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*Original Article*

# Cocaine Abuse in 448 Alcoholics: Evidence for a Bipolar Connection

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## Abstract

**Background:**
**Several studies indicate a specific relationship between bipolar disorder and stimulant use and abuse. It has generally been assumed that cocaine use represents self-enhancement or attempts to optimize one's level of hypomania, cyclothymia, or hyperthymia. This topic required further examination among alcoholics because cocaine abuse is commonly comorbid with alcoholism.**

**Methods:**
**Cocaine abuse by bipolar participants was investigated in a group of 448 consecutive treatment-seeking alcoholics. We collected data with (1) the Drug Addiction History Rating Scale; and (2) the semi-structured interview for depression that inquires systematically among others, about hypomania, cyclothymia, hyperthymia, and depressive temperament. Participants were aged 44 ± 9 years, and were predominantly male (75.4%).**

**Results:**
**Univariate and multivariate analyses provided correlations in favor of a link between current cocaine abuse and bipolar spectrum ($P<0.01$).**

**Limitation:**
**The modality of access to cocaine in different communities and the difficulty to distinguish cocaine use from abuse and dependence may have limited the interpretation of results. Blindness to the chronologic sequence of alcohol and cocaine use is also a major limitation.**

**Conclusions:**
**It can be hypothesized that cocaine use is an attempt to maintain a baseline level of mood elation similar to a hyperthymic temperament or hypomanic state. Alcohol use, especially in youngsters, may be an instrument to cope with chronic dysphoria corresponding to an affective temperament. The attempt to induce and maintain hypomania by cocaine use would lead to full-blown bipolar disorders. In this context, alcohol use may favor the engagement into cocaine use by cyclothymics owing to its sedating effect, but would eventually become a further prodysphoric factor.**

**Key Words: alcoholism, cocaine, affective temperaments, bipolar disorders, bipolar spectrum**

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## BACKGROUND

Polydrug abuse associated with alcohol consumption is a relevant problem, especially among the majority of adolescent drinkers.[1–3]

Alcohol and cocaine are frequently used in combination[4,5] both in clinical samples[6–9] and in the general population,[10,11] with rates up to 60% in an inpatient setting.[5]

Cocaine abuse severity predicts the outcome of polyabusers applying for detoxification from both substances.[12] Cocaine use is yet related to increased suicidal behavior in alcoholics with depressive pictures.[13] Concomitant alcohol use is related to a poorer prognosis in treatment-seeking cocaine abusers.[14,15] Moreover, an enhanced somatic risk comes from the chemical interaction between alcohol and cocaine generating coca-ethylene, a highly toxic metabolite.[16,17]

A few studies investigated the psychiatric correlates and dynamics of concurrent alcohol and cocaine use in clinical samples of alcoholics.[12,13,15] A substance-independent association between polyabuse patterns and psychiatric comorbidity has been reported.[18] Chen et al reported a prevalence rate of about 30% of polydrug use in psychiatric inpatients, with an inverse relationship between frequency of drug use and schizophrenia.[19] The association between substance use and bipolar disorder is widely documented in literature,[20–22] and alcohol and cocaine are common substances of abuse in this category of patients.[20,23–25]

Recently, a group of affective syndromes varying in severity and typology of prominent symptoms, but sharing a



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similar evolution toward mood instability, chronic dysphoria, and impulsiveness has been conceptualized as the bipolar spectrum.[26–30] The bipolar spectrum also comprises a series of biological conditions, possibly consisting of temperamental cyclothymia, or early-onset anxiety disorders with a cyclic course, which are predictive of a subsequent bipolar evolution, in the attempt to identify the early precursors of mood instability.[31,32] In this view, temperamental disposition and drug-induced mood excitement are regarded as elements of the bipolar spectrum along prototypes, II ½ to IV (the II ½ prototype corresponds to depression upon a cyclothymic temperament, usually evident for the fluctuation of symptom intensity of partial recurrent remission; prototype III corresponds to substance/antidepressant-induced manic/hypomanic phases or cycles; prototype 4 corresponds to depression upon hyperthymic temperament. In the prototype III, it is implied that spontaneous or substance-induced manic phases share common backgrounds and evolution toward spontaneous bipolar disorder, although participants who do not experience mania out of substance intoxication have a lower level of spontaneous disposition).[28] Substance use itself may be regarded as one of the typical expression of temperamental elation, both on the legal and illegal side. Therefore, especially in adolescents and young adults, affective instability is often anticipated and elicited by substance use. Given the peculiar analogies between cocaine intoxication and manic states, a bipolar-stimulant spectrum accounting for the strong association between the two has been proposed.[33]

This study aims to verify the clinical correlates of alcoholics with cocaine abuse, with special regard to the distribution of psychiatric diagnoses. Our hypothesis was that participants with cocaine abuse would have a higher rate of bipolarity.

## METHODS

### Design of the Study

A comparative cohort study was designed to compare demographic, clinical, and diagnostic characteristics of alcoholics with and without cocaine abuse. All patients included in the study signed informed consent. Both the consent form and the experimental procedures were approved by the competent ethics committees in accordance with internationally accepted criteria for ethical research. All patients were evaluated after the resolution of acute withdrawal by standard benzodiazepine-based treatment to avoid, in the diagnostic process, possible interferences owing to the acute phase of their illness. Since 2004, the Center for the assessment and treatment of Alcohol-Related Pathology, University ''La Sapienza,'' ''Umberto I,'' University Hospital in Rome, Italy has been using a clinical protocol that has the characteristics of single setting integrated treatment, with a long-term perspective and a treatment-maintenance oriented approach. Different facilities are provided within the same environment, with scheduled appointments and the possibility of further evaluations, are prompted along the patient's request. Thus, psychological, pharmacologic, and other medical interventions can be administered in real-time synergy and the threshold of minimum requested compliance is lowered by the one doctors' shopping setting. Patients displaying major psychomotor excitement, aggressive, and suicidal behavior, or major psychotic symptoms were shunted to the local psychiatric inpatient unit. For them, the outpatient treatment initiation was postponed after possible discharge from the inpatient ward.

### Participants

The study included 448 consecutive alcoholics, according to DSM-IV TR criteria, who had been referred for treatment to our outpatient clinic during the years 2005 to 2007, 338 (75.4%) were male patients and 110 (24.6) were females. The mean age was 44 ± 9 (min 19 max 74). Most of them were single (155, 34.6%), with less than 8 years of education (230, 51.3%), and employed (344, 76.8%).

A total of 144 alcoholics had cocaine abuse according to DSM-IV criteria. Of these, 123 (85.4%) were males.

Mean age was 40 ± 8 years. In addition, they were characterized by concomitant use of heroin (31.3%), benzodiazepines (BDZ) (18.7%), and cannabinoids (57.3%). A total of 304 alcoholics never used cocaine. Of these, 215 (70.7%) were male participants. Mean age was 46 ± 9 years.

## Instruments

These instruments were used to collect data on the variables to be studied:

### Drug Addiction History Rating Scale (DAH-RS) Alcohol Version

Alcoholism-related information was collected by means of the Drug Addiction History Rating Scale (DAH-RS)-alcohol version, administered by a psychiatrist. The DAH-RS.[34] Is a multiscale questionnaire comprising these categories: sociodemographic information, physical health, mental health, substance abuse, treatment history, social adjustment, and environmental factors. DAH-RS was specifically elaborated to register information regarding illicit drugs users. For alcoholic patients, we registered also the number of alcohol units in-token per day at evaluation time and the maximum lifetime.

### Psychiatric Diagnostic Evaluation

#### *Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Clinician Version*

This user-friendly instrument[35] will help clinicians make standardized, reliable, and accurate diagnoses and avoid the common problem of ''premature closure''-the premature focus on 1 diagnostic possibility. Specifically adapted from the research standard for Axis I structured clinical interviewing for use in clinical settings, the SCID-I covers those DSM-IV diagnoses most commonly seen by clinicians and includes the diagnostic criteria for these disorders with corresponding interview questions. The SCID-I is divided into 6 self-contained modules that can be administered in sequence: mood episodes; psychotic symptoms; psychotic disorders; mood disorders; substance use disorders; and anxiety, adjustment, and other disorders.

We considered there to be a ''dual diagnosis'' when we have determined the presence of both alcohol dependence and an autonomous psychiatric disorder. Autonomy of additional psychiatric syndromes was assessed with reference to an independent course with respect to substance abuse, and the specificity of symptoms with respect to expected intoxication or withdrawal pictures.

#### *Bipolar spectrum diagnoses*

As for bipolar spectrum diagnoses, history of earlier hypomanic episodes, and temperamental characteristics were explored using the criteria listed in the SID, the Semistructured Interview for Depression.[36] All information was gathered from the patient and at least 1 close relative (usually parents, siblings); in addition, all available clinical records were carefully examined. Inquiry on temperamental attributes was made about the habitual self of the patient-during periods free of affective episodes-from patient and significant others. Our operational criteria for affective temperaments represent the University of Tennessee[27] modification of the Schneiderian descriptions.[37] The SID, developed as part of the Pisa-Memphis (now San Diego) collaborative study on affective disorders, has been used with over 2000 patients at the time of writing: its reliability for diagnostic assessment of patients and their temperaments has been documented elsewhere.[38,39]

### Urine Analyses

Toxicologic urine analyses were carried out at evaluation time. The enzyme-linked multiplied immunoassay was used.

## Data Analysis

Regarding the psychiatric evaluation, the patients were evaluated while free of an acute phase, for which hospitalization was required, so to reduce the diagnostic ambiguity between intoxication-related symptoms and spontaneous mental disorders. In case in which further relevant clinical information emerged from subsequent interviewing, diagnoses were reassessed.

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We compared alcoholics with and without abuse of cocaine regarding sociodemographic information, physical health, psychiatric diagnoses, substance abuse, and social adjustment. The variables that showed statistically significant differences ($P<0.05$) for an association with cocaine use were included in separate logistic backward regression analyses comprising the appurtenance to alcohol plus cocaine group as dependent variable. Statistical analyses were carried out using the SPSS package. As this is an exploratory study, statistical tests were considered significant at the $P<0.05$ level.

## RESULTS

Patients showed the first-level psychiatric comorbidity: bipolar II disorder (N = 91, 20.3%), bipolar 1 disorder (N = 19, 4.2%), cyclothymia (N = 16, 3.5%), major depression, recurrent (N = 12, 2.6%), dysthymia (N = 12, 2.6%), schizophrenia (N = 8, 1.7%), schizoaffective disorder (N = 3, 0.6%), and other (N = 2, 0.4%). Additional comorbidities were panic disorder (N = 30 6.6%), social phobia (N = 10, 2.2%), obsessive-compulsive disorder (N = 7, 1.5%), generalized anxiety disorder (N = 5, 1.1%), eating disorders (N = 3, 0.6%), Somatization (N = 2, 0.4%), others (N = 4, 0.8%). Considering Akiskal and Mallya criteria, 162 alcoholics (36.2%) were diagnosed as ''bipolar spectrum.''

Table 1 shows differential sociodemographic characteristics, psychiatric comorbidity, social adjustment, and drug addiction history between alcoholics with and without cocaine abuse. No differences emerged as for educational level, rates of unemployment, age of first sip (age of first contact with alcohol), and the rate of dual diagnosis. An additive psychiatric diagnosis can be assessed for 61 (42.4%) of alcoholics with cocaine abuse and 124 (40.8%) of alcoholics without cocaine abuse.

Cocaine-dependent alcoholics were younger, more frequently males, and single. Less frequently they were living with their families. They show a statistically significant higher rate of current or past use of heroin, benzodiazepines, and cannabinoids. The transition from use to abuse takes place earlier for cocaine-dependent alcoholics, and they

**TABLE 1.** Univariate Association Between Abuse of Cocaine in Alcoholics and Sociodemographic Characteristics, Psychiatric Comorbidity, Social Adjustment, and Drug Addiction History

| | **Alcohol Cocaine N = 144** | **Alcohol N = 304** | **χ/T** |
|---|---|---|---|
| Age (Mean ± SD) | 40 ± 8 | 46 ± 9 | −6.30** |
| Sex (male) | 123 (85.4) | 215 (70.7) | 11.38** |
| Marital status (single) | 76 (52.7) | 95 (31.2) | 17.48** |
| Living in family | 94 (65.3) | 224 (74.7) | 4.24* |
| Concomitant use of heroin | 45 (31.3) | 15 (4.9) | 58.33** |
| Concomitant use of BDZ | 27 (18.7) | 9 (2.9) | 36.11** |
| Concomitant use of THC | 82 (57.3) | 24 (7.9) | 131.44** |
| Age alcohol continuous use | 23 ± 6 | 25 ± 7 | −2.23* |
| Drinking duration | 25 ± 9 | 30 ± 10 | −4.99** |
| Alcoholism duration | 17 ± 8 | 21 ± 11 | −4.27** |
| Initial alcohol units/daily | 10.11 ± 9.1 | 6.09 ± 3.2 | 4.69* |
| Max alcohol units/daily | 25.17 ± 11.8 | 20.54 ± 9.3 | 4.11** |
| Physical severe complications | 33 (22.9) | 47 (15.5) | 3.70* |
| Problematic social adjustment | 74 (51.4) | 111 (36.5) | 8.91* |
| Bipolar spectrum | 84 (58.3) | 78 (25.7) | 45.19** |

Only significant ($P<0.05$) differences are reported.
*<0.05.
**<0.001.
BDZ indicates benzodiazepines; THC, cannabinoids.

have a shorter dependence history when applying for treatment. They consume a higher amount of alcohol at the beginning of their dependence history, and reach a higher top level of alcohol consumption, ever along their dependence history. As regards the consequences of their pathologic drinking, they report a higher level of somatic impairment and worse social adjustment.

First level ($\chi^2$ 11.38 df 8 $P = 0.18$), and second level ($\chi^2$ 13.90 df 9 $P = 0.125$) comorbidity was not different between groups. Despite a similar rate of dual diagnosis, alcoholics using cocaine display a significant higher rate of bipolar spectrum.

Table 2 shows the most important predictors of concomitant cocaine abuse in our alcoholics. Older age at the time of present treatment is the only correlate of no concurrent cocaine use. In other words, alcohol-cocaine abuse is rather typical of younger generation of alcoholics. A diagnosis of bipolar disorder and concurrent benzodiazepine and cannabis use is the strongest correlate of alcohol-cocaine abuse. A minor link was also found with male sex, a history of heroin use, and an early heavier involvement with alcohol.

## DISCUSSION

As expected, cocaine-dependent alcoholics are predominantly male patients and younger, have been never married and do not live with their families, and are more severely impaired on social grounds. They engage in habitual alcohol use earlier and display a higher level of global somatic impairment. Their alcohol dependence is characterized by a higher level of consumption at the beginning of their habitual alcohol use, and a higher peak level of consumption ever along the course of their disorder. Polyabuse is more likely. Earlier and heavier regular drinking may mirror the well-known relationship between bipolar disorders and substance use. In fact, young bipolars have a strong disposition to engage in substance use.[40] Other authors hypothesize that substance use itself may be the trigger for full-blown bipolar disorders later on.[41,42] In this study, the found correlation between the bipolar spectrum and alcohol-cocaine abuse of alcoholics allows to support a slightly different hypothesis. Minor syndromes belonging to the bipolar spectrum (hypomania and affective temperaments) may develop into full-blown bipolar disorders as a consequence of occasional or periodic cocaine use.[28,33] In other words, substance-induced manic episodes may make the difference between a latent disposition displaying as minor cyclothymia and a full-blown bipolar disorder, by a self-maintaining effect that causes progressive clinical worsening.[43] Exposure to stimulants, in fact is not enough to elicit a manic episode in the absence of a bipolar disposition, which can be revealed by means of rating scales for subthreshold cyclothymia or affective temperaments.[44] Bipolar participants using alcohol or cocaine loom as a phenotypic variant of the bipolar spectrum, rather than a mere clinical subtype accounting for substance-induced mood symptoms. A similar observation has been

**TABLE 2.** Most Important Predictors of Concomitant Abuse of Cocaine in 448 Alcoholics Applying for Treatment

| Predictors | Odds Ratio | Min | Max | *P* |
|---|---|---|---|---|
| Age | 0.95 | 0.93 | 0.97 | 0.007 |
| Sex (male) | 1.47 | 1.12 | 1.82 | 0.035 |
| ''Bipolar Spectrum'' | 2.16 | 1.77 | 2.55 | 0.000 |
| Concomitant use of benzodiazepines | 2.03 | 1.50 | 2.56 | 0.009 |
| Concomitant use of cannabinoids | 2.31 | 2.00 | 2.62 | 0.000 |
| N° initial alcohol units/daily | 1.05 | 1.03 | 1.07 | 0.001 |
| Past use of opioid | 1.84 | 1.55 | 2.13 | 0.000 |

Statistic: $\chi^2$ 173.03 df 7 $P<001$.

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made for heroin addicts abusing cocaine,[45] whereas heroin addicts and alcoholics in general have been shown to have a higher level of temperamental cyclothymia than control participants[46,47] and a similar hypothesis about a bipolar-stimulant spectrum had also been made.[28,33] Consistently with literature data and suggestions, out data indicate that a minor, or latent bipolar disposition, as that expressed as cyclothymia, may cause proneness to multiple substance use in substance-dependent individuals, along with a general substance-abuse trend linked to cyclothymia itself and the bipolar spectrum.

All in all, having a bipolar spectrum disorder would be a risk disposition to substance use[48] which, in its turn, would secondarily increase the rate of axis I bipolar disorder. Such a vicious circle would be possible owing to a general disposition toward bipolar disorder, instead of a specific toxic effect of drugs of abuse, with no sharp distinction between substance-induced bipolar disorders and spontaneous forms. Underlying cyclothymia, shared by substance abuses regardless of major affective disorders, rather than the direct effect of substance, may be the missing link between substance use and bipolar disorder.

The awareness of a bipolar spectrum diagnosis of apparently depressed alcoholics or the assessment of affective temperaments as a routine in treatment-seeking alcoholics may have an influence on treatment decisions. In fact, the choice between possible antidepressant treatment and mood stabilizing treatment is likely to be a major issue for treatment retention and compliance to alcohol-dependence treatment. Hypomanic and manic episodes induced by antidepressant-only treatment in fact may increase the relapse rate, cause a regression in the patient's insight, and worsen the stability of the therapeutic relationship.

### Limitations

The patterns of drug use in different communities may influence our results. In fact, in countries in which cocaine is a second-line drug with respect of alcohol, the bipolar-stimulant link may just mirror a higher level of bipolarity in this deviant subgroup. However, for participants of such an age as our sample's cocaine and alcohol are equally likely to be first-line drugs. In addition, the diagnostic process may have a limitation in distinguishing actual cocaine dependence from abuse and use: therefore, some cases of past cocaine abuse or current controlled use may be omitted since self-rated as negligible, and the interviewer may focus on current or relevant periods of cocaine intoxication rather than generically on chronic exposure to cocaine. As a consequence, results may be limited to a relationship between current pathologic engagement into cocaine use and bipolar disorder. Last, the chronology of engagement into cocaine use, through different stages, and engagement into alcohol use, is missing from our assessment, so that interpretation about primary vs. secondary use is not possible. Obviously, prospective data are needed to shed further light on the hypotheses derived from our clinical sample.

## CONCLUSIONS

This paper illustrates a significant relationship between alcohol-cocaine abuse and the bipolar spectrum, with special regard to subthreshold and minor syndromes. It can be hypothesized that cocaine use is an attempt to maintain a baseline level of mood elation similar to a hyperthymic temperament or hypomanic state. Alcohol use, especially in youngsters, may be an instrument to cope with chronic dysphoria corresponding to an affective temperament. The attempt to induce and maintain hypomania by cocaine use would lead to full-blown bipolar disorders. In this context, alcohol use may favor the engagement into cocaine use by cyclothymics owing to its sedating effect, but would eventually become a further prodysphoric factor.

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