = 137)	$\chi^2$	р	
Gender					45.83	< .0001					109.44	< .0001	
Female	52.55	38.75	41.85	34.39			56.82	42.57	35.05	35.75			
Male	47.45	61.25	58.15	65.61			43.18	57.43	64.95	64.25			
Education					21.76	.0196					57.00	<.0001	
Less than high school	18.46	17.98	22.39	23.46			16.10	12.06	13.80	16.38			
High school graduate	35.37	33.72	37.44	51.25			27.81	30.17	30.63	26.84			
Some college	34.11	36.37	32.30	19.67			28.76	31.71	33.23	33.99			
College or higher	12.06	11.92	7.87	5.62			27.34	26.07	22.33	22.79			
Employment					3.92	.6866					29.06	.0004	
Full-time	55.28	57.63	61.32	57.89			51.88	56.21	27.14	54.10			
Part-time	11.65	10.94	10.69	8.24			10.73	9.30	9.37	15.80			
Not working	33.07	31.44	27.99	33.87			37.39	34.49	33.49	30.10			
Marital status					21.35	.0042					73.03	< .0001	
Married	51.72	57.43	56.16	55.31			62.18	66.99	55.63	40.83			
Previously married	21.26	22.32	17.61	16.76			16.55	17.18	18.01	21.86			
Never married	27.02	20.26	26.23	27.93			21.27	15.83	26.36	37.31			
Race/ethnicity <sup>d</sup>													
White race	87.78	87.82	83.57	76.99	7.95	.0561	82.19	84.54	81.71	59.49	31.75	< .0001	
Black race	9.36	8.13	12.85	14.52	8.18	.0512	11.93	11.27	14.03	27.65	17.55	.0013	
Hispanic ethnicity	6.24	4.71	5.62	3.28	6.73	.0916	13.70	8.76	8.85	9.33	29.01	< .0001	

Table 2. Sociodemographic Characteristics of the Sample by Nicotine Dependence and Level	of Gambling Pathology <sup>a,b</sup>
--	--------------------------------------

<sup>a</sup>Numbers in the table represent weighted percentages, stratified by gender.

<sup>b</sup>There were 93 nicotine-dependent and 973 non-nicotine-dependent respondents with missing data on gambling.

Non/LF gamblers = nongamblers or low-frequency gamblers.

<sup>d</sup>Race and ethnicity categories are not mutually exclusive.

and an interaction between nicotine dependence and gambling were the independent variables of interest, adjusting for previously identified sociodemographic variables. Our analysis began with examining psychiatric disorders grouped into 4 categories: any mood disorder, any anxiety disorder, any substance use disorder, and any personality disorder. Only when a significant association was found between these categories and gambling severity and nicotine status did we pursue an analysis of the individual disorders. Because only 4 comparisons were initially made, and these were significant, we did not adjust our  $\alpha$  level to account for the multiple subsequent comparisons. Analyses were performed using SUDAAN software<sup>29</sup> and the NESARC-calculated weights in order to adjust the data for the design effects of the NESARC.

#### RESULTS

## **Rates of Gambling Pathology Based on Nicotine Status**

Of the 43,093 respondents, 4962 (12.8%) were nicotine dependent.<sup>12</sup> Compared with non-nicotine-dependent respondents, the nicotine-dependent group was significantly more likely to be male, white, working part-time or full-time, and previously or never married (Table 1). Of the 43,093 respondents, 30,885 (71.7%) were non/lowfrequency gamblers, 9964 (23.1%) were low-risk gamblers, 945 (2.2%) were at-risk gamblers, and 233 (0.5%) were problem/pathological gamblers. Percentages of subjects with low-risk, at-risk, and problem/pathological gambling severity were higher among nicotine-dependent respondents. Among respondents who were nicotinedependent (N = 4962), prevalence estimates for non/lowfrequency gambling, low-risk gambling, at-risk gambling, and PPG were 59.7%, 31.6%, 4.9%, and 1.9%, respectively, compared to estimates of 73.2%, 22.0%, 1.8%, and 0.4%, respectively, in the non-nicotinedependent group (N = 38,131).

## Sociodemographic Variables Based on **Gambling Pathology and Nicotine Dependence Status**

Table 2 presents the sociodemographic characteristics of the groups divided on nicotine dependence status and stratified by level of gambling pathology. Among nicotine-dependent respondents, significant associations with gambling status at p < .05 were observed related to gender, education, and marital status. Among nonnicotine-dependent respondents, significant associations with gambling status were observed on all sociodemographic measures. Some gambling-related differences appear similar in both nicotine-dependent and nondependent groups. For example, higher proportions of men and blacks were observed in the at-risk and problem/ pathological gamblers regardless of nicotine dependence.

Diagnosis		1	Nicotine Dep	pendent			Non-Nicotine Dependent						
	Non/LF	Low-Risk	Problem/ sk At-Risk Pathological				Non/LF	Low-Risk	At-Risk	Problem/ Pathological			
	Gamblers <sup>b</sup>	Gamblers	Gamblers	Gamblers	$\chi^2$	р	Gamblers <sup>b</sup>	Gamblers	Gamblers	Gamblers	$\chi^2$	р	
Any mood disorder	22.35	18.60	25.24	23.65	2.56	.0628	7.44	7.32	14.10	25.23	12.64	< .0001	
Major depression	18.46	13.93	16.71	14.77	9.7	.0279	5.81	5.23	8.88	16.11	17.2	.0015	
Dysthymia	4.91	3.99	5.08	4.46	1.68	.6429	1.41	1.38	2.18	6.85	6.15	.1154	
Mania	4.69	4.50	2.76	10.43	4.47	.2253	1.09	1.49	3.65	7.03	19.00	.0008	
Hypomania	3.04	2.86	6.07	0.27	21.78	.0003	0.80	0.97	3.04	4.23	11.4	.0144	
Any anxiety disorder	22.56	20.68	24.91	38.66	3.04	.0353	8.99	11.24	16.90	23.09	13.34	< .0001	
Panic disorder <sup>c</sup>	6.53	4.70	9.87	11.37	8.47	.0455	1.46	1.63	4.44	3.85	8.46	.0458	
Social phobia	6.12	5.29	6.83	8.73	1.95	.5853	2.21	2.62	3.62	10.26	8.72	.0411	
Simple phobia	14.01	14.00	18.82	28.33	7.59	.065	5.74	7.28	10.55	15.96	28.2	< .0001	
Generalized anxiety	5.38	5.26	3.54	11.65	2.82	.2912	1.54	1.79	2.62	4.60	4.9	.1901	
Any AUD or SUD	23.53	26.39	39.69	45.11	7.71	.0002	5.66	9.71	17.91	24.29	28.90	< .0001	
Alcohol ab/dep	20.76	22.91	38.27	42.52	24.93	.0001	5.08	9.21	16.24	21.48	82.1	< .0001	
Drug ab/dep	7.32	8.92	13.40	7.47	5.09	.1767	0.97	1.28	3.47	4.71	16.3	.0021	
Any Axis II disorder	31.34	30.76	40.73	60.95	8.14	.0001	11.19	15.43	27.03	48.63	28.26	< .0001	
Avoidant	6.47	4.16	8.59	10.49	11.67	.0128	1.92	1.63	3.12	9.02	8.19	.0509	
Dependent	1.70	1.76	1.03	3.77	2.10	.5557	0.37	0.16	0.40	2.17	13.9	.0053	
Antisocial	10.93	13.29	18.15	25.79	13.6	.006	1.87	3.58	7.21	16.74	50.4	< .0001	
Obsessive-compulsive	14.42	13.44	20.16	25.82	9.99	.0249	6.30	8.78	14.39	23.64	52.3	< .0001	
Paranoid	12.26	9.98	14.77	28.60	13.38	.0065	3.09	3.73	8.19	23.79	30.8	< .0001	
Schizoid	7.77	7.10	9.10	17.64	5.04	.1799	2.28	2.93	4.63	14.32	21.6	.0003	
Histrionic	5.76	4.31	8.12	18.86	11.22	.0153	1.17	1.47	4.38	9.10	18.2	.0153	

Table 3. Rates of Psychiatric Diagnoses by Level of Gambling Pathology and Nicotine Dependence<sup>a</sup>

<sup>a</sup>Numbers in the table represent weighted percentages, stratified by gender.

<sup>b</sup>Non/LF gamblers = nongamblers or low-frequency gamblers.

"With or without agoraphobia.

Abbreviations: ab/dep = abuse or dependence, AUD = alcohol use disorder, SUD = substance use disorder.

Other gambling-related differences appeared different in the 2 nicotine-related groups. For example, the relatively lower proportions of married individuals in the at-risk gambling and PPG groups in the non–nicotine-dependent group were not evident in the nicotine-dependent group.

# Psychiatric Disorders, Nicotine Dependence Status, and Level of Gambling Pathology

Differences in the associations between gambling severity and psychopathology were observed in the groups stratified by nicotine dependence status (Table 3). Within both the nicotine-dependent and non–nicotine-dependent groups, and as compared to non/low-frequency gambling and low-risk gambling groups, estimates of co-occurring psychopathology were higher in the at-risk gambling group and higher still in the PPG group. In virtually all instances, nicotine-dependent respondents had numerically higher estimates of co-occurring psychiatric disorders at each gambling severity level.

Logistic regression models examined the influences of nicotine dependence, gambling severity, and their interaction upon the odds ratios for other psychiatric disorders (Table 4). Significant gambling-by–nicotine-group interactions were observed for mood, anxiety, substance use, and personality disorders (Figure 1). Subsequent analyses identified significant interactions for the following Axis I conditions: major depression, mania, hypomania, social phobia, simple phobia, generalized anxiety disorder, alcohol abuse/dependence, and drug abuse/dependence. Significant gambling-by-nicotine-group interactions were also observed for most Axis II disorders: antisocial, obsessive-compulsive, paranoid, schizoid, and histrionic. In all cases in which a significant interaction was observed, a stronger association between gambling severity and psychopathology was observed in the non-nicotinedependent group as compared to the nicotine-dependent one.

The patterns of associations between gambling severity and psychopathology appeared substantially influenced by nicotine dependence. Differences were observed at the severe end of the gambling spectrum for many disorders. In the PPG versus non/low-frequency gambling comparisons, the non–nicotine-dependent group demonstrated significant odds ratios of > 3.3 for every Axis I and II disorder. In contrast, only 1 Axis I disorder (alcohol abuse/dependence) and 1 Axis II disorder (histrionic personality disorder) demonstrated an odds ratio  $\geq 3$  in comparisons within the nicotine-dependent group.

A pattern of a stepwise progression for increasingly larger odds ratios was observed for increasing gambling severity in the at-risk and PPG groups for virtually all Axis I and II psychiatric disorders in the non–nicotinedependent group. This pattern was less consistently observed in the nicotine-dependent group. Unique features were observed for each disorder in the patterns of associations in the nicotine-dependent and nondependent groups. For example, gambling severity did not confer additional risk for major depression in the nicotine-dependent group

	Nicotine	Dependent (N	ID), OR	Non-Nicot	ine Dependent	t (NND), OR			
	Problem/			-		Problem/	ND vs NND Interaction, OR		
Diagnosis	Low-Risk vs Non/LF Gamblers	At-Risk vs Non/LF Gamblers	Pathological vs Non/LF Gamblers	Low-Risk vs Non/LF Gamblers	At-Risk vs Non/LF Gamblers	Pathological vs Non/LF Gamblers	Low-Risk Gamblers	At-Risk Gamblers	Problem/ Pathologica Gamblers
Any mood disorder	0.87	1.33	1.14	1.12	2.04***	3.92***	0.78*	0.65*	0.29**
Major depression	0.78*	1	0.8	1.09	1.8***	3.43***	0.78	0.6*	0.26**
Dysthymia	0.86	1.17	0.87	1.15	1.74*	5.83***	0.81	0.71	0.16*
Mania	1.13	0.65	2.48	1.71***	3.65***	6.42***	0.68	0.18***	0.4
Hypomania	1.12	2.24*	0.09*	1.52*	3.81***	4.39*	0.75	0.6	0.02**
Any anxiety disorder	0.92	1.21	2.27**	1.34***	2.07***	3.04***	0.69***	0.59*	0.75
Panic disorder	0.75	1.8*	2.01	1.36*	3.91***	3.42*	0.61*	0.49	0.68
Social phobia	0.89	1.17	1.45	1.33**	1.83*	5.97***	0.72	0.67	0.27*
Simple phobia	1.03	1.5	2.54**	1.51***	2.36***	3.8***	0.77*	0.69	0.79
Generalized anxiety	1.03	0.71	2.41	1.39**	2.04**	3.6*	0.82	0.38*	0.77
Any AUD or SUD	1.37***	2.55***	3.26***	2.18***	3.61***	4.87***	0.63***	0.71	0.67
Alcohol ab/dep	1.32	2.83	3.51	2.06***	3.04***	3.88***	0.57***	0.87	0.83
Drug ab/dep	1.64	2.3	1.00	1.64**	3.12***	3.33**	0.9	0.66	0.27*
Any Axis II disorder	1.04	1.59**	3.60***	1.57***	2.96***	7.10***	0.66***	0.54**	0.51*
Avoidant	0.7*	1.49	1.65	1.01	1.77	5.34***	0.73	0.88	0.33
Dependent	1.24	0.72	2.1	0.56	1.21	7.16***	2.31	0.62	0.31
Antisocial	1.42***	1.93***	2.89***	2.05***	3.46***	8.25***	0.61**	0.5*	0.31**
Obsessive-compulsive	0.93	1.56*	2.21**	1.46**	2.54***	4.65***	0.64***	0.62*	0.48*
Paranoid	0.89	1.3	2.88***	1.5***	2.99***	9.26***	0.62	0.45**	0.33*
Schizoid	0.98	1.22	2.53**	1.42***	2.09***	6.35***	0.69*	0.58	0.4
Histrionic	0.85	1.59	3.99***	1.51**	3.79***	6.93***	0.57*	0.42*	0.58

Table 4. Adjusted Associations Between Gambling and Psychiatric Diagnoses, by Nicotine Dependenceab

<sup>a</sup>Odds ratios (ORs) are adjusted for age, race/ethnicity, marital status, education, employment, and income.

<sup>b</sup>Non/LF gamblers = nongamblers or low-frequency gamblers.

\*\*\*p < .001.

Abbreviations: ab/dep = abuse or dependence, AUD = alcohol use disorder, SUD = substance use disorder.

(Table 4), with significant between-nicotine-group differences observed for both the at-risk and the PPG comparisons. Within the nicotine-dependent group, the most statistically significant association with major depression was a decreased odds in the low-risk versus non/lowfrequency gambling comparison (OR = 0.78; p < .05). Similarly, social phobia demonstrated a significant interaction effect for the PPG versus nongambling comparison; however, no significant association was observed between social phobia and problem gambling severity within the nicotine-dependent group. Largely similar stepwise progressions were observed between problem gambling severity and alcohol abuse/dependence in nicotine-dependent and nondependent groups, with a significant between-group difference observed only in the low-risk versus nongambling comparison. With antisocial personality disorder, significant positive associations were observed across all gambling severity groups in both the nicotine-dependent and nondependent groups, with significantly stronger associations observed in the nonnicotine-dependent group comparisons.

## DISCUSSION

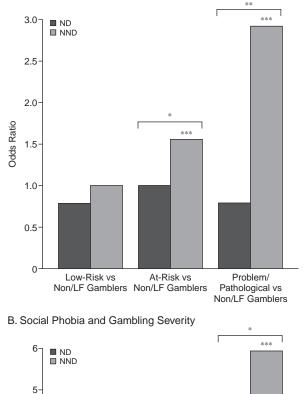
This study is, to our knowledge, the first to examine the association between nicotine dependence, problem gambling severity, and a broad range of Axis I and II psychiatric disorders in a nationally representative sample. The multiple strengths of the survey, including the high response rate, large population-based sample, and diagnostic measures obtained, allow for examination of the interactive influences of psychiatric disorders. This study found that more severe problem gambling is associated with more psychopathology in both nicotine-dependent and non–nicotine-dependent respondents, and this pattern applies to a broad range of Axis I and II disorders. Previous studies found that PPG is associated with an increased risk for multiple psychiatric disorders.<sup>6,9,10</sup> Consistent with these previous studies, this study found that individuals with PPG had elevated rates of co-occurring psychiatric disorders.

In the non-nicotine-dependent group, the association between gambling severity and psychopathology was seen for the majority of Axis I and II disorders and was particularly robust for major depression and antisocial personality disorders. The finding that the nicotinedependent group had higher prevalence estimates of psychiatric disorders, and yet psychopathology generally had a weaker association with gambling in the nicotinedependent group, suggests that some of the gamblingrelated risk for these disorders is attributable to nicotine dependence.

Tobacco use may co-occur with gambling for multiple reasons. Biological (e.g., genetic factors) such as those

<sup>\*</sup>p < .05.

<sup>\*\*</sup>p < .01.



A. Major Depression and Gambling Severity

Figure 1. Interactions With Nicotine Dependence in the Associations Between Psychiatric Diagnoses and Gambling Severity<sup>a</sup>

🔳 ND NND .... 3.5 3.0 2.5 Odds Ratio \*\*\* 2.0 1.5 1.0 0.5 0 Low-Risk vs At-Risk vs Problem/ Non/LF Gamblers Non/LF Gamblers Pathological vs Non/LF Gamblers

4.0 \*\*\*\*

C. Alcohol Abuse/Dependence and Gambling Severity

D. Antisocial Personality Disorder and Gambling Severity

\*\*\*

Problem/

Pathological vs Non/LF Gamblers

10

8

6

4

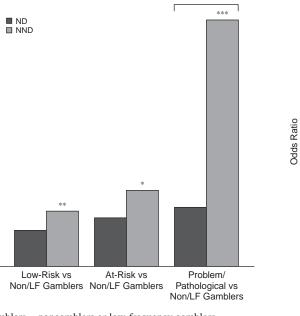
2

0

Low-Risk vs

ND

NND



 $^{a}$ Non/LF gamblers = nongamblers or low-frequency gamblers. \*p < .05. \*\*p < .01.

4

3

2

1

0

Odds Ratio

Abbreviations: ND = nicotine dependence, NND = non-nicotine dependence.

contributing to impulsivity or related constructs may contribute to participation in both behaviors.<sup>30</sup> Preclinical data suggest that nicotine use may enhance dopamine response to reinforcers by facilitating burst firing of dopamine neurons.<sup>31,32</sup> The ventral striatum, a dopaminergically innervated brain region, has been identified in some studies of pathological gambling,<sup>33</sup> although a role for striatal dopamine involvement in pathological gambling has yet to be empirically demonstrated. Gambling and smoking may be related to common social or environmental factors, such as gambling and smoking together among friends or in casinos. Specific influences of tobacco smoking (calming, stimulating, attention-related, coping with stress) may enhance gambling experiences.

\*\*\*

At-Risk vs

Non/LF Gamblers Non/LF Gamblers

<sup>\*\*\*\*</sup>p < .001

The extent to which the relationship between gambling and smoking is mediated by specific environmental, genetic, or other biological factors warrants further examination.

Examination of the relationships between smoking, gambling, and other psychiatric disorders may provide insight into how these disorders fit in the structure of psychiatric conditions. Data indicate that common psychiatric disorders aggregate in 2 main groups: internalizing and externalizing disorders (i.e., disorders characterized by either withdrawal from society or in conflict with society, respectively).<sup>34,35</sup> Where PPG fits within this structure is not completely understood, particularly as assessments of gambling problems have often been omitted from major psychiatric epidemiologic studies.<sup>36</sup> Problem/ pathological gambling shares with externalizing disorders (for example, substance use disorders and antisocial personality disorder) a disinhibited personality style and lack of constraint.<sup>35</sup> Problem/pathological gambling also shares with internalizing disorders (for example, major depressive disorder and social phobia) an uncomfortable mood or anxiety state that often precedes gambling. Existing data suggest strong genetic contributions between pathological gambling and internalizing<sup>37</sup> and externalizing<sup>11,38</sup> disorders, respectively. Further study, particularly using DSM-based measures of pathological gambling in conjunction with DSM-based measures of other psychiatric disorders, may provide important insight into how best to categorize pathological gambling.

The relationship between nicotine dependence and externalizing/internalizing disorders is also unsettled, with findings arguably suggesting a stronger clustering with externalizing disorders. Associations between daily cigarette smoking and most psychiatric disorders have been demonstrated in multiple studies.<sup>39,40</sup> Although nicotine dependence has also been associated with internalizing disorders like major depressive disorder and anxiety disorders,<sup>15,41,42</sup> strong associations between daily tobacco smoking or nicotine dependence have been found for substance use disorders, attention-deficit/hyperactivity disorder, conduct disorder, oppositional defiant disorder, and antisocial personality disorder.<sup>15,39,41,43</sup> A strong association exists between progression to daily smoking and externalizing disorders, with externalizing disorders predicting the development of nicotine dependence from daily smoking.39

In this study, the nicotine-dependent group demonstrated high estimates of major depression regardless of gambling severity. In other words, more severe gambling behaviors did not increase the risk for depression among nicotine-dependent subjects, suggesting an overlap in the factors contributing to nicotine dependence and problem gambling behaviors as they relate to depression. In that low-risk gamblers had a low odds ratio for major depression compared to nongamblers among nicotine-dependent subjects, it suggests that low-level gambling behaviors either have a mood-protecting influence in smokers or that a depressed mood among smokers interferes with participation in low-risk gambling. Previous studies have suggested that neuroticism may be a common predisposition to both nicotine dependence and major depression<sup>15</sup> and that smoking may assist in managing mood symptoms.<sup>12</sup> Further research is needed to examine the extent to which these or other factors mediate the relationship between tobacco smoking, depression, and gambling.

Although more severe gambling behaviors increased the risk for all anxiety disorders in both nicotine-dependent and nondependent groups, the association between gambling and anxiety disorders was substantially stronger in the nondependent group. Research indicates that nicotine use has anxiolytic properties.<sup>44,45</sup> The greater odds ratios for anxiety disorders within the nondependent group suggest that gambling severity level may be indicative of the anxiolytic properties of gambling behaviors and implicate a neurobiological pathway common to gambling and tobacco use. Given the high rates of anxiety disorders in individuals with disordered gambling,<sup>6</sup> these findings may have treatment implications for preventing gambling relapse in PPG groups.

## **Clinical Implications**

The data yield several important conclusions. First, PPG in non-nicotine-dependent adults was associated with a broad range of psychopathology. Second, even low-risk gambling in non-nicotine-dependent respondents was positively associated with multiple psychiatric disorders, including drug and alcohol use disorders, anxiety, and mania. Given the increased popularity of gambling as a recreational activity, there has been significant concern about the potential public health threat posed by subsyndromal levels of gambling.<sup>1</sup> To date, there has been relatively little research exploring low-risk gambling patterns and correlates,<sup>7</sup> and existing studies have frequently not used diagnostic measures of psychopathology.7,46 Consistent with these studies,<sup>7,46</sup> the current findings indicate that even low-risk gambling is associated with significant psychopathology in certain groups; e.g., non-nicotine-dependent subjects. Although there are no diagnostic criteria for levels of gambling pathology except pathological gambling, this finding suggests that gambling may be more accurately seen as a spectrum of disease.<sup>7-9</sup> Regardless of the underlying mechanism for the association, these results raise concern that low-risk gambling in nonsmoking individuals may be more reflective of psychopathology than such gambling in nicotine-dependent groups. This has implications for (1) primary care, in which screening and brief interventions around gambling, smoking, and other psychiatric disorders could be implemented; and (2) public policy related to the expansion in availability of gambling venues.

## **Strengths and Limitations**

Our study is the first to find that nicotine dependence influences the association between gambling severity and psychopathology. The study's strengths are its survey design, large nationally representative sample, the inclusion of a wide range of DSM-IV Axis I and II disorders, and the response rate (81%). Despite these strengths, this study has several important limitations. First, the crosssectional nature of the data precludes our ability to establish temporal patterns between problem gambling behavior, psychopathology, and nicotine dependence. It is therefore possible to suggest several competing, although not necessarily mutually exclusive, explanations, all of which are consistent with the data. Second, low rates of pathological gambling were reported, necessitating combining problem and pathological gambling into a single category. It is possible that there exist significant differences in psychopathology between problem and pathological gambling. Third, although pathological gambling in this study was based on DSM-IV criteria, the exclusionary criterion of DSM-IV (i.e., diagnosis of pathological gambling is not given if it occurs during a manic episode) was not assessed. Therefore, pathological gambling in this study may differ from DSM-IV pathological gambling. Fourth, there are no established standards for categorizing gambling behavior across a continuum. Although these groupings have been used in previous studies,<sup>7,23,27</sup> they are not based on empirically-derived thresholds.

This study highlights the need for future research. In particular, research focusing on a possible biological basis for the associations between gambling, nicotine dependence, and other psychopathology is needed. Additionally, given the clinical and public health concerns of these associations, future research should address both primary and secondary interventions.

*Disclosure of off-label usage:* The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this article.

#### REFERENCES

- Shaffer HJ, Hall MN, Vander Bilt J. Estimating the prevalence of disordered gambling behavior in the United States and Canada: a research synthesis. Am J Public Health 1999;89(9):1369–1376
- Petry NM, Stinson FS, Grant BF. Comorbidity of DSM-IV pathological gambling and other psychiatric disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 2005;66(5):564–574
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-Text Revision. Washington, DC: American Psychiatric Association; 2000
- Shaffer HJ, Hall MN. Updating and refining prevalence estimates of disordered gambling behaviour in the United States and Canada. Can J Public Health 2001;92:168–172
- Potenza MN, Kosten TR, Rounsaville BJ. Pathological gambling. JAMA 2001;286:141–144
- 6. Argo T, Black DW. Clinical characteristics. In: Grant JE,

Potenza MN, eds. Pathological Gambling: A Clinical Guide to Treatment. Washington, DC: American Psychiatric Publishing; 2004:39–54

- Desai RA, Maciejewski PK, Dausey DJ, et al. Health correlates of recreational gambling in older adults. Am J Psychiatry 2004;161:1672–1679
- Shaffer HJ, Korn DA. Gambling and related mental disorders: a public health analysis. Annu Rev Public Health 2002;23:171–212
- Crockford DN, El-Guebaly N. Psychiatric comorbidity in pathological gambling: a critical review. Can J Psychiatry 1998;43:43–50
- Cunningham-Williams RM, Cottler LB, Compton WM III, et al. Taking chances: problem gamblers and mental health disorders: results from the St. Louis Epidemiologic Catchment Area study. Am J Public Health 1998;88(7):1093–1096
- Slutske WS, Eisen S, True WR, et al. Common genetic vulnerability for pathological gambling and alcohol dependence in men. Arch Gen Psychiatry 2000;57:666–673
- Grant BF, Hasin DS, Chou SP, et al. Nicotine dependence and psychiatric disorders in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2004; 61:1107–1115
- Breslau N. Psychiatric comorbidity of smoking and nicotine dependence. Behav Genet 1995;25:95–101
- Breslau N, Kilbey MM, Andreski P. DSM-III-R nicotine dependence in young adults: prevalence, correlates and associated psychiatric disorders. Addiction 1994;89:743–754
- Breslau N, Kilbey MM, Andreski P. Nicotine dependence, major depression, and anxiety in young adults. Arch Gen Psychiatry 1991;48: 1069–1074
- Smart RG, Ferris J. Alcohol, drugs and gambling in the Ontario adult population, 1994. Can J Psychiatry 1996;41:36–45
- Petry NM, Oncken C. Cigarette smoking is associated with increased severity of gambling problems in treatment-seeking gamblers. Addiction 2002;97:745–753
- Grant JE, Potenza MN. Tobacco use and pathological gambling. Ann Clin Psychiatry 2005;17:237–241
- Potenza MN, Steinberg MA, McLaughlin SD, et al. Characteristics of tobacco-smoking problem gamblers calling a gambling helpline. Am J Addict 2004;13:471–493
- Morasco BJ, Pietrzak RH, Blanco C, et al. Health problems and medical utilization associated with gambling disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychosom Med 2006;68(6):976–984
- Blanco C, Hasin DS, Petry N, et al. Sex differences in subclinical and DSM-IV pathological gambling: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychol Med 2006;36: 943–953
- 22. Grant BF, Stinson FS, Hasin DS, et al. Immigration and lifetime prevalence of DSM-IV psychiatric disorders among Mexican Americans and non-Hispanic whites in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2004;61:1226–1233
- Desai RA, Desai MM, Potenza MN. Gambling, health, and age: data from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychol Addict Behav 2007;21:431–440
- 24. Grant BF, Moore TC, Shepard J, et al. Source and Accuracy Statement: Wave 1 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Bethesda, Md: National Institute on Alcohol Abuse and Alcoholism; 2003. Available at: www.niaaa.nih.gov. Accessed Jul 6, 2006
- 25. Grant BF, Dawson DA, Stinson FS, et al. 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 Alcohol Depend 2003;71:7–16
- National Opinion Research Center. Gambling Impact and Behavior Study. Chicago, Ill: University of Chicago; 1999
- Desai RA, Maciejewski PK, Pantalon MV, et al. Gender differences among recreational gamblers: association with the frequency of alcohol use. Psychol Addict Behav 2006;20:145–153
- National Research Council of the National Academies, Committee on National Statistics. Measuring Racial Discrimination. Blank RM, Dabady M, Citro CF, eds. Washington, DC: National Academies Press; 2004
- 29. Research Triangle Institute. Software for Survey Data Analysis (SUDAAN), Version 8.1. Research Triangle Park, NC:

Research Triangle Institute; 2002

- Kreek MJ, Nielsen DA, Butelman ER, et al. Genetic influences on impulsivity, risk taking, stress responsivity and vulnerability to drug abuse and addiction. Nat Neurosci 2005;8:1450–1457
- Rice ME, Cragg SJ. Nicotine amplifies reward-related dopamine signals in striatum. Nat Neurosci 2004;7:583–584
- Zhang H, Sulzer D. Frequency-dependent modulation of dopamine release by nicotine. Nat Neurosci 2004;7:581–582
- Reuter J, Raedler T, Rose M, et al. Pathological gambling is linked to reduced activation of the mesolimbic reward system. Nat Neurosci 2005;8:147–148
- Potenza MN. Impulse control disorders and co-occurring disorders: dual diagnosis considerations. J Dual Diagnosis 2007;3(2):47–57
- Krueger RF, Hicks BM, Patrick CJ, et al. Etiologic connections among substance dependence, antisocial behavior, and personality: modeling the externalizing spectrum. J Abnorm Psychol 2002;111:411–424
- Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. Arch Gen Psychiatry 1994; 51(1):8–19
- Potenza MN, Xian H, Shah K, et al. Shared genetic contributions to pathological gambling and major depression in men. Arch Gen Psychiatry 2005;62:1015–1021
- Slutske WS, Eisen S, Xian H, et al. A twin study of the association between pathological gambling and antisocial personality disorder.

J Abnorm Psychol 2001;110:297-308

- Rohde P, Kahler CW, Lewinsohn PM, et al. Psychiatric disorders, familial factors, and cigarette smoking, 2: associations with progression to daily smoking. Nicotine Tob Res 2004;6:119–132
- Lasser K, Boyd JW, Wollhandler S, et al. Smoking and mental illness. JAMA 2000;284:2606–2610
- Kendler KS, Neale MC, Sullivan P, et al. A population-based twin study in women of smoking initiation and nicotine dependence. Psychol Med 1999;29:299–308
- Breslau N, Peterson EL, Schultz LR, et al. Major depression and stages of smoking: a longitudinal investigation. Arch Gen Psychiatry 1998; 55:161–166
- Brown RA, Lewinsohn PM, Seeley JR, et al. Cigarette smoking, major depression and other psychiatric disorders among adolescents. J Am Acad Child Adolesc Psychiatry 1996;35(12):1602–1610
- Booker TK, Butt CM, Wehner JM, et al. Decreased anxiety-like behavior in beta3 nicotinic receptor subunit knockout mice. Pharmacol Biochem Behav 2007;87:146–157
- 45. Buckley TC, Holohan DR, Mozley SL, et al. The effect of nicotine and attention allocation on physiological and self-report measures of induced anxiety in PTSD: a double-blind placebo-controlled trial. Exp Clin Psychopharmacol 2007;15:154–164
- 46. Lynch WJ, Maciejewski PK, Potenza MN. Psychiatric correlates of gambling in adolescents and young adults grouped by age at gambling onset. Arch Gen Psychiatry 2004;61:1116–1122

For the CME Posttest for this article, see pages 438–440.