

## CLINICAL CORRELATES OF CIGARETTE SMOKING AND NICOTINE DEPENDENCE IN ALCOHOL-DEPENDENT MEN AND WOMEN

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**Abstract** — This paper examines the clinical characteristics associated with tobacco use and nicotine dependence in a large sample of alcohol-dependent subjects. The goal was to determine if the characteristics of the alcohol use history were associated with the smoking status, even after controlling for additional characteristics, such as the antisocial personality disorder, other drug dependence and gender. As part of the Collaborative Study on the Genetics of Alcoholism, a semi-structured interview, including a detailed history of alcohol and tobacco use, was administered to 1005 alcohol-dependent men and women, made up of 658 (65.5%) current smokers, 167 (16.6%) former smokers, and 180 (17.9%) non-smokers. Among former smokers, 50.3%, and among current smokers, 72.8% had ever been nicotine-dependent (DSM-III-R). Current smokers and nicotine-dependent subjects had a greater severity of alcohol dependence, even as evaluated through logistic regression analyses in which gender and associated diagnoses were considered. The data also enabled us to study the relationships among depression, nicotine dependence, and alcohol dependence, with most of the correlation occurring for substance-induced, not independent, mood disorders.

### INTRODUCTION

An estimated 80% of alcohol-dependent men and women use tobacco products regularly, a figure which has been fairly stable in recent decades (Hurt *et al.*, 1994; Gulliver *et al.*, 1995; Hughes, 1995, 1996; Toneatto *et al.*, 1995; Pomerleau *et al.*, 1997). This combination of regular nicotine use and alcoholism has important clinical implications, including a heightened mortality rate from cancer and several other physical disorders (Blot *et al.*, 1988; Klatsky and Armstrong, 1992). Alcohol-dependent individuals who also regularly smoke cigarettes have a higher quantity and frequency of alcohol intake compared to non-smoking alcoholics (York and Hirsch, 1995), and have been reported in some (but not all) studies to have greater difficulty in giving up alcohol if they continue smoking (Gulliver *et al.*, 1995; Sobell *et al.*, 1995; Sher *et al.*, 1996; Stuyt *et al.*, 1997; Bobo *et al.*, 1998). Alcoholics with more intense nicotine dependence report higher levels of urges to drink alcohol, and demonstrate higher quantities and frequencies of alcohol use if they relapse (Abrams *et al.*, 1992; Gulliver *et al.*, 1995). Alcohol dependence or evidence of heavy drinking among smokers is also associated with an increased number of cigarettes per day and a greater likelihood of nicotine dependence (Batel *et al.*, 1995; Hurt *et al.*, 1995; Hughes, 1996; Pomerleau *et al.*, 1997). Finally, both alcohol and nicotine dependence can be associated with

mood disorders (Glassman, 1993; Schuckit *et al.*, 1997a,b; Patton *et al.*, 1998a).

Although few clinicians or researchers question the importance of the relationship between cigarette use and alcohol dependence, most studies have been of relatively modest size and, thus, were unable to control for potentially important additional variables. For example, there are gender differences in the clinical course of alcohol and nicotine dependence (Carmody *et al.*, 1985; Breslau *et al.*, 1994; Patton *et al.*, 1998b; Schuckit *et al.*, 1998a), raising the question of whether the correlates of conjoint alcoholism and heavy smoking apply equally to men and women. A second potentially confounding factor is the possibility that the more severe clinical course of conjoint alcohol and nicotine dependence might reflect the impact of a third disorder. Thus, for example, the concurrence of alcohol and nicotine dependence carries with it a 5-fold increased risk for bipolar disorder, a 6-fold increased risk for use of illegal drugs, and an almost 20-fold increased rate of the antisocial personality disorder (ASPD) (Helzer *et al.*, 1991).

This study reports data from a large heterogeneous sample of alcoholics where extensive clinical interviews were used to gather detailed data on these potentially important issues. The major purpose was to evaluate whether the characteristics of alcohol use history are associated with smoking status even after controlling for the potential impact of ASPD, additional drug dependence diagnoses, and gender.

### METHOD

The data were generated from subjects who took part in the six-centre-wide Collaborative Study on the Genetics of Alcoholism (COGA). As described in additional publications, this is a family pedigree study that begins with an alcohol-dependent proband in treatment, and gathers data from that subject and all available first degree relatives (Bucholz *et al.*, 1994; Schuckit *et al.*, 1997a,b, 1998b). Potential COGA subjects were included regardless of additional diagnoses, with the only exclusions occurring for individuals who were unable

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†The Collaborative Study on the Genetics of Alcoholism (COGA) (H. Begleiter, SUNY HSCB Principal Investigator; T. Reich, Washington University, Co-Principal Investigator) includes six different centres where data collection takes place. The six sites and Principal Investigator and Co-Investigators are: Indiana University (J. Nurnberger Jr, T.-K. Li, P. M. Conneally, H. Edenberg); University of Iowa (R. Crowe, S. Kuperman); University of California at San Diego and Scripps Institute (M. Schuckit, F. Bloom); University of Connecticut (V. Hesselbrock); State University of New York, Health Sciences Center at Brooklyn (H. Begleiter, B. Porjesz); Washington University in St Louis (T. Reich, C. R. Cloninger, J. Rice).

to speak English, those with evidence of severe debilitating diseases such as acquired immune deficiency syndrome, those with recent heavy intravenous drug use, and subjects who had fewer than two relatives available for interview. Controls were selected from a variety of sources including general medical and dental clinics, drivers' licence records, and random population surveys.

All subjects and their available first and second degree relatives gave informed consent and participated in a structured face-to-face interview, using the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) instrument given by well-trained interviewers (Bucholz *et al.*, 1994). The SSAGA screens for 17 Axis I DSM-III-R diagnoses (American Psychiatric Association, 1987), including misuse and dependence on substances. Subjects were questioned regarding recent drinking histories, patterns of alcohol use, periods of abstinence, a series of 44 life experiences related to alcohol, and the nine criteria relevant to establishing the DSM-III-R diagnoses of alcohol and nicotine dependence (Schuckit *et al.*, 1998a,b). Similar data were gathered regarding dependence on most drugs of misuse, and information was obtained regarding most major psychiatric disorders. Regarding major depressive disorder (MDD) among alcohol-dependent subjects, a distinction was made between major depressive episodes that only occurred during periods of alcohol or drug use (substance-induced MDD), versus those observed before the onset of alcohol dependence or during periods of at least 3 months of abstinence (independent MDD) (Schuckit *et al.*, 1997a).

Consistent with several other studies, cigarette smoking was defined as daily cigarette use for at least 1 month at any time in a person's life (Robins *et al.*, 1989; Breslau *et al.*, 1994). The smoking history section of the SSAGA was expanded to include the Fagerström Test for Nicotine Dependence (FTND) (Payne *et al.*, 1994). The FTND was used to generate a modified score based on five instead of six questions, as the item asking which cigarette is the most difficult to give up (explaining 6.7% of the variance of the total score) was not included in the interview. Indeed, it is hard to believe that subjects who smoked cigarettes daily for several years were not considered nicotine dependent. For these analyses, nicotine dependence was defined according to DSM-III-R criteria, which apply only to smokers experiencing severe repercussions of their tobacco use, i.e. on their social functioning, physical or psychological health. Therefore, the distinction between smokers with and without DSM-III-R nicotine dependence might reflect stages in the severity of nicotine dependence, rather than a categorical distinction between those with and without nicotine dependence.

Statistical analyses compared data between groups defined according to smoking status or nicotine dependence.  $\chi^2$ -Tests were applied for categorical data across groups, whereas *F*-values were used to determine the two-tailed significance of differences in group means for continuous variables. If more than two groups were compared, for items that were significant overall, post-hoc tests of pairwise comparisons were applied using Tukey's Honestly Significant Difference Test for continuous variables and the  $\chi^2$  for proportions for dichotomous variables. Consistent with the COGA approach to data analyses, demographic, alcohol- and drug-related items were compared across groups without correction for multiple comparisons in order to avoid a conservative approach where

meaningful differences across groups are missed. Finally, logistic regression was used to determine the potential importance of the variables which were significant at the univariate level in predicting current smoking status or nicotine dependence. The approach used to evaluate the proportion of the variance explained by the logistic regression analyses followed the recommendations of Hosmer and Lemeshow (1989) through which an  $R^2 = 100(1 - L_p/L_0)$ .

## RESULTS

Data were available from 2251 SSAGA interviews that included detailed histories of tobacco use and DSM-III-R criteria of nicotine dependence. Among these, 1005 individuals met DSM-III-R criteria for alcohol dependence and were eligible for the present analyses. The sample of 1005 alcohol-dependent individuals included 292 original probands (29.1%), 656 relatives of probands (65.3%), and 57 controls (5.7%). There were 393 women (39.1%), and the racial distribution was 79.2% Caucasian, 17.9% African-American, and 2.9% of other ethnic backgrounds. The mean age ( $\pm$  SD) of these alcohol-dependent men and women was 38.6 ( $\pm$  11.50) years, and 70.9% of the participants had graduated from high school. At the time of the interview, 40.3% of the subjects were married, 28.4% were separated or divorced, 1.7% were widowed, and 29.7% had never been married. Of the sample of 1005 subjects, 454 (45.2%) had no history of treatment related to alcohol (i.e. Alcoholics Anonymous, outpatient or inpatient programmes).

Table 1 compares demographic background, alcohol and tobacco use histories, and associated diagnoses across five groups of subjects. These include 180 alcoholics who were non-smokers (Group 1), 167 former smokers (divided into those in Group 2 who were never nicotine dependent versus those in Group 3 who fulfilled such criteria), and similar non-dependent and dependent subdivisions of 658 current smokers (Groups 4 and 5). Looking across Groups 1 through 5, it is apparent that almost 18% of these alcohol-dependent men and women had never regularly smoked cigarettes, and that a lower proportion of former smokers had ever been nicotine dependent (84 of 167 or 50.3%), compared to current smokers (479 of 658 or 72.8%) ( $\chi^2 = 31.10$ ;  $P < 0.001$ ). Regarding demographics, former smokers were older than the remaining subjects (indicating that one might expect higher rates of former smoking in Groups 4 and 5 over time), and, within both former and current smokers, women were more likely to have ever been nicotine dependent. The remaining two demographic items demonstrate that, among Groups 2 to 5, current smokers and nicotine-dependent subjects had lower proportions of individuals who were employed or who had received a high school diploma.

The data also demonstrate that, among smokers, current smokers and those who were nicotine dependent had the earliest age of onset of alcohol dependence, and the highest number of alcohol-related life problems with higher maximum drinks per day in current smokers. The problems included in the list of 44 major life events relating to alcohol have been described in more detail in another publication (Schuckit *et al.*, 1998a). Only current smokers were more likely than the remaining groups to have ever been treated for alcoholism.

Table 1. Comparison of demographic characteristics, alcohol and tobacco use histories, and associated diagnoses across non-smokers, former smokers, and current smokers in 1005 alcohol-dependent subjects

Parameter	Non-smokers <sup>†</sup>	Former smokers <sup>‡</sup>		Current smokers <sup>§</sup>		Statistical test: <i>F</i> or $\chi^2$	Group differences
	(Group 1)	Non-nicotine-dependent (Group 2)	Nicotine-dependent (Group 3)	Non-nicotine-dependent (Group 4)	Nicotine-dependent (Group 5)		
<i>n</i> (%)	180 (17.9)	83 (8.3)	84 (8.3)	179 (17.8)	479 (47.7)		
<b>Demographics</b>							
Age at interview	37.4 ± 11.06	45.3 ± 14.54	44.1 ± 13.00	37.8 ± 11.39	37.3 ± 10.13	14.96***	a,b,f,g,h,i,k,m
% female	37.2	38.6	51.2	29.6	41.8	13.58**	b,h,j,m
% presently employed	67.8	61.4	66.7	58.7	46.1	34.07***	d,g,i,j,k,l,m
% with high school diploma	84.4	83.1	75.0	72.1	62.6	38.74***	c,d,g,i,j,k,l,m
<b>Alcohol use history</b>							
Age of first intoxication	17.1 ± 5.47	15.8 ± 4.04	15.9 ± 4.67	15.3 ± 3.67	15.2 ± 4.48	5.95***	c,d,l
Age of onset alcohol dependence	23.9 ± 8.16	25.7 ± 9.54	24.6 ± 9.99	23.0 ± 8.09	21.7 ± 7.18	7.09***	d,g,i,k,m
Maximum drinks (24 h)	22.9 ± 17.99	21.2 ± 12.87	21.5 ± 16.06	31.5 ± 26.55	32.5 ± 24.41	11.63***	c,d,f,g,h,i,k,l
No. of DSM-III-R alcohol dependence criteria (9)	5.2 ± 2.00	4.7 ± 1.80	5.4 ± 1.99	6.0 ± 2.01	6.8 ± 1.88	38.20***	c,d,f,g,i,j,k,l,m
No. of alcohol problems (44)	17.2 ± 7.86	15.2 ± 7.33	18.2 ± 8.15	20.1 ± 7.45	23.6 ± 8.12	37.24***	c,d,f,g,i,j,k,l,m
% treated for alcohol problem	36.1	33.7	31.0	61.5	67.2	92.59***	c,d,f,g,h,i,k,l,m
<b>Tobacco use history</b>							
Age started smoking daily	—	17.6 ± 5.27	16.8 ± 4.09	17.2 ± 5.14	15.7 ± 4.04	8.20***	g,j,k,m
No. of years smoked daily	—	11.7 ± 12.16	16.1 ± 11.86	18.8 ± 11.68	20.5 ± 10.43	16.95***	e,f,g,i,k,m
No. of cigarettes per day	—	14.8 ± 13.86	27.5 ± 14.28	18.0 ± 11.07	22.3 ± 11.28	21.72***	e,g,h,i,j,m
% tried to quit	—	90.4	98.8	68.2	83.1	43.97***	e,f,h,i,j,k,m
No. of attempts to quit smoking	—	2.7 ± 4.28	5.5 ± 8.40	3.0 ± 3.17	5.1 ± 11.01	4.77**	h,j,m
No. of DSM-III-R nicotine dependence criteria (9)	—	1.8 ± 1.56	5.5 ± 1.59	2.82 ± 1.72	6.04 ± 1.64	271.18***	e,f,g,h,i,j,k,m
Modified Fagerström	—	2.0 ± 2.00	4.8 ± 2.37	3.7 ± 2.11	5.2 ± 2.07	70.98***	e,f,g,h,j,k,m
<b>Associated diagnoses</b>							
% ASPD	8.9	8.4	11.9	12.3	22.1	26.55***	d,g,i,j,k,l,m
% with an additional drug dependency	42.2	27.7	39.3	48.0	67.6	78.88***	a,d,f,g,i,j,k,l,m
No. of additional drug dependencies (5)	0.8 ± 1.14	0.5 ± 0.89	0.9 ± 1.34	0.9 ± 1.21	1.45 ± 1.37	18.95***	d,g,i,j,k,l,m
% with alcohol-induced depression	25.0	13.3	19.0	19.6	40.5	52.53***	a,d,g,i,j,k,m
% with independent major depression	18.9	10.8	21.4	14.5	20.9	7.35**	g,m

<sup>†</sup>Never smoked daily for 30 days; <sup>‡</sup>smoked daily for at least 30 days, not in the last 12 months; <sup>§</sup>smoked daily for at least 30 days over the last 12 months.

*F*-test or  $\chi^2$  significant at \**P* < 0.05; \*\**P* < 0.01; \*\*\**P* < 0.001.

Post-hoc comparisons all significant at *P* < 0.05: <sup>a</sup>Group 1 vs Group 2; <sup>b</sup>Group 1 vs Group 3; <sup>c</sup>Group 1 vs Group 4; <sup>d</sup>Group 1 vs Group 5;

<sup>e</sup>Group 2 vs Group 3; <sup>f</sup>Group 2 vs Group 4; <sup>g</sup>Group 2 vs Group 5; <sup>h</sup>Group 3 vs Group 4; <sup>i</sup>Group 3 vs Group 5; <sup>j</sup>Group 4 vs Group 5;

<sup>k</sup>Groups (2 + 3) vs Groups (4 + 5) (former smokers vs current smokers); <sup>l</sup>Group 1 vs Groups (2 + 3 + 4 + 5) (non-smokers vs smokers);

<sup>m</sup>Groups (2 + 4) vs Groups (3 + 5) (non-nicotine-dependent vs nicotine-dependent).

DSM-III-R, *Diagnostic and Statistical Manual of Mental Disorders III—revised*; ASPD, antisocial personality disorders.

Table 1 also offers information about tobacco use histories among current and former smokers. Reflecting the way the groups were defined, nicotine-dependent subjects had a more severe course of nicotine use with, for most items, a greater maximum intake and more lifetime tobacco-related problems illustrated by more DSM-III-R criteria of nicotine dependence for current versus former smokers. However, problems were still apparent for non-nicotine-dependent smokers.

Of central interest is whether the group differences on alcohol use and problems might actually reflect additional associated diagnoses. Antisocial personality disorders (ASPD) and substance dependence diagnoses were more likely in smokers, especially those whose use was current, and, among smokers, in nicotine-dependent individuals. For Groups 2 to 5, dependent subjects were also more likely to have independent and substance-induced mood disorders, with the latter diagnoses more likely among current, versus former, smokers. Thus, it is possible that the association of some aspects of more evidence of social impairment (unemployment, low level of education), higher levels of alcohol use, and more intense tobacco use with a history of current (versus former) smoking

and with nicotine dependence might reflect differences between groups regarding gender, ASPD, and dependence on drugs other than alcohol and nicotine.

To test this, the top portion of Table 2 evaluates the characteristics associated with being a former smoker, and the bottom relates to the pattern of those characteristics associated with a history of nicotine dependence using logistic regression analyses. In predicting former (versus current) smokers among individuals who had ever regularly consumed cigarettes, and in predicting nicotine dependence among smokers, each of the items from Table 1 that were significantly associated with the relevant dependent variable (e.g. nicotine dependence) were entered into the logistic regression analyses, with Table 2 presenting only those items that significantly contributed to the final equation. Regarding the ability to become a former smoker after regularly consuming cigarettes, the regression analysis explained 17.8% of the variance. Items that significantly added to the equation indicated a greater probability of smoking cessation in older alcoholics, those who were employed, and were also associated with a lower maximum of drinks per day, fewer alcohol-related problems, fewer of the

Table 2. Logistic regression analyses for characteristics significantly associated with former smokers and with nicotine dependence in alcohol-dependent subjects

Dependent variable	Predictor variable	$\chi^2$	Odds ratio
Former smokers <sup>a</sup> ( <i>n</i> = 825) ( <i>df</i> = 13)	Age at interview	42.07***	1.07
	Present employment	8.09**	1.86
	Age of onset of alcohol dependence	4.13*	0.97
	Maximum drinks (24 h)	3.88*	0.99
	No. of alcohol problems ( <i>n</i> = 44)	9.30**	0.95
	No. of DSM-III-R nicotine dependence criteria	5.14*	0.88
Nicotine dependence <sup>b</sup> ( <i>n</i> = 825) ( <i>df</i> = 12)	Modified Fagerström	10.95***	0.84
	Female gender	19.06***	2.33
	Present employment	6.74**	0.62
	No. of alcohol problems ( <i>n</i> = 44)	6.98**	1.03
	No. of additional drug dependencies	10.37**	1.30
	Ever had a substance-induced depression	13.27***	1.21
	No. of cigarettes per day	38.47***	1.06
No. of attempts to quit smoking	15.10***	1.11	

\* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .

<sup>a</sup>Overall regression  $\chi^2 = 180.47$ ; variance accounted for by predictor variables = 17.8%.

<sup>b</sup>Overall regression  $\chi^2 = 193.74$ ; variance accounted for by predictor variables = 15.8%.

DSM-III-R, *Diagnostic and Statistical Manual of Mental Disorders III—revised*.

nine DSM-III-R nicotine dependence criteria, and a lower modified Fagerström score. The age of onset of alcohol dependence acted as a suppressor variable in the context of current age, and, thus, the direction of the odds ratio was reversed. It is interesting to note that these predictors were unaffected by the presence or absence of ASPD, dependencies on drugs other than alcohol, prior treatment for alcohol, or gender, as none of these latter items entered the final regression analysis.

The prediction of nicotine dependence among smokers created a regression analysis that explained 15.8% of the variance. Those alcoholics most likely to develop nicotine dependence were more likely to be women, unemployed, to have a higher number of alcohol problems, a greater number of additional drug dependencies, and to have experienced a substance-induced (but not an independent) depression. Not surprisingly, the decision to include all relevant items from Table 1 that were significantly associated with dependence also resulted in a higher number of cigarettes per day and a greater number of times attempting quitting smoking entering the equation as well. The results regarding nicotine dependence demonstrate that a diagnosis of ASPD had little impact, and that a greater number of alcohol problems and some evidence of a lower level of social functioning (e.g. fewer individuals employed) continued to relate to nicotine dependence, even in the context of consideration of gender and additional drug dependencies. It is also important to note that a history of a substance-induced major depressive episode (but not independent major depressions) significantly predicted nicotine dependence even after considering gender, other drug dependencies, and other relevant factors.

## DISCUSSION

This paper presents data generated from detailed personal interviews with >1000 alcohol-dependent men and women. The findings in Table 1 corroborate prior reports of an ~80% lifetime rate of regular smoking among alcoholics, and demonstrate a greater severity of alcohol-related life problems

among current, versus former, smokers and among those who ever fulfilled criteria for nicotine dependence.

Reflecting the limited number of subjects in most investigations as well as the research methodologies invoked, prior studies were usually unable to determine whether the greater intensity of alcoholism associated with current smoking and nicotine dependence might be an indirect reflection of additional characteristics, such as ASPD, other drug dependencies, and gender. The results in Table 1 support the relationship between nicotine and alcohol use disorders. Table 2 reveals that, even after considering the impact of gender, ASPD, and additional drug dependencies, both current smokers and nicotine-dependent smokers continued to show evidence of a greater number of alcohol-related life problems.

Another interesting result concerns the relationship of gender to nicotine dependence in the logistic regressions. Similar results have also been reported in the literature (Swan *et al.*, 1997). It is postulated that women smokers might respond to a wider range of environmental cues, which increased their desire for cigarettes, and are thus more likely to develop dependence and, perhaps, even less likely to respond to nicotine replacement treatment. In any event, the current results support the need to consider gender when evaluating issues related to smoking behaviours in general, including those among alcohol-dependent individuals.

Several studies have also discussed the relationship between mood disorders and smoking (e.g. Glassman, 1993), as well as mood disorders and heavy drinking (Schuckit *et al.*, 1997a). Using methods established for alcohol, the current study distinguished between independent major depressive episodes as described in the DSMs and temporary, substance-induced mood disorders that are observed in  $\geq 30\%$  of alcoholics (Schuckit *et al.*, 1997a). The univariate analyses in Table 1 show fairly strong group differences in substance-induced mood disorders among smokers, and some, perhaps less intense, differences for independent major depression. Table 2 indicates that, after considering additional group differences, only the differential in induced depressions remains robust. The first implication of these results is the need for future

researchers to distinguish between substance-induced and independent depressive episodes in looking at nicotine-dependent individuals, at least among those with alcohol or drug dependence.

Although the current sample was large and the subjects diverse regarding demography and associated diagnoses, several caveats should be considered. First, the data were generated from families with a high density of alcoholism selected through an alcoholic proband. Second, more detail was available regarding alcohol, drugs, and mental health problems than was true for the nicotine history. Third, most of the subjects had modest levels of education. Thus, the generalizability of the current results to other populations will need to be tested. Moreover, other variables related to subjects' personality, social, and cultural characteristics with potentially important influences on the smoking status were not considered in these analyses. Nonetheless, the data presented here document that, within this sample, the reported heightened intensity of alcohol-related problems among smoking alcoholics appears to be independent of ASPD, additional drug dependencies, prior alcohol treatment, and that some similar generalizations apply to both genders.

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