Pretreatment Clinical and Risk Correlates of Substance Use Disorder Patients With Primary Depression*

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ABSTRACT. Objective: The current study examined the distinction between primary and secondary depression among substance use patients to test whether the primary depressed subgroup presents to treatment with a unique profile of clinical and vulnerability characteristics. **Method:** The heterogeneous sample comprised 286 individuals (76% male) with alcohol and/or drug abuse or dependence (according to criteria from the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised) across four treatment outcome studies conducted at the alcohol research center at the Rutgers University Center of Alcohol Studies. Participants were classified as having comorbid lifetime history of primary depression (21%), secondary depression (24%), or no depression (55%). **Results:** Participants in the primary depression and secondary depression groups were comparable in severity of substance use, and both of these groups had more severe substance use problems than the no-depression group. The primary depression group presented with more severe depression histories, higher levels of current depressive

symptoms, and higher rates of additional Axis I comorbidity at treatment entry. In terms of vulnerability indices, the primary depression subgroup had a uniquely high family history risk for major depressive disorder; underlying personality vulnerability to depression was also evident in the primary depression group, with higher neuroticism and lower extraversion relative to secondary depression patients. **Conclusions:** The findings suggest that careful assessment of lifetime depression symptoms vis-à-vis substance use history and severity yields important information identifying the primary depression subtype of substance use patients as a group with a unique and more severely affected clinical presentation of depression and other Axis I psychopathology relative to secondary depression patients. Effectiveness of substance use interventions may be augmented with depression treatment for primary depression patients, given their more severe clinical presentation and vulnerability characteristics. (*J. Stud. Alcohol Drugs*, 72, 151-157, 2011)

DEPRESSIVE DISORDERS ARE HIGHLY comorbid with drug and alcohol use disorders (i.e., substance use disorders [SUDs]; Grant, 1995; Grant and Hartford, 1995; Grant et al., 1996; Substance Abuse and Mental Health Services Administration, 2008). This comprises a major public health concern, given that a considerable percentage of individuals who receive a combination of depression and substance use interventions do not respond successfully (Nunes and Levin, 2004). Heterogeneity among individuals with comorbid SUDs and depression may contribute to this uneven response. Research using both community and treatment-seeking samples of substance users has focused on distinguishing between those with “primary” and “secondary” depression on a variety of concurrent and predictive

indices (Epstein et al., 2010; Nunes and Levin, 2004, 2006; Ramsey et al., 2004; Schuckit et al., 2007) to unravel the role of diagnostic variability on treatment planning and response in substance users with comorbid depression.

In population-based samples, unique features of an SUD and primary (vs. secondary) depression include female gender, lower socioeconomic status, single marital status, and treatment seeking for depression (Gilman and Abraham, 2001; Grant et al., 1996; Hanna and Grant, 1997; Kasperowicz-Dabrowiecka and Rybakowski, 2001). In a large ($N = 2,110$) sample combining non-treatment-seeking ($n = 1,756$) and treatment-seeking ($n = 354$) alcohol- or drug-dependent individuals, Schuckit et al. (1997, 2007) found the same gender difference as reported for community samples, little difference between primary and secondary depression groups regarding history of depressive symptoms, less severe alcohol use patterns, and greater familial risk of major depressive disorder (MDD) among those classified with primary depression.

Although the studies using community and non-treatment-seeking samples in general support a distinction between clinical symptoms of primary and secondary depression, few treatment-seeking samples have been studied to assess the primary/secondary depression distinction in terms of pretreatment clinical symptoms, clinical history profile, and vulnerability risk factors. One exception is the study by Kahler et al. (2002), who found no differences in

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current depressive or alcohol use symptoms between “substance-induced MDD” and primary MDD at baseline but did find that participants with primary MDD scored higher on dysfunctional (i.e., depressogenic) attitudes (i.e., thoughts) and lower on “antidepressive coping.” Other studies using clinical samples focus mostly on differences in treatment response among individuals with alcohol and/or drug use disorders classified with either primary or secondary depression at baseline (see Hasin et al., 2002; Helzer and Pryzbeck, 1988; Nunes and Levin, 2006).

Personality variables may also have important implications for the presentation and treatment of individuals with comorbid alcohol problems and MDD (Costa et al., 2005; Quilty et al., 2008). High neuroticism coupled with low conscientiousness and agreeableness are robustly indicative of substance use problems (Hopwood et al., 2007; Malouff et al., 2005), emotional difficulties and psychiatric diagnosis (Morey et al., 2002), and symptoms and risk for MDD (Costa et al., 2005). Thus, as the clinical presentation of primary depression has been shown to be the most severe of the depression subtypes (Schuckit et al., 1997, 2007), we would expect a more maladaptive personality constellation in individuals with primary depression. To our knowledge, no study has examined differences on these personality dimensions among primary and secondary depression subtypes in a clinical treatment-seeking sample.

The current study examined the distinction between primary and secondary depression in SUD patients at treatment entry based on clinical profile (i.e., current and lifetime substance use, depression symptoms, and other Axis I problems), as well as robust risk factors such as family history of depression and an alcohol use disorder and underlying personality vulnerability indicators that have been associated with independent depression and substance use behavior (Costa et al., 2005; Malouff et al., 2005). Because many alcohol- or drug-dependent patients do have comorbid depressive disorders that could be independent of, or secondary to, their SUD, treatment efforts may be complicated if underlying symptom and risk correlates are not well delineated. The identification of a unique, multidimensional set of diagnostic and vulnerability risk factors in substance users with primary depressive disorders should aid in more effective treatment planning targeted toward the specific clinical profile of this subtype.

Method

Participants

The sample of 286 patients (76% male) who met lifetime or current (prior 6 months) alcohol abuse or dependence diagnostic criteria (according to the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised [DSM-III-R]; American Psychiatric Association, 1987) with

or without a non-alcohol/drug use diagnosis ($n = 263$, 92%) or met criteria for current or lifetime nonalcohol drug use disorder only ($n = 23$, 8.0%) was drawn from a larger study of 418 consented participants in four treatment outcome studies conducted through the alcohol research center at the Rutgers University Center of Alcohol Studies (see Epstein et al., 2002, for more complete description). Participants missing data relevant for the current study ($n = 105$) or who had no diagnosable SUD ($n = 9$) were excluded, as were 18 participants who could not be classified conclusively as primary versus secondary depressive disorder.

Average age of participants was 40 years ($SD = 13.89$); 93 (32.5%) were married, 97 (33.9%) were separated or divorced, 8 (2.8%) were widowed, and 84 (29.4%) were single. Data were missing for four participants for the marital status variable. One hundred twenty-nine (45%) worked full or part time, and 100 (38%) were unemployed or disabled, 4 (1.4%) were students, and 22 (7%) were retired. Twenty-two individuals (7%) had missing data for the employment status variable. Most attained a high school ($n = 87$, 30.4%) or college ($n = 113$, 39.5%) degree; 45 (15.7%) completed some high school, and 40 (13.9%) attained graduate education. One person was missing data for education. One hundred seventy-eight (62%) were White, 89 (31.1%) were Black, 12 (4.2%) were Hispanic, and 5 (1.7%) were “other.” Two individuals had missing data for the race/ethnicity variable. Treatment sites included three inpatient rehabilitation programs ($n = 174$, 61.0%), an ambulatory medical clinic ($n = 24$; 8.4%), an intensive outpatient program for older adults ($n = 29$, 10.1%), and an inpatient Veterans Affairs (VA) program ($n = 59$, 20.6%).

Measures

The Structured Clinical Interview for DSM-III-R (SCID; First et al., 1995; Spitzer et al., 1990; Williams et al., 1992) yielded lifetime and current diagnoses for SUDs and Axis I disorders. Sections were modified to obtain age at onset for each SUD symptom and the temporal history of depression episodes and/or dysthymia with respect to alcohol and drug use. Interviews were audio-taped, and 10% were coded by a second interviewer (κ for diagnoses = .87).

The Timeline Followback interview (Sobell and Sobell, 1996) yielded percentage drinking days, mean drinks per drinking day, and percentage days abstinent from alcohol or drugs in either the 3 months ($n = 107$) or 6 months ($n = 179$) before baseline.

The Rutgers Consequences of Use questionnaire (Rhines et al., 1997) measured alcohol and drug consequences in the 6 months before baseline, on a frequency scale of 0-4.

The Michigan Alcoholism Screening Test–brief version (Pokorny et al., 1972; Selzer, 1971) measured lifetime severity of alcoholism.

The Structured Treatment History Interview was specifi-

cally created for the assessment battery to assess frequency, type, and duration of inpatient and outpatient treatment episodes for alcohol and drug problems (see Table 2).

The NEO Personality Inventory-Revised (NEO-PI-R; Costa and McCrae, 1992) assessed the personality traits of neuroticism, extraversion, openness, agreeableness, and conscientiousness. It has high test-retest reliability and internal consistency across domains (Costa and McCrae, 1992).

The Family History-Research Diagnostic Criteria (Andreason et al., 1977, 1986) interview yielded percentage of first- and second-degree relatives with an alcohol use disorder and MDD. This interview demonstrates good psychometric properties for alcohol and depression (Cuijpers and Smit, 2001; Ptak et al., 2001).

Procedure

Participants were recruited, provided consent, and completed the baseline assessment at their respective treatment sites. Interviewers met weekly with the second author (E.E.E.) to review diagnoses. Participants were followed up at 6 and 12 months after baseline (see Epstein et al., 2002). The present study focuses on pretreatment variables.

Primary and secondary depression classification

We used the current standard for distinguishing between depression subtypes, which is based on temporal patterning of diagnoses and substance use behavior (see Schuckit et al., 1997, 2007). Primary depression ($n = 60$, 21%) was defined as current or past depressive episode that met MDD or dysthymia criteria that occurred independent of an SUD, either preceding the onset of an SUD or occurring after at least a 6-month period of abstinence. Secondary depression ($n = 68$, 23.8%) was defined as current or past depressive episode that met MDD or dysthymia criteria that occurred after onset of an SUD or within a 3-month window of heavy alcohol or drug use. No depression ($n = 158$, 55%) was defined as no history of MDD or dysthymia. Excluded from analyses were individuals whose classification was inconclusive based on having no history of primary depression and current or past MDD or dysthymia that occurred during nonproblematic substance use (fewer than three times per week) or after a 3-month period of abstinence.

Data analysis

Separate univariate analyses of variance (ANOVAs) were used to examine differences among subtypes on drug-related indices with a Bonferroni correction of $p < .01$. We did not use multivariate analysis of variance (MANOVA) because listwise deletions substantially reduced baseline sample size (the alcohol-only subsample had missing values for drug use variables) and because baseline variables were intercor-

related below the level at which MANOVA is recommended (Keppel and Wickens, 2004). Significant omnibus ANOVA results ($p < .01$) were followed with Tukey's least significant difference post hoc procedure for planned comparisons. Significance levels of $p < .05$ are noted for descriptive purposes and are considered significant at a trend level given our Bonferroni correction; however, only p values $< .01$ are interpreted as significant.

Results

Treatment site and demographics

Treatment site and demographic variables were compared across the depression subtypes for descriptive purposes, with site differences, $\chi^2(12) = 26.44$, $p < .01$, showing a greater proportion of no-depression patients in traditional rehabilitation programs than in the VA (51% vs. 27%), and approximately equal percentages of primary depression patients (48% for traditional rehabilitation programs and 40% for VA) and secondary depression patients (40% for traditional rehabilitation programs and 46% for VA) in these two sites. The no-depression group was most likely to be employed, $\chi^2(14) = 18.05$, $p < .01$, and the secondary depression group was most likely to be unemployed. The primary depression, secondary depression, and no-depression subtypes did not differ significantly by gender, age, relationship status, education, or ethnicity. Among the subset of participants who had some form of depression, the difference in gender remained nonsignificant (61.3% of women had primary depression and 38.7% had secondary depression, whereas 42.3% of men had primary depression and 57.7% had secondary depression), $\chi^2(1) = 3.41$, $p = .065$, as did other demographic variables.

Alcohol and drug use history, severity, and treatment

Table 1 shows results of ANOVAs and chi-square tests of differences among the three depression subtypes for pretreatment and lifetime alcohol and substance use variables. The primary depression and secondary depression groups were similar to one another, and both were more severe on all alcohol and drug use history and current use indices compared with the no-depression group.

Depression history, severity, and DSM symptoms

Table 2 shows results of ANOVAs and chi-square tests of differences between primary depression and secondary depression subtypes for depression history, severity, and DSM symptoms of depression and/or dysthymia. Compared with the secondary depression group, the primary depression group was more likely to have sought mental health treatment for depression, reported more time feeling depressed since age 18, had a longer course (in weeks) of depressive

TABLE 1. History and severity of alcohol and drug use

Characteristic	Primary depression <i>M (SD)</i>	Secondary depression <i>M (SD)</i>	No depression <i>M (SD)</i>	ANOVA	
				<i>df</i>	<i>F</i>
Age at onset of AUD diagnosis	22.82 (8.83)	22.18 (11.10)	25.70 (13.87)	2, 256	2.23
Percentage drinking days past 3 months	52.74 (37.57)	63.78 (34.62)	50.82 (36.38)	2, 285	3.12*
Mean drinks/drinking day past 3 months	17.17 (14.91)	17.71 (17.30)	12.83 (11.40)	2, 266	3.74*
Brief MAST	18.06 (8.30) ^a	20.16 (7.44) ^a	15.78 (8.06) ^b	2, 252	6.87**
Number AUD treatment episodes	3.25 (2.83)	3.25 (2.51)	2.53 (2.49)	2, 285	2.75
Number drug classes used past 6 months	0.97 (1.03)	0.97 (1.02)	0.77 (0.98)	2, 285	1.29
Number times used drugs past 6 months	44.00 (48.04)	62.26 (46.69)	53.41 (51.38)	2, 144	1.24
Alcohol use consequences past 6 months	1.61 (0.11) ^a	1.62 (0.11) ^a	1.13 (0.07) ^b	2, 275	10.64**
Drug use consequences past 6 months	1.48 (0.15)	1.59 (0.14)	1.14 (0.10)	2, 182	3.85*

Notes: ANOVA = analysis of variance; AUD = alcohol use disorder; MAST = Michigan Alcoholism Screening Test. Means in a row with different superscripts are significantly different at $p < .01$.

* $p < .05$; ** $p < .01$.

episodes, and had more total lifetime symptoms of depression or dysthymia. The primary depression group endorsed more DSM symptoms of depression (diminished pleasure/interest, self-worth/self-esteem/guilt, impaired concentration/decision making) and two more at a trend level of $p < .05$ (depressed mood/sad, sleep disturbance).

Axis I psychiatric comorbidity and risk factors

Chi-square tests revealed that, compared with the secondary depression and no-depression groups, primary depression individuals were more likely to have a third Axis I disorder (in addition to MDD and SUD), $\chi^2(2) = 13.95$, $p < .01$ (28% for primary depression vs. 10.3% for secondary depression vs. 9.5% for no depression). We could not determine differences among depression subtypes across each Axis I disorder because sample sizes were too small.

ANOVA tests were used to compare the three subtypes on risk factors of family history and personality. Those with primary depression, compared with the secondary depression and no-depression groups, had a higher percentage of relatives affected with MDD, $F(2, 233) = 6.15$, $p < .01$ (20% for primary depression vs. 7% for secondary depression and 10% for no depression), and, at a trend level, the primary depression group had a higher percentage of relatives affected with an alcohol use disorder compared with the no-depression group (35% vs. 24%) but was not different from the secondary depression group (29%), $F(2, 266) = 3.92$, $p < .05$. Compared with the secondary depression and no-depression groups, primary depression individuals were also lower on extraversion ($M_{PD} = 45.13$ vs. $M_{SD} = 47.11$ and $M_{ND} = 53.39$), $F(2, 238) = 10.92$, $p < .01$, and higher on neuroticism ($M_{PD} = 68.19$ vs. $M_{SD} = 63.13$ vs. $M_{ND} = 56.66$), $F(2, 238) = 23.75$, $p < .01$. Primary depression and

TABLE 2. Clinical presentation of depression history and lifetime DSM-III-R symptoms of depression and dysthymia ($n = 128$)

Variable	Frequency (column %) or <i>M (SD)</i>		χ^2 or <i>F</i>	
	Primary depression	Secondary depression	<i>df</i>	χ^2/F
Earliest age outpatient treatment	27.23 (10.95)	34.69 (14.37)	1, 45	3.95*
% Received inpatient depression treatment	13.00 (22%)	07.00 (10%)	1, 127	3.28
% Ever seen mental health specialist	38.00 (63%)	19.00 (28%)	1, 127	16.16**
Average course of depression, in weeks	30.56 (33.32)	14.54 (18.42)	1, 94	7.69**
% Time depressed since age 18 ^a	03.71 (01.20)	03.05 (01.41)	1, 123	7.80**
Number DSM symptoms of MDD or dysthymia	10.85 (03.45)	08.31 (03.13)	1, 126	18.89**
Depressed mood	51 (88%)	48 (74%)	1, 123	3.87*
Diminished interest/pleasure	57 (97%)	49 (75%)	1, 124	11.23**
Change in appetite/weight	37 (64%)	36 (56%)	1, 122	0.72
Insomnia/hypersomnia	47 (81%)	41 (65%)	1, 122	3.88*
Psychomotor agitation/retardation	41 (70%)	35 (55%)	1, 123	2.85
Fatigue	43 (74%)	40 (62%)	1, 123	2.22
Self-worth/self-esteem/guilt	49 (83%)	38 (59%)	1, 124	8.93**
Impaired concentration/decision making	50 (85%)	40 (62%)	1, 124	8.37**
Suicide idea/plan/attempt	35 (59%)	30 (46%)	1, 124	2.15

Notes: DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised; MDD = major depressive disorder. ^aScale score of 4 = about half the time; scale score of 3 = minimum of time.

* $p < .05$; ** $p < .01$.

secondary depression groups were not different from each other and were both lower than the no-depression group on conscientiousness ($M_{PD} = 34.67$ and $M_{SD} = 38.38$ vs. $M_{ND} = 42.08$), $F(2, 238) = 7.57, p < .01$.

Discussion

This study examined the concurrent validity of a distinction between primary and secondary depression on a set of clinical and vulnerability variables in a heterogeneous, treatment-seeking sample of individuals with an SUD. In general, results suggest that treatment-seeking individuals with depression that is primary to an SUD are unique relative to both nondepressed and secondary depressed patients, in that primary depression individuals had more severe and disruptive depression as evidenced by greater number of symptoms and longer time spent depressed, greater Axis I comorbidity, higher levels of family risk for MDD, and lower extraversion and higher neuroticism. Of note, the unique aspects of primary depression emerged as a result of an in-depth assessment of temporal patterns of depression vis-à-vis substance use problems, of lifetime severity and pattern of depression indicators, and of variables related to underlying risk factors.

A unique family history risk and personality vulnerability profile of the primary depression individuals was also evident. Although the primary depression and secondary depression groups were similar in their family risk for alcohol use disorder (and both groups were higher than the no-depression group), the primary depression group had the greatest family risk for MDD. This finding supports the possibility of a unique etiological pathway of the primary depression group to substance use problems that is different from the secondary depression group. Further, and as expected, greater underlying personality pathology of the primary depression group (higher neuroticism and lower extraversion) than both the secondary depression and no-depression groups may represent a precursor to development of a particularly virulent form of depression that leads to later drug and alcohol use problems in individuals who have a family risk for alcohol use disorders and MDD. Longitudinal studies would be necessary to explore this further. Because some personality constructs, such as neuroticism, are thought to be fairly stable across the life span (Costa and McCrae, 1997) and can indicate risk for psychopathology (Harkness et al., 2002; Sen et al., 2003), results from this study have implications for early identification and targeted prevention efforts for primary depression *before* substance use problems develop.

In this clinical sample, of which 82% were inpatients, primary depression and secondary depression groups did not differ on drinking and drug use severity. This finding is in contrast to studies of primarily non-treatment-seeking samples showing greater substance use severity among

secondary depression individuals (Grant et al., 1996; Schuckit et al., 2007). It may be that severity is similar and less variable across groups at the higher end of substance use severity associated with entry into treatment (Tucker, 2003). However, Table 2 illustrates that the primary depression group suffered from a more severe and disruptive set of depression indicators and symptom pattern—including more treatment, longer course of depressive episodes, and more symptoms overall—and a greater likelihood to endorse several particular symptoms of MDD. This suggests that the primary depression individuals may indeed need their own unique treatment targeted toward depression symptoms, in addition to their SUD.

Strengths of the current study include a demographically and diagnostically heterogeneous sample; the use of a treatment-seeking sample of individuals with alcohol and/or drug diagnoses; and rigorous methodology for classification of primary, secondary, or no-depression groups (Schuckit et al., 2007). In addition, this study, like that of Kahler et al. (2002), goes beyond symptom counts to examine less observable correlates of the primary depressed group. Taken together, results support the potential value of the primary and secondary depression distinction in a treatment-seeking population, which requires a temporal patterning approach to assessment of both current and lifetime symptoms, because the distinction between primary and secondary depression is not obvious when it is based simply on the assessment of symptoms of an MDD diagnosis at baseline (Nunes and Levin, 2004; Schuckit et al., 2007).

Limitations of the current study include the reliance on retrospective reports to diagnose whether depression was primary or secondary to the onset of an alcohol use disorder. Depression subtypes were not equally distributed across treatment sites; site should be entered as a covariate in subsequent treatment outcome analyses. In contrast to other studies on mostly nonpatient samples (Grant et al., 1996; Hanna and Grant, 1997; Schuckit et al., 1997, 2007), gender did not emerge as a risk factor for primary depression in the current study, and sample size may have been a factor. Women were more likely than men to present with primary than secondary depression at a p level of .065, a finding that is not interpretable because of Bonferroni correction. Last, the effect of depression subtype on treatment outcome is not addressed in the current study. Subsequent research should examine heterogeneity among treatment-seeking substance users and link depression subtypes with treatment response.

In summary, results suggest that individuals with primary depression at entry to treatment for an SUD do not differ in basic substance use severity from patients with secondary depression but appear to have a more pathological clinical presentation than both secondary depression and no-depression subtypes in terms of depression history and severity, other psychiatric comorbidity, and vulnerability factors (family history and personality profile) that becomes apparent

only when we “scratch the clinical surface” and examine lifetime clinical correlates. Treatment implications include a need to use a lifetime assessment approach to the diagnosis of SUDs and comorbid MDD in order to identify patients with depression that is primary to their SUD and then to consider administration of auxiliary depression interventions (either psychosocial and/or pharmacological) for this particular subgroup. Future studies should examine causal pathways that differentially link early affect and personality vulnerability to later SUD and MDD among individuals at risk for both disorders and should investigate symptom change throughout the course of treatment to determine specificity of tailored interventions.

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