

Depressed Patients With Co-Occurring Alcohol Use Disorders: A Unique Patient Population

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Objective: Alcohol use and depressive disorders are frequently comorbid. Few studies have assessed the impact of comorbid alcohol use disorders (AUDs) on clinical aspects of major depression. We compared depressed subjects with and without co-occurring AUDs with respect to demographic and clinical parameters.

Method: 505 individuals participated. 318 subjects had DSM-IV major depressive disorder (MDD) without a history of any alcohol or substance abuse/dependence (MDD only), and 187 individuals had MDD and a history of alcohol abuse/dependence (MDD/AUD). Demographic, clinical, and psychiatric history measures of patients in the 2 groups were examined and compared. The study was conducted from January 1990 to June 2005.

Results: MDD/AUD patients were younger at their first psychiatric hospitalization ($p = .014$), their first major depressive episode ($p = .041$), and their first suicide attempt ($p = .001$). They reported more previous major depressive episodes ($p = .001$), suicide attempts ($p = .001$), and recent life events ($p = .001$); and had higher lifetime aggression ($p < .001$), impulsivity ($p < .001$), and hostility ($p < .001$) scores. MDD/AUD patients were also more likely to report tobacco smoking ($p < .001$), a lifetime history of abuse ($p = .004$), and a history of AUD among first-degree relatives ($p < .001$) compared to MDD only patients. MDD/AUD individuals also had higher childhood ($p < .001$), adolescent ($p < .001$), and adult ($p < .001$) aggression scores and reported more behavioral problems during their childhood compared to their counterparts. Logistic regression analysis demonstrates that the number of previous depressive episodes, lifetime aggression, and smoking drive the difference between the groups.

Conclusion: Our findings suggest that comorbid MDD/AUD may result from worse antecedents and lead to early onset, more comorbidity, and a more severe course of illness.

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Major depression affects approximately 10 million Americans, or roughly 5% of the population, and is the leading cause of disability in the United States.¹ Similarly, alcohol problems, including at-risk drinking, alcohol abuse, and alcohol dependence, are highly prevalent.^{2,3} Prevalence estimates for alcohol abuse and dependence in the general population range between 7% for current and 16% to 24% for lifetime alcohol problems.^{1,3} Patients with depression frequently have alcohol problems.^{1,4,5} One household survey reported a prevalence of 16% for any alcohol diagnosis in depressed patients.⁵ These conditions have been found to coexist in different age, sex, and racial groups.^{4,5} Alcohol problems in depressed patients present diagnostic and management challenges and may adversely affect the course of depression and its response to standard therapies. Five studies that examined the risk of suicide/death in persons with co-occurring depression and alcohol use disorders (AUDs) concluded that a current or lifetime alcohol problem in patients with depression was associated with an increased risk of severe suicidal symptoms or acts.^{6–10} In our previous paper,⁹ we reported higher morbidity and suicidality in depressed subjects with co-occurring alcoholism compared to depressed individuals without a history of alcoholism and that this bore a close relationship to aggression. Our finding was consistent with reports linking aggression and suicidality,^{11–13} with the model of suicidal

behavior proposed by Conner and Duberstein,¹⁴ and with the stress-diathesis model of suicidal behavior.¹¹ Considerable evidence suggests that suicide attempters as a group are more aggressive than nonattempters.^{11–13} Chronic alcohol intake may lead to a state of lowered central serotonergic functioning characterized by a propensity toward disinhibited behavior, thus increasing the potential for aggressive behavior.^{15–19} The relationship between aggression and lower serotonergic function is also present in psychiatric patients who do not have a history of a suicide attempt.^{20–22} Given the evidence linking low serotonergic activity separately to suicidal behavior, aggression, and AUDs,^{12,16–19,23–27} low serotonergic activity may underlie all 3 conditions. Low serotonergic activity may mediate genetic and developmental effects on suicide, aggression, and AUDs. It is plausible that the causal substrates for suicidal behavior, aggression, and alcoholism involve a developmental sequence, or an interplay of predisposing factors.

In the current study, we include a substantially larger sample of patients with major depressive disorder (MDD), with or without co-occurring AUDs, and a larger number of clinical parameters and psychiatric history measures. The large sample size and a comprehensive evaluation of the subjects permit multivariate analysis. This was not possible in most studies reported in the literature in which the sample size and the number of variables were much smaller. Besides, the current study includes only subjects with MDD while our previous report included both patients with MDD and subjects with bipolar depression. We sought to expand and explore our previous finding that patients with co-occurring major depression and AUDs represent a unique patient population that is not only different clinically and neurobiologically from patients with major depression only, but also suffers from a more severe course of illness with earlier onset and greater morbidity and mortality.

METHOD

Subjects

Participants were recruited through advertising and referrals and participated in mood disorders research in an urban university hospital. All subjects gave written informed consent as required by the Institutional Review Board for Biomedical Research. In all, 505 individuals participated in the study, which was conducted from January 1990 to June 2005. Three hundred eighteen subjects ($N = 80$ males and $N = 238$ females) had MDD without a history of any alcohol or substance abuse/dependence (MDD only) and 187 individuals ($N = 71$ males and $N = 116$ females) had MDD and a history of alcohol abuse/dependence (MDD/AUD). Three hundred forty-eight of the subjects were included in our previous report. Since they were participating in biological studies, all

subjects were free from alcohol or substance abuse for at least 2 months. The duration of the drug-free status of the subjects was established by a combination of urine and blood toxicologic screenings, observation in hospital, and a history obtained from the participant, the participant's family, and the referring physician. All subjects were free of medical illness, based on history, physical examination, and laboratory tests including liver function tests, hematologic profile, thyroid function tests, urinalysis, and toxicology.

Measures

Psychiatric disorders including MDD and AUDs were diagnosed using the Structured Clinical Interview for DSM-IV.²⁸ All subjects had a physical examination and routine laboratory screening tests, including urine and blood toxicologic screenings to rule out neurologic or medical illness that could affect their mental status. Current severity of depression was assessed by the Hamilton Rating Scale for Depression (HAM-D)²⁹ and the Beck Depression Inventory.³⁰ Lifetime aggression and impulsivity were assessed with the Brown-Goodwin Lifetime History of Aggression Scale, revised,³¹ and the Barratt Impulsivity Scale,³² respectively. Hostility was rated with the Buss-Durkee Hostility Inventory.³³ Hopelessness during the previous week was measured with the Beck Hopelessness Scale.³⁴ A lifetime history of all suicide attempts, including number of attempts and the method of the attempt, was recorded on the Columbia Suicide History Form.³⁵ A suicide attempt was defined as a self-destructive act that was committed with some intent to end one's life. Additionally, the Beck Lethality Rating Scale³⁶ was used to measure the degree of medical damage caused by each suicide attempt. The scale was scored from 0 to 8 (0 = no medical damage, 8 = death), with different anchor points for various suicide attempt methods. The degree of suicide intent for the worst and most recent attempt was rated with the Suicide Intent Scale.³⁷ The Scale for Suicide Ideation³⁸ was used to measure the severity of suicidal ideation during the week prior to index hospitalization. Life events were scored on the St. Paul-Ramsey Life Events Scale.³⁵ Reasons for living were evaluated using the Reasons for Living Inventory.³⁹ Interviewers were master's or Ph.D.-level psychologists. Interrater reliability was good to excellent (intraclass correlation coefficient range, 0.71–0.97).

Statistical Analysis

Demographic data were compared using Student t test and χ^2 test, as appropriate. A general linear model compared clinical variables controlling for age and gender. The relationship between childhood aggression score subscales and AUDs was evaluated using multivariate regression analysis. To evaluate whether the larger number of major depressive episodes and the larger number of suicide attempts in the MDD/AUD group are related to the

Table 1. Demographic Characteristics of Depressed Subjects With and Without a History of Alcohol Use Disorders (AUDs)

Variable	Subjects Without a History of AUDs (N = 318) ^a	Subjects With a History of AUDs (N = 187) ^b	Analysis		
			df	t/χ ²	p
Age, mean ± SD, y	41.75 ± 14.24	37.96 ± 10.58	503	3.16	.002
Gender, male, N (%)	80 (25.2)	71 (38.0)	1	9.22	.002
Race, white, N (%)	231 (81.1)	139 (77.2)	1	0.99	.318
Marital status, married, N (%)	113 (35.8)	60 (32.3)	1	0.64	.425
Educational status, patients who completed at least some college, N (%)	214 (67.9)	113 (60.8)	1	2.66	.103

^aMDD only group.^bMDD/AUD group.

Abbreviation: MDD = major depressive disorder.

longer duration of illness, we used analysis of variance (ANOVA). The duration of illness was defined as the time interval between the onset of the first major depressive episode and the time of the enrollment into the study. We also used ANOVA to evaluate whether early onset of alcohol/drug abuse is related to aggression scale scores.

Using the list of variables that differentiated depressive subjects with AUDs from those without AUDs, we performed a backward stepwise logistic regression using the Wald test. The purpose of the analysis was to identify associations. The final model had 3 variables: number of previous depressive episodes, lifetime aggression, and smoking. SPSS program was used to perform statistical analysis (SPSS, Inc., Chicago, Ill.).

RESULTS

Demographic Characteristics

Demographic measures are presented in Table 1. There was a higher percentage of males in the MDD/AUD group compared to the MDD only group. MDD/AUD patients were younger at the time of entry to the study. There was no significant difference between the groups with regard to race, marital status, and level of education. Because of the differences in age and sex, we controlled for age and sex in the clinical comparisons.

Course of Illness

Clinical and psychiatric history measures are presented in Table 2. MDD/AUD patients had more previous major depressive episodes, were younger at the time of their first psychiatric hospitalization, and reported more suicide attempts compared to MDD only patients. The duration of illness was longer among MDD/AUD patients compared to their counterparts. MDD/AUD patients still had more previous major depressive episodes and more suicide attempts after controlling for the duration of illness ($F = 5.75$, $df = 1,453$; $p = .017$ and $F = 6.93$, $df = 1,460$; $p = .009$, respectively). The percentages of MDD/AUD patients who began drinking/using drugs before ages 13 and 18 were 8.6% and 48.8%, respectively.

Associated Clinical Features

MDD/AUD patients reported lower HAM-D and higher lifetime aggression, impulsivity, and hostility scale scores compared to MDD only patients (Table 2). MDD/AUD individuals also had higher childhood, adolescent, and adult aggression scores (Table 2) and more frequently reported behavioral problems during their childhood compared to their counterparts (Table 3). Among MDD/AUD individuals, those who began drinking/using drugs before age 18 had higher adolescent aggression scores compared to the subjects who started drinking/using drugs after age 18 ($F = 6.65$, $df = 1,113$; $p = .011$). Suicidal behavior measures are also presented in Table 2. MDD/AUD subjects were more likely to report past suicide attempts and were younger at the time of their first suicide attempt compared to the MDD only group.

Comorbidity

MDD/AUD patients were more likely to report tobacco smoking and were more likely to be moderate or heavy smokers compared to MDD only patients (Table 4).

Environmental Stressors

MDD/AUD patients were more likely to report a lifetime history of childhood abuse, a history of AUDs among first-degree relatives, and more recent life events compared to their counterparts (Table 4).

Logistic Regression Analysis

We entered the variables significant on bivariate tests in a backward, stepwise, multiple logistic regression analysis with lifetime AUD as the dependent variable. Stressful life event variable was not included due to missing data. The final model results are summarized in Table 5. More prior major depressive episodes, greater lifetime aggression, and smoking were each independently associated with a lifetime AUD history among depressed subjects, adjusting for all other variables in the model (data available on request). Each additional major depressive episode was associated with a nearly 10% increase in the odds of having a lifetime history of AUD. Each point of

Table 2. Measures of Course of Illness and Associated Clinical Features of Subjects With and Without a History of Alcohol Use Disorders (AUDs) (adjusted for age and gender)

Variable	Subjects Without a History of AUDs (N = 318) ^a	Subjects With a History of AUDs (N = 187) ^b	Analysis		
			df	F	p
Course of illness, mean ± SD					
Age at onset of first depressive episode	28.91 ± 15.16	24.64 ± 11.80	3,469	4.18	.041
No. of previous depressive episodes	3.98 ± 4.32	5.34 ± 6.40	3,463	10.33	.001
Age at first psychiatric hospitalization	35.90 ± 15.04	30.82 ± 11.71	3,342	6.04	.014
No. of psychiatric hospitalizations	1.91 ± 3.24	2.25 ± 3.62	3,429	2.06	.152
Duration of illness, y	12.74 ± 11.61	13.48 ± 11.55	3,466	4.19	.041
Associated clinical features, mean ± SD					
Hamilton Rating Scale for Depression score	17.88 ± 8.13	16.59 ± 7.49	3,499	3.97	.047
Beck Depression Inventory score	25.42 ± 12.16	25.09 ± 12.28	3,437	0.07	.791
Beck Hopelessness Scale score	11.29 ± 6.14	11.20 ± 6.12	3,440	0.04	.842
Barrat Impulsivity Scale score	49.44 ± 16.41	57.63 ± 17.76	3,403	21.44	< .001
Buss-Durkee Hostility Inventory score	33.10 ± 11.84	39.86 ± 12.26	3,418	26.46	< .001
Aggression history scale score					
Lifetime	16.18 ± 4.45	21.92 ± 6.20	3,445	119.13	< .001
Child ^c	12.50 ± 3.31	14.51 ± 4.91	2,340	19.76	< .001
Adolescent ^c	13.54 ± 3.71	18.34 ± 6.12	2,340	80.02	< .001
Adult ^c	14.34 ± 3.50	17.21 ± 4.95	2,310	34.47	< .001
Suicidality					
Suicide attempt status, attempts, N (%)	128 (40.5)	106 (56.7)	3,502	10.60	.001
Age at first suicide attempt (in attempts), mean ± SD	29.31 ± 14.39	24.82 ± 11.77	3,228	12.22	.001
No. of suicide attempts (in attempts), mean ± SD	0.87 ± 1.51	1.42 ± 1.91	3,497	11.07	.001
Reasons for Living Inventory score, mean ± SD	165.26 ± 47.87	158.39 ± 45.63	3,281	1.04	.307
Suicide Ideation Scale score, mean ± SD	6.49 ± 10.10	7.90 ± 11.67	3,291	0.42	.516
Suicide Intent Scale score, mean ± SD	16.31 ± 5.44	15.65 ± 5.49	3,213	2.58	.110
Maximum lethality of suicide attempts, mean ± SD	3.10 ± 2.15	3.37 ± 2.03	3,161	0.29	.588

^aMDD only group.^bMDD/AUD group.^cAdjusted for gender only.

Abbreviation: MDD = major depressive disorder.

Table 3. Brown-Goodwin Lifetime History of Aggression Scale Scores in Childhood of Subjects With and Without a History of Alcoholism (adjusted for gender)

Brown-Goodwin Lifetime History of Aggression Scale Items	Subjects Without a History of Alcoholism (N = 216), % ^a		Subjects With a History of Alcoholism (N = 127), % ^b		Analysis					
	Never/ Rarely	Occasionally/ Often	Never/ Rarely	Occasionally/ Often	df	Wald	p	Odds Ratio	95% CI	95% CI
Ever been a discipline problem in school	89.8	10.2	76.4	23.6	1	9.861	.002	2.708	1.454	5.042
Ever had severe arguments with family and friends	80.9	19.1	71.2	28.8	1	4.028	.045	1.699	1.013	2.849
Ever gotten into physical fights	84.1	15.9	74.6	25.4	1	4.361	.037	1.783	1.035	3.075
Ever destroyed someone's or own property	97.2	2.8	88.0	12.0	1	9.598	.002	4.677	1.762	12.41
Ever done things against the law and not gotten caught	98.6	1.4	84.3	15.7	1	16.606	< .001	13.077	3.797	45.03

^aMDD only group.^bMDD/AUD group.

Abbreviations: AUD = alcohol use disorder, MDD = major depressive disorder.

Table 4. Family History of Alcoholism, Comorbidity, and Environmental Stressors of Depressed Patients With and Without a History of Alcohol Use Disorders (AUDs) (adjusted for age and gender)

Variable	Subjects Without a History of AUDs (N = 318) ^a	Subjects With a History of AUDs (N = 187) ^b	Analysis		
			df	F	p
First-degree relatives with a history of AUDs, mean ± SD					
Comorbidity, N (%)	75.0 ± 25.7	217.0 ± 74.3	3,466	18.226	< .001
Prevalence of cigarette smokers	63 (21.4)	91 (49.7)	3,477	43.21	< .001
Prevalence of moderate and heavy cigarette smokers	36 (12.2)	59 (32.2)	3,477	37.40	< .001
Environmental stressors					
Prevalence of a lifetime history of childhood abuse, N (%)	124 (45.6)	91 (58.3)	3,427	8.55	.004
St. Paul-Ramsey Scale score (recent life events), mean ± SD	2.38 ± 0.79	2.74 ± 0.88	3,263	10.58	.001

^aMDD only group.^bMDD/AUD group.

Abbreviation: MDD = major depressive disorder.

Table 5. Final Model Summary of Backward, Stepwise, Multiple Logistic Regression Analysis of Lifetime Alcohol Use Disorder History in Subjects With Major Depressive Disorder (N = 326)

Independent Variable	Wald	Odds Ratio	95% CI	p
No. of previous depressive episodes	12.582	1.097	1.042 to 1.154	< .001
Aggression history scale	52.449	1.245	1.174 to 1.322	< .001
Cigarette smokers	11.362	2.783	1.535 to 5.047	.001

increase in lifetime aggression score was associated with an almost 25% increase in the odds of having a lifetime history of AUD. Being a smoker was associated with a nearly 3-fold increase in the odds for a lifetime history of AUD.

DISCUSSION

Depression is associated with increased risk for AUDs and vice versa.^{1,40–42} However, there is still sparse knowledge on what separates those who suffer from MDD/AUD from those who suffer from MDD only. We found that the comorbid group is distinct in a number of ways. Many of these differences have clear clinical implications.

Consistent with previous observations, we have demonstrated that MDD/AUD patients were younger at the time of entry to the study, their first psychiatric hospitalization, their first major depressive episode, and their first suicide attempt; reported more previous major depressive episodes, suicide attempts, and recent life events; had higher lifetime aggression, impulsivity, and hostility scale scores; and were more likely to report tobacco smoking, a lifetime history of abuse, and a history of AUD among first-degree relatives compared to MDD only patients. The larger number of major depressive episodes and the larger number of suicide attempts appeared not to be attributable to longer duration of illness among MDD/AUD subjects compared to their counterparts.

We believe that this is a first report that MDD/AUD individuals have higher childhood, adolescent, and adult aggression scores and report more behavioral problems during their childhood compared to MDD patients. These data also suggest that the number of previous depressive episodes, lifetime aggression, and smoking drive the difference between the groups.

Demographic and Background Characteristics

In our study, young age was associated with an elevated rate of comorbid AUD, and there was a higher prevalence of males in the MDD/AUD group compared to their counterparts. These findings are consistent with research reports showing that AUDs are more common in men and in younger age groups.^{43,44} For example, in a study of the 12-month prevalence and trends in DSM-IV

alcohol abuse and dependence in the United States, AUDs were more common among males and among younger respondents.⁴³

Course of Illness

We found that comorbid subjects had more major depressive episodes and were younger at the time of their first psychiatric hospitalization, their first major depressive episode, and their first suicide attempt compared to MDD only subjects. The number of previous depressive episodes is 1 of 3 measures that drive the difference between the 2 groups. Our findings are consistent with results from other studies suggesting that subjects with co-occurring depression and AUDs may have more chronic impairment than individuals who suffer from either of the disorders alone.^{9,45–47} It has also been shown that alcohol dependent subjects with prior depressive episodes or suicidal behavior differ from subjects without such comorbid problems.^{46,48} Depressed alcoholic patients, compared with never-depressed alcoholic patients, had a higher daily alcohol intake, and more had attempted suicide and reported alcoholism in both parents.⁴⁶

The fact that MDD/AUD subjects were younger at the time of their first depressive episode, their first hospitalization, and their first suicide attempt; were more aggressive during their childhood and adolescent years; and more frequently had behavioral problems during their childhood compared to their counterparts suggests that comorbid subjects may have inherited or acquired (e.g., as a result of childhood abuse) neurobiological abnormalities that contribute to their morbidity. Indeed, twin and adoption studies suggest that 50% to 60% of risk to develop alcohol dependence is due to heritable factors, and linkage and association studies have identified chromosomal regions and individual genes that most likely contribute to the development of this condition.^{49–51} In a previous study, we have shown that MDD/AUD subjects had lower cerebrospinal fluid (CSF) homovanillic acid (HVA) levels compared with MDD only subjects.⁴⁷ An earlier study reported that depressed subjects with alcoholism had significantly lower concentrations of HVA than never-depressed subjects with alcoholism.⁴⁶ Low CSF HVA may have more to do with psychopathology related to alcoholism as opposed to mood disorder biology.⁴⁷ In another study, we found an anterior medial prefrontal cortical area where MDD/AUD subjects had more severe hypofrontality compared to MDD only patients.²⁶ This group difference disappeared after fenfluramine administration. The fact that the observed group difference disappeared after the fenfluramine challenge suggests that serotonergic mechanisms play a role in the observed differences between the groups. Many behaviors and emotional mechanisms that participate in inducing alcohol abuse are known to be critically dependent on the prefrontal cortical areas.^{52,53} This means that prefrontal cortex

abnormalities could be present in individuals with AUD before they start drinking. Although it is possible that some individuals begin drinking before age 13 and their behavioral problems are related to alcohol use, this is not very likely, because in our MDD/AUD sample only 8.6% of subjects began drinking/using drugs before age 13.

The observation that MDD/AUD subjects had more major depressive episodes compared to their counterparts suggests that therapeutic interventions targeting both depression and alcohol misuse may help reduce morbidity in the MDD/AUD group. Early interventions with alcohol abusing adolescents who experienced childhood abuse and/or grew up with a family member suffering from AUD may also be important to reduce morbidity.

Associated Clinical Features

Our study demonstrates that MDD/AUD subjects exhibit more suicidal behavior compared to MDD only subjects. Considerable evidence suggests that suicide is associated with both depression and AUDs.^{9,11,54,55} Studies have shown that suicidal behavior is very common among subjects with co-occurring depression and AUDs,^{45,56} and that AUDs predict suicidal behavior even after controlling for sociodemographic factors and co-occurring mental disorders.^{57,58} The mechanisms underlying this relationship are still debated. Some argue that alcohol use affects suicidality by increasing the likelihood of acting on suicidal ideation,⁴⁵ while others, after controlling for major depression, have found that alcohol use is associated with suicidal thoughts.⁵⁴

Our results can also be compared to those of Preuss et al.^{48,56} In a large sample of alcohol dependent subjects, they found a number of differences between those who had attempted suicide and those who had not. Differences included a number of socioeconomic variables, as well as earlier onset of AUDs and more problems related to drinking, drug use, and psychiatric status in the suicidal group. This included a higher risk of lifetime depression among suicide attempters, which independently was associated with suicide risk.

Based on a comprehensive review of the literature, Conner and Duberstein¹⁴ proposed a model to explain the elevated risk of suicide among alcohol dependent subjects. This model includes aggression/impulsivity, severe alcoholism, negative affect, and hopelessness as key predisposing factors and major depressive episodes and stressful life events, particularly interpersonal difficulties, as key precipitating factors for suicide. In light of this, the higher rate of previous suicide attempts among MDD/AUD subjects is possibly explained by the higher level of predisposing and precipitating factors in this group compared to the MDD only group.

Our observation that MDD/AUD subjects have higher lifetime impulsivity scores than MDD only subjects is consistent with reports that, apart from its role in suicidal

behavior, impulsivity is an important risk factor for the development of alcoholism.⁵⁹ We also found that aggression is a measure that drives the difference between the 2 groups, and that subjects with alcohol dependence were more aggressive during their childhood and adolescent years compared to the subjects who did not develop alcohol dependence. This suggests that impulsive-aggressive individuals are at elevated risk for the development of alcohol dependence. This also suggests that aggression is not merely a sequelae of intoxication or the secondary neurobiological consequences of intoxication.

Two causal links between impulsive aggression and AUD have been proposed: (1) individuals who develop AUDs possess higher premorbid levels of impulsive-aggression than those who do not develop AUDs, and (2) impulsive-aggression differentiates both populations, because it develops as a consequence of alcoholism.⁶⁰ The results of our study support the first suggestion.

Zucker et al.⁶¹ suggested that the prospective relation between childhood impulsivity and later alcohol problems marks an etiologic process whereby these traits lead to poor school performance and relational problems. These troubles in turn may lead such individuals to associate with similar peers who are likely to begin using alcohol and other drugs early in adolescence. This theory is consistent with our observation that the odds of developing AUDs are much higher among children who had behavioral problems.

We observed that there was no significant difference in maximum lethality of suicide attempts between the 2 groups. This supports the notion that the occurrence of a suicide attempt, and not the lethality of suicidal acts, is related to impulsive aggression.¹²

Comorbidity

Our findings that smoking is a factor that drives the difference between the MDD only and MDD/AUD groups and that MDD/AUD subjects are more likely to report tobacco smoking and more likely to be moderate or heavy smokers compared to their counterparts are consistent with multiple reports suggesting that there is a strong association between alcohol misuse and cigarette smoking.⁶²⁻⁶⁴ Approximately 80% of alcohol-dependent patients are reported to smoke cigarettes.^{62,63} Cigarette use is a predictor of unrecognized AUD.⁶⁵ The prevalence of smoking among substance abusers is approximately 2 to 3 times that of the general population.⁶² Alcoholism is estimated to be 10 times more common among smokers than among nonsmokers.⁶⁶

Smoking is an important predictor of suicidal behavior.⁶⁷ Being a cigarette smoker increases the risk of eventual suicidal acts by more than 2-fold.⁶⁷ A prospective study of army recruits also showed that those who committed suicide were twice as likely to be smokers (82%), compared with recruits who died from accidents (40%) or

comparison subjects (40%).⁶⁸ The effect of smoking on suicidal behavior may be mediated through pharmacologically induced disinhibition or depletion of monoamines, or it may be due to a common diathesis or to an association with relevant psychopathology such as aggression/impulsivity. Perhaps some of the predictive power of cigarette smoking stems from its association with these other risk factors. Indeed, cigarette smokers have been found to have lower serotonergic functioning than nonsmokers²³ and more aggressive/impulsive traits.^{69,70}

Additionally, concomitant AUDs and cigarette smoking have a major impact on the development of medical diseases. For example, simultaneous use of tobacco and alcohol contributes to an increased incidence of several malignancies, especially head and neck cancers.^{71,72} Given the prevalence of smoking in individuals with AUDs, programs that target smoking cessation in this group have the potential for significant impact on public health.

Environmental Stressors

A history of abuse is an independent risk factor for both AUDs⁷³ and major depression.⁷⁴ In a longitudinal study of a nonclinical sample, Johnson and Pandina⁷⁵ found that hostility and a lack of warmth were some of the family characteristics associated with higher levels of alcohol and drug use. Individuals in treatment for alcohol abuse are more likely than those in the general population to be victims of sexual abuse and physical violence.⁷⁶ One prospective study found that a history of trauma or maltreatment predicted a lower rate of remission from major depression over a 5-year period.⁷⁷ In light of this, it seems reasonable that we found a higher rate of previous abuse in the comorbid group.

Strengths and Limitations

There were several strengths to this study. The study includes a large sample that is well characterized using state-of-the-art instruments. The large sample size permits multivariate analyses, something not possible with smaller studies in the literature.

There are important clinical implications to our findings. Many subjects in the MDD/AUD group had a history of suicide attempts. A history of suicide attempt has been found to increase the likelihood of a future attempt as much as 4 times.^{67,78} MDD/AUD subjects have multiple risk factors for suicidal behavior in much greater proportions than MDD only patients. It is impressive that many powerful risk factors described in the literature are elevated in the MDD/AUD group compared to the other group. Given the substantially elevated risk of suicidal behavior among these MDD/AUD subjects, this group needs to be closely monitored, and they require more intense management.

Limitations also need to be addressed. A significant limitation of our study is that AUDs are treated as a cat-

egorical variable (yes/no). Future studies should include assessment of the characteristics of AUD patients that may modulate the disorder and treatment response, such as family support for recovery, living with an alcoholic partner, severity of dependence, etc. Due to the correlational design of our study, we are not able to address the question of causality. Participants were recruited in an urban area. Only patients who voluntarily agreed to participate in the studies and had a capacity to sign informed consents were recruited. Therefore, the results of this study may not be generalizable to all depressed patients.

CONCLUSION

MDD/AUD individuals demonstrate significantly higher morbidity and higher rates of co-occurring pathology compared to MDD only subjects. Most likely, MDD/AUD subjects were impaired before they developed AUD, because they had behavioral problems before age 13 more frequently than those individuals who did not develop AUD. Additionally, MDD/AUD subjects were younger when they developed MDD and when they needed inpatient treatment.

MDD patients with co-occurring AUDs report more suicidal behavior than MDD patients without co-occurring AUDs. This increased suicidality may be related to higher aggression, impulsivity, and hostility in the MDD/AUD group, which is consistent with the stress-diathesis model of suicidal behavior. Chronic alcohol intake may lead to a state of lowered central serotonergic functioning characterized by a propensity toward disinhibited behavior, thus increasing the potential for aggressive, impulsive, and hostile behavior.

Our findings suggest that in addition to obtaining a history of depression and suicidal behavior, clinicians should assess comorbidity with AUDs and personality traits such as aggression and impulsivity. This may help identify patients at higher risk for suicidal behavior. Our findings also suggest that MDD/AUD patients represent a unique patient population that may need to be studied separately in order to reduce morbidity and mortality in individuals with co-occurring major depression and AUDs.

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