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Rate of Progression from First Use to Dependence on Cocaine or Opioids: A Cross-substance Examination of Associated Demographic, Psychiatric, and Childhood Risk Factors

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Abstract

Background—A number of demographic factors, psychiatric disorders, and childhood risk factors have been associated with cocaine dependence (CD) and opioid dependence (OD), but little is known about their relevance to the rate at which dependence develops. Identification of the subpopulations at elevated risk for rapid development of dependence and the risk factors that accelerate the course of dependence is an important public health goal.

Methods—Data were derived from cocaine dependent (n=6,333) and opioid dependent (n=3,513) participants in a multi-site study of substance dependence. Mean age was approximately 40 and 40% of participants were women; 51.9% of cocaine dependent participants and 29.5% of opioid dependent participants self-identified as Black/African-American. The time from first use to dependence was calculated for each substance and a range of demographic, psychiatric, and childhood risk factors were entered into ordinal logistic regression models to predict the (categorical) transition time to CD and OD.

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Contributors

Dr. Sartor conducted the literature searches and statistical analyses and wrote the first draft of the manuscript. Drs. Gelernter and Kranzler designed the study, wrote the protocol, oversaw data collection, and edited the manuscript. All authors contributed to and have approved the final manuscript.

Conflicts of Interest

Dr. Kranzler has been a consultant or advisory board member for Alkermes, Lilly, Lundbeck, Pfizer, and Roche. He is also a member of the American Society of Clinical Psychopharmacology's Alcohol Clinical Trials Initiative, which is supported by Lilly, Lundbeck, Abbott, and Pfizer.

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Results—In both the cocaine and opioids models, conduct disorder and childhood physical abuse predicted rapid development of dependence and alcohol and nicotine dependence diagnoses were associated with slower progression to CD or OD. Blacks/African Americans were at greater risk than European Americans to progress rapidly to OD.

Conclusions—Only a subset of factors known to be associated with CD and OD predicted the rate at which dependence developed. Nearly all were common to cocaine and opioids, suggesting that sources of influence on the timing of transitions to dependence are shared across the two substances.

Keywords

cocaine dependence; opioid dependence; transition

1. Introduction

An estimated 1.1 million Americans meet DSM-IV criteria for cocaine abuse or dependence, according to the National Survey on Drug Use and Health (NSDUH) (Substance Abuse and Mental Health Services Administration, 2010). Opioid use disorders are even more prevalent (Compton, Thomas, Stinson, & Grant, 2007), and will likely remain a significant public health issue as the misuse of prescription opioids continues to rise (Blanco et al., 2007; Compton & Volkow, 2006; Martins, Keyes, Storr, Zhu, & Gruzca, 2010). Understanding the development of cocaine and opioid use disorders, including identification of the subpopulations at elevated risk for rapid development of dependence and the psychiatric and childhood risk factors that accelerate the course of dependence are important public health goals.

1.1 Prevalence of cocaine dependence and opioid dependence by sex and race/ethnicity

Studies examining differences by sex or race/ethnicity in prevalence of cocaine and opioid use disorders have produced mixed results. A recent study by Lev-Ran and colleagues (2013) based on data from a large nationally representative sample, the National Epidemiological Study of Alcohol and Related Conditions, reported a higher prevalence of cocaine use disorders in men than women. However, a study by Wagner and Anthony (2007) based on another large nationally representative sample, the National Comorbidity Survey (NCS), found no evidence for sex differences in dependence risk among users. Further, studies of adolescent or college-aged samples have shown higher rates of cocaine dependence (CD) in females (Chen & Kandel, 2002; Kasperski, Vincent, Caldeira, Garnier-Dykstra, O'Grady, & Arria, 2011). Far less attention has been given to sex differences in opioid use disorders. The one known study in this area reported a higher prevalence in men (Lev-Ran, Imiatz, Rehm, & Le Foll, 2013).

The literature on racial/ethnic differences in the prevalence of cocaine use disorders, though sparser, is more consistent. Investigations using two different large-scale community-based samples (National Household Survey on Drug Abuse (NHSDA) and National Epidemiological Survey of Alcohol and Related Conditions) reported higher rates of CD among African-American than European-American cocaine users (Chen & Kandel, 2002; Lopez-Quintero et al., 2011). Racial/ethnic differences in the prevalence of opioid dependence (OD) have not been investigated, but according to an NHSDA-based study, African Americans are more likely than European Americans to use heroin (Ma & Shive, 2000). Identifying possible distinctions by race/ethnicity in the pathway to cocaine or opioid dependence is an important step toward developing tailored prevention efforts.

1.2 Psychiatric comorbidity with cocaine dependence and opioid dependence

Both CD and OD frequently co-occur with other substance use disorders (SUDs). Elevated rates of alcohol use disorders, nicotine dependence, cannabis dependence, and OD have been observed in dependent cocaine users (Bierut, Strickland, Thompson, Afful, & Cottler, 2008; Goldstein, Dawson, Chou, & Grant, 2012; Tang, Kranzler, Gelernter, Farrer, & Cubells, 2007). Similarly, in clinical samples of dependent opioid users, the lifetime prevalence of alcohol dependence, cannabis dependence, and CD is high, ranging from approximately 40–70%, 20–50%, and 65–80%, respectively (Brooner, King, Kidorf, Schmidt, & Bigelow, 1997; Kidorf, Disney, King, Neufeld, Beilenson, & Brooner, 2004; Rodriguez-Llera et al., 2006).

In addition to SUDs, high rates of comorbidity of attention-deficit hyperactivity disorder (ADHD) (Falck, Wang, & Carlson, 2008; Goldstein et al., 2012), major depressive disorder (Kandel, Huang, & Davies, 2001), and posttraumatic stress disorder (PTSD) (Back, Dansky, Coffey, Saladin, Sonne, & Brady, 2000; Najavits et al., 1998; Wasserman, Havassy, & Boles, 1997) have been reported in cocaine dependent individuals. Rates of ADHD (Carpentier, VanGogh, Knapen, Buitelaar, & DeJong, 2011; Rodriguez-Llera et al., 2006) and major depressive disorder (Brooner et al., 1997; Kidorf et al., 2004; Rodriguez-Llera et al., 2006; Sordo et al., 2012) are also elevated in individuals with OD, but there is no evidence for heightened risk for PTSD in this population (Kidorf et al., 2004; Rodriguez-Llera et al., 2006). However, the prevalence of conduct disorder is extremely high, estimated at 54% (Modestin, Matutut, & Wumle, 2001) and 60% (Carpentier et al., 2011) in two treatment-seeking samples. Elevated rates of exposure to childhood physical and sexual abuse have also been observed in individuals dependent on cocaine or opioids (Afifi, Henriksen, Asmundson, & Sareen, 2012; Shin, Hong, & Hazen, 2012), likely due at least in part to the high degree of overlap in risk factors for child maltreatment and substance use disorders, such as poor parental monitoring and parental substance use problems (Fergusson et al., 1996; Walsh et al., 2003).

1.3 Rate of progression from first use to dependence

Examination of the rate of progression from first use to dependence is important for the development of etiological models of CD and OD, as this phenotype captures the dynamic nature of substance dependence and can be informative for the identification of risk factors that accelerate its development. Risk for developing dependence is higher among cocaine users and opioid users than cannabis users (Anthony, Warner, & Kessler, 1994; Tsuang et al., 1999; Wagner & Anthony, 2002), but about equal to the risk for alcohol dependence among drinkers and far lower than nicotine dependence risk among tobacco users (Lopez-Quintero et al., 2011). However, the transition to dependence occurs much more rapidly for cocaine than alcohol (Ridenour, Lanza, Donny, & Clark, 2006; Wagner & Anthony, 2002). For example, Lopez-Quintero and colleagues (2011) reported that 7.1% of cocaine users developed dependence within the first year, compared to less than 2% of alcohol, nicotine or cannabis users. The rate of progression to OD has not been well documented, but one small high-risk family study of adolescents reported that the transition to dependence was shorter for opioids than cocaine, cannabis, tobacco, or alcohol (Ridenour et al., 2006).

Several studies have shown that women progress more rapidly from first cocaine use to abuse or dependence (known as “telescoping”) (McCance-Katz, Carroll, & Rounsaville, 1999; O’Brien & Anthony, 2005) and from regular use to treatment onset (Haas & Peters, 2000), but the relevant literature for OD is limited to one study that found a faster transition from regular use to treatment for women (Hernandez-Avila, Rounsaville, & Kranzler, 2004). We are also aware of only one study to examine racial/ethnic differences in the rate of progression to CD or OD (O’Brien & Anthony, 2005), in which a more rapid progression

from first cocaine use to CD was observed in non European-American (African-American and other race/ethnicity) than European-American cocaine users. None of the existing studies examining progression to CD or OD have incorporated psychiatric conditions or childhood risk factors.

In short, few of the demographic factors and none of the psychiatric or childhood risk factors associated with CD and OD have been investigated with respect to the rate of transition from first use to dependence, despite the potential utility of such an approach for understanding the development of CD and OD. The current study was designed to address that gap in the literature, using data from a sample in which all individuals met dependence criteria, thus avoiding the need to distinguish factors that contribute to the rate of transition to dependence from those that contribute to the risk to *ever* develop dependence.

2. Materials and methods

2.1 Sample

Data for the current study were derived from cocaine dependent and opioid dependent participants in a multi-site study of alcohol dependence, CD, and OD conducted through Yale University School of Medicine, the University of Connecticut Health Center, the University of Pennsylvania Perelman School of Medicine, the Medical University of South Carolina, and McLean Hospital. The sample for the multi-site study was comprised of alcohol, cocaine, or opioid dependent individuals and unaffected controls recruited for case-control genetic studies of SUDs and cocaine or opioid dependent probands and their relatives from family-based genetic studies. (See Sun et al. (2012) for details on ascertainment and procedures.) The study protocol and informed consent document were approved by the institutional review board at each participating institution.

Given our goal of examining progression from initiation to dependence onset in affected individuals, we limited our CD analyses to participants meeting CD criteria and our OD analyses to those meeting OD criteria. The two groups of participants are therefore described separately, although they are not mutually exclusive. (Diagnostic overlap is discussed in 2.4.2.)

2.1.1 Cocaine dependent subsample—CD criteria were met by 6,333 individuals, 41.1% of whom were women. The mean age of cocaine dependent participants was 40.4 (SD=9.0). Just over half (51.9%) self-identified as Black/African-American, 39.7% as European-American, and 8.4% as being of another race/ethnicity. Approximately half reported an annual household income under \$10,000; 44.5% had completed fewer than 12 years of education.

2.1.2 Opioid dependent subsample—OD criteria were met by 3,513 individuals, 38.0% of whom were women. The mean age of opioid dependent participants was 39.1 (SD=10.0) years. Of these, 29.5% self-identified as Black/African-American, 60.9% as European-American, and 9.6% as being of another race/ethnicity. Just over half reported an annual household income under \$10,000 and 45.6% reported fewer than 12 years of education. Approximately 80% identified heroin as the opiate drug they used the most.

2.2 Assessment

Data were collected by trained interviewers, who conducted in-person interviews with an electronic version of the Semi-structured Assessment for Drug Dependence and Alcoholism (SSADDA). The SSADDA queries demographic information, diagnostic criteria for DSM-IV psychiatric disorders, and history of exposure to environmental factors associated with

SUDs (e.g., traumatic events). A detailed history of substance use, including age at first use and age at onset of dependence for all classes of drugs of abuse is also queried in the SSADDA. More in-depth descriptions of the SSADDA, including administration methods and reliability, have been previously reported (Feinn., Gelernter, Cubells, Farrer, & Kranzler, 2009; Pierucci-Lagha et al., 2005; Pierucci-Lagha et al., 2007).

2.3. Operationalization of Variables

2.3.1 Substance use and dependence—Age at first use was asked of all participants who endorsed use of a given substance. Age at dependence onset, defined as the age at which full dependence criteria were met (3 or more symptoms in the same 12-month period), was queried for all participants meeting dependence criteria. The transition time from first use of cocaine or opioids to dependence was calculated as the difference between age at first use and age at dependence onset. There are no standard definitions of rapid or slow rate of transition to dependence for either cocaine or opioids. To create an indicator of transition time that could be interpreted as the rate relative to other dependent users, we broke the continuous transition time distribution into quartiles to construct categorical variables. For CD, the four categories were: <1, 1–3, 4–8, and 9 or more years. For OD, they were <1, 1–2, 3–6, and 7 or more years.

2.3.2 Other domains—Race/ethnicity was categorized as European-American, Black/African-American, or other racial/ethnic background. Psychiatric diagnoses were derived according to DSM-IV diagnostic criteria. Exposures to childhood risk factors were assessed with yes/no questions. Given our goal of building *predictive* models of the rate of progression from first use to dependence on cocaine or opioids, we did not include marital status, household income, or education level, as only current status was queried in the interview. (Knowing only marital status, educational attainment, and household income at the time of interview, we were unable to determine their ordering with respect to the onset of CD or OD.) Ages at onset of psychiatric disorders were reported and exposures to childhood risk factors were assessed with reference to a specific timeframe (e.g., “by the time you were 13”), so we created variables representing their presence or absence prior to the onset of dependence (separately for each substance). Only psychiatric disorders and childhood risk factors experienced before the onset of dependence were coded positive for that construct.

2.4 Data Analysis

2.4.1 Determination of the best analytic approach to account for comorbidity of CD and OD—Because of the substantial degree of overlap between CD and OD cases (see Table 1), we first conducted the ordinal regression analyses (described in 2.4.3) stratified by OD status for the CD analyses and by CD status for the OD analyses. Results from comorbid cases did not differ significantly from single diagnosis cases, so for ease of interpretation, we analyzed them together, including OD status as a covariate in CD analyses and CD status as a covariate in OD analyses to account for the overlap.

2.4.2 Demographic, psychiatric, and childhood risk factors by transition time—Descriptive analyses were conducted in SAS (SAS Institute, 2008). Potential distinctions by (categorical) transition time in the rates of demographic, psychiatric, and childhood risk factors were examined by conducting chi-square tests of association. Differences across transition times in age at time of assessment, age at first use of cocaine or opioids, and age at onset of CD or OD were tested using analyses of variance. A Bonferroni correction was applied to control for inflation in Type 1 error due to multiple testing, setting the critical value to 0.002.

2.4.3 Predictors of the rate of progression from first use to onset of dependence

Ordinal logistic regression analyses aimed at identifying correlates of the rate of progression from first use to dependence onset were conducted in Stata (StataCorp, 2007), using the Huber-White correction to adjust for non-independence of observations in family members. Separate models were conducted for cocaine and opioids. Analyses proceeded in two steps. In the first step, two ordinal logistic regression analyses were conducted using variables representing (1) SUDs and other psychiatric disorders and (2) childhood risk factors. (See Tables 1 and 2 for lists of covariates.) All analyses were adjusted for age and age at first use. In the second step, the significant covariates from the domain-specific analyses were entered into a final ordinal logistic regression model along with age, age at first use, sex, and race/ethnicity.

3. Results

3.1. Characteristics of dependent users by timing of transition to dependence

3.1.1 Cocaine—As seen in Table 1, the slowest transition group reported the youngest age at first use: 19.1 years (SD=4.7). European Americans were underrepresented in the slowest transition group and women were overrepresented in the very rapid (<1 year) and very slow (>8 years) progression groups. Rates of ADHD and conduct disorder were highest in individuals reporting <1 year and 1–3 year transition times, but the prevalence of major depressive disorder was highest in those reporting the slowest transition time. A linear relationship was observed between length of transition time and rates of alcohol dependence and OD, with the lowest rates in the rapid onset and the highest in the slow progression groups.

3.1.2 Opioids—As seen in Table 2, the group with the slowest transition to OD reported the youngest age at first use and women were overrepresented in the rapid progression (<1 year and 1–3 years) groups. In addition, we found a markedly higher prevalence of alcohol dependence and CD in the slowest progression group (60.2% vs. 35–44% for alcohol dependence and 55.6% vs. 29–33% for CD).

3.2 Predicting rate of progression from first use to onset of dependence

3.2.1. Cocaine—Results from the final ordinal logistic regression model predicting the rate of transition from first use of cocaine to CD are shown in Table 3. Conduct disorder (odds ratios (OR)=1.56; 95% confidence intervals (CI): 1.28–1.90) and severe childhood physical abuse (OR=1.32; CI: 1.02–1.70) were associated with an accelerated rate of progression from first use to dependence. Onset of alcohol dependence (OR=0.53; CI: 0.44–0.64), nicotine dependence (OR=0.63; CI: 0.53–0.76), and OD (OR=0.27; CI: 0.22–0.32) before CD were associated with a slow transition to CD.

3.2.2 Opioids—Results from the final ordinal logistic regression model predicting the rate of transition from first use of opioids to OD are shown in Table 4. The results were very similar to those from the final CD model. Conduct disorder and severe childhood physical abuse were associated with rapid progression to dependence (ORs=1.22 (CI: 1.02–1.46) and 1.50 (CI: 1.17–1.91), respectively) and all three of the SUDs included in the model predicted a slow transition to OD. The ORs for alcohol dependence (0.54; CI: 0.46–0.65) and nicotine dependence (OR=0.64; CI: 0.54–0.77) were nearly identical to those estimated in the CD model. The odds ratio for CD was 0.50 (CI: 0.42–0.60). In addition, a more rapid onset of OD was observed in Blacks/African Americans than European Americans (OR=1.31; CI: 1.07–1.61).

4. Discussion

The current study expands the existing literature on the development of two SUDs of major public health concern, cocaine dependence and opioid dependence, by examining a phenotype that captures the dynamic nature of these disorders and informs our understanding of the heterogeneity in the pathways leading to their onset. Ours is the first investigation to examine any psychiatric or childhood risk factors associated with the rate of progression to either CD or OD. It is also the first to assess potential differences by sex or race/ethnicity in the rate of progression to OD. Furthermore, our exclusive use of dependent cases allowed for the identification of distinctions among affected individuals with respect to the contributions of demographic, psychiatric, and childhood risk factors specific to the timing of transition to dependence rather than dependence risk in general. Finally, as we examined both CD and OD, results from this study can address the question of whether predictors of transition time from first use to dependence vary across the two substances.

Results from both the CD and OD models revealed conduct disorder and severe childhood physical abuse to be significant predictors of rapid progression from first use to onset of dependence. In addition, for both cocaine and opioids, dependence on other substances was associated with a slower rate of progression. The only substance-specific finding was a faster rate of progression to OD in Blacks/African Americans than European Americans. The high degree of similarity in predictors across substances is consistent with findings from an earlier study by our group that examined the rate of transition from first use to problem use of alcohol and cannabis, in which all but one of the correlates of transition time for cannabis were also observed for alcohol (Sartor et al., 2013).

4.1 Sex and race/ethnicity differences

Contrary to expectations, women were no more likely than men to progress rapidly to dependence on either cocaine or opioids. Although studies examining sex differences in the prevalence of CD and OD have produced inconsistent results (Chen & Kandel, 2002; Kasperski et al., 2011; Lev-Ran et al., 2013; Wagner & Anthony, 2007), studies examining the rate of progression from first cocaine use to CD (McCance-Katz et al., 1999; O'Brien & Anthony, 2005) and from first use of cocaine or opioids to treatment (Haas & Peters, 2000; Hernandez-Avila et al., 2004) have shown a telescoping effect in women. Discrepancies between our study and earlier investigations may be attributable to the fact that adjustments for psychiatric and psychosocial correlates were not made in these earlier investigations. In our sample, sex was a significant predictor of the rate of progression both to CD and OD in univariate analyses, but not in adjusted models, indicating that apparent sex differences in the rate of progression may be explained by sex differences in the psychiatric and childhood risk factors included in the models.

A more rapid progression to OD was observed in Blacks/African Americans than European Americans, making this the first study to document distinctions by race/ethnicity in the rate of progression to OD. Consistent with the one known study to examine racial/ethnic differences in the rate of progression to CD, which was based on NHSDA data (O'Brien & Anthony, 2005), we found no differences by race/ethnicity in timing of the transition from first use to CD onset. Interestingly, in two other nationally representative studies (Chen & Kandel, 2002; Lopez-Quintero et al., 2011) (one of which was also based on NHSDA data), a higher prevalence of CD was found in African Americans than European Americans, illustrating the fact that prevalence of a given demographic or risk factor is not indicative of its relevance to the progression of the disorder. Differential accessibility has been proposed as a possible explanation of differences in heroin and cocaine dependence by race/ethnicity, as African Americans are overrepresented in socioeconomically disadvantaged neighborhoods where illicit drugs are relatively easily obtained (Chen & Kandel, 2002;

Lopez-Quintero et al., 2011). This explanation seems applicable as well to the rate of progression to dependence, so it is unclear why a more rapid progression to dependence in Blacks/African Americans compared to European Americans was observed only for opioid dependence. Racial/ethnic differences in physiological aspects of cocaine and opioid dependence, for example, potential distinctions by substance in the extent to which genetic influences vary by race/ethnicity, merit exploration.

4.2 Distinguishing psychiatric and childhood risk factors

The strong association of the rate of progression to CD and OD with other SUDs is consistent with the high rates of comorbidity of CD and OD with other illicit drugs, alcohol, and nicotine reported in the literature (Bierut et al., 2008; Brooner et al., 1997; Goldstein et al., 2012; Kidorf et al., 2004; Rodriguez-Llera et al., 2006). However, the direction of effect we observed was unexpected, again demonstrating the distinction between lifetime prevalence and rate of progression phenotypes. We can only speculate on why the presence of other SUDs prior to CD or OD onset appears to slow progression of dependence, as there are no comparable studies of the rate of progression phenotype for CD or OD. One possibility is that many heavy drug users experiment with a range of substances and eventually develop problems related to that substance, but at any given point in time they have a drug of choice and may not be sufficiently motivated to regularly acquire other substances. The possibility that pharmacological interactions between substances explains this pattern of findings should also be considered.

Again recognizing that it is difficult to draw a clear parallel between risk factors for ever developing a disorder and those that contribute to its progression—but lacking more relevant literature—we compare the significant psychiatric and childhood risk factors identified in our study with those previously linked to lifetime CD or OD diagnoses. The overlap is modest. Elevated rates of conduct disorder have been reported in opioid dependent (Carpentier et al., 2011; Modestin et al., 2001) but not cocaine dependent individuals. In our study, conduct disorder was associated with a rapid progression both to CD and OD, which is consistent with earlier studies of alcohol and nicotine linking conduct disorder to rapid progression to dependence (Sartor et al., 2007; Sartor et al., 2008). The most likely link is the high degree of affiliation with deviant peers among individuals with conduct disorder, which provides easy and consistent access to alcohol and drugs. Although the prevalence of both ADHD (Carpentier et al., 2011; Falck et al., 2008; Goldstein et al., 2012; Rodriguez-Llera et al., 2006) and major depressive disorder (Brooner et al., 1997; Kandel, 2001; Kidorf et al., 2004; Rodriguez-Llera et al., 2006; Sordo et al., 2012) are elevated in cocaine dependent and opioid dependent individuals, we found no significant association between either ADHD or major depressive disorder and the timing of transition to CD or OD. Similarly, in contrast to the highly elevated rates of PTSD documented in clinical samples of cocaine dependent patients (Back et al., 2000; Najavits et al., 1998; Wasserman et al., 1997), we found no evidence of PTSD conferring risk for the rapid development of CD.

Childhood physical and sexual abuse are the only two childhood risk factors examined in our study that have been included in prior studies of CD or OD. Both are overrepresented in cocaine dependent and opioid dependent individuals (Afifi et al., 2012; Shin et al., 2012) and childhood physical abuse emerged as a significant predictor of the transition time from first use to CD or OD in the current study. The association can likely be attributed to common risk factors such as low parental monitoring and parental substance use problems that are more common in families where childhood maltreatment occurs (Fergusson et al., 1996; Walsh et al., 2003). It is unclear why physical but not sexual abuse would be associated with the rate of progression to dependence, but one possibility is related to sex differences in the prevalence of sexual abuse. Nearly five times as many women as men report a history of sexual abuse (Fergusson, Lynskey, & Horwood, 1996; Kessler, Sonnega, Bromet, Hughes,

& Nelson,1995) and in one of the few studies to examine sexual abuse and OD (Afifi et al., 2012), the association was specific to females. In a sample such as ours, in which 60% of participants are male, the association may not be easily detected.

4.3 Limitations

Findings from the current study should be interpreted with certain considerations in mind. As in the case of all retrospective studies, the use of retrospective reports may have introduced a recall bias that could have affected results if it varied systematically by any of the significant covariates (e.g., if Blacks/African Americans were more likely than European Americans to underreport time from first opioid use to dependence). Second, the sample was composed of individuals from high-risk families, so severe cases of CD and OD were likely overrepresented. The factors that contribute to the progression of the disorder are unlikely to differ significantly between high-risk family and general population-based samples – the difference being in the concentration rather than the nature of these risk factors - but the rate of progression in a high-risk family sample may be faster. Third, as the methods of administration of cocaine and opioids were not queried, we were unable to assess potential differences by administration method on rate of progression to dependence. Fourth, the specific drug used the first time a participant tried an opiate drug was not queried, so we could not assess possible distinctions in rates of progression by type of opiate drug used the first time, nor could we determine the continuity of use of a given drug from first use to dependence onset. Finally, although the stratified analyses did not reveal significant differences between comorbid and single diagnosis cases of CD and OD and we adjusted for co-occurrence of CD and OD in the analyses, study findings may better represent subpopulations of CD and OD users with high rates of comorbidity than those with only one of the two disorders.

4.4 Conclusions

Our findings indicate that although numerous psychiatric conditions and childhood risk factors are associated with CD and OD, only a few are associated with the rate of progression from first use to dependence: conduct disorder, comorbid SUDs, and childhood physical abuse. As the predictors were not substance-specific, our findings further indicate that sources of risk and protective factors for rapid onset of dependence are common to cocaine and opioids. In addition, our study revealed that Blacks/African Americans are more prone to rapid progression to OD than European Americans, a finding that merits further investigation, as race/ethnicity is often correlated with modifiable factors such as access to healthcare.

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Highlights

- Conduct disorder and physical abuse predicted rapid onset of cocaine dependence
- These same two risk factors predicted rapid onset of opioid dependence
- Dependence on other substances predicted slower transitions to cocaine dependence
- This same pattern was observed for opioid dependence
- African Americans were at elevated risk for rapid onset of opioid dependence

Table 1

Characteristics of cocaine dependent participants by timing of transition from first use of cocaine to onset of dependence

	Years from First Use to Onset of Dependence			
	<1	1–3	4–8	>8
	n=1,466	n=1,774	n=1,617	n=1,438
Mean Age at Onset (SD)				
Cocaine use *	22.6 (6.7)	20.7 (6.3)	19.8 (5.2)	19.1 (4.7)
Cocaine dependence *	22.6 (6.7)	22.6 (6.3)	25.5 (5.3)	33.0 (6.4)
Demographics				
Age: mean (SD) *	39.5 (9.7)	38.2 (9.7)	40.5 (8.0)	44.1 (7.1)
Female *	44.5%	39.0%	38.8%	42.8%
Race/ethnicity *				
European-American	24.5%	30.6%	25.0%	19.9%
Black/African-American	22.2%	25.9%	26.5%	25.4%
Other race/ethnicity	24.1%	30.6%	23.9%	21.4%
DSM-IV Psychiatric Disorders with Onset Prior to CD Onset				
Attention deficit hyperactivity disorder *	9.6%	9.8%	6.9%	6.0%
Agoraphobia	5.0%	4.1%	3.4%	4.3%
Bipolar disorder	2.2%	2.5%	2.0%	2.6%
Conduct disorder *	21.1%	22.9%	18.3%	17.2%
Generalized anxiety disorder	0.9%	0.5%	0.8%	0.2%
Major depressive disorder *	5.4%	4.1%	4.6%	7.2%
Obsessive compulsive disorder	1.4%	2.0%	1.4%	1.4%
Panic disorder	4.3%	2.5%	3.7%	4.1%
Posttraumatic stress disorder	14.3%	12.6%	11.4%	12.4%
Social phobia	5.0%	4.8%	4.2%	3.6%
<i>Substance use disorders</i>				
Alcohol dependence *	31.2%	37.4%	41.4%	51.3%
Cannabis dependence	31.9%	38.4%	35.7%	33.3%
Nicotine dependence	30.1%	29.2%	33.3%	44.0%
Opioid dependence *	17.7%	26.7%	37.4%	58.9%
Childhood Risk Factors Experienced Prior to CD Onset				
Death of a parent < age 6	4.5%	4.4%	5.0%	4.3%
Witnessed violent crime < age 14	23.3%	25.1%	24.6%	22.3%
Victim of violent crime < age 14	9.1%	8.3%	8.2%	6.7%
Sexually abused < age 14	19.4%	19.4%	19.5%	18.6%
Severely physically abused < age 14	14.5%	12.2%	11.7%	11.7%

	Years from First Use to Onset of Dependence			
	<1	1-3	4-8	>8
	n=1,466	n=1,774	n=1,617	n=1,438
Cocaine use in household < age 14	11.3%	11.7%	9.7%	7.7%
Heroin use in household < age 14	6.1%	6.9%	5.9%	4.3%

*
p < 0.002 (critical value after Bonferroni correction)

Table 2

Characteristics of opioid dependent participants by timing of transition from first use of opioids to onset of dependence

	Years from First Use to Onset of Dependence			
	<1	1–2	3–6	>6
	n=695	n=493	n=510	n=460
Mean Age at Onset (SD)				
Opioid use *	23.8 (7.6)	21.1 (6.8)	19.6 (6.3)	18.5 (4.8)
Opioid dependence *	23.8 (7.6)	22.5 (6.8)	23.8 (6.40)	31.1 (6.8)
Demographics				
Age: mean (SD) *	39.7 (9.6)	36.6 (10.8)	37.6 (10.2)	42.5 (8.2)
Female *	43.4%	40.8%	31.8%	32.0%
Race/ethnicity				
European-American	57.9%	63.0%	63.6%	61.6%
Black/African-American	32.6%	26.2%	27.0%	30.0%
Other race/ethnicity	9.5%	10.8%	9.4%	8.4%
DSM-IV Psychiatric Disorders with Onset Prior to OD Onset				
Attention deficit hyperactivity disorder	8.8%	10.4%	9.9%	9.1%
Agoraphobia	5.5%	5.9%	3.4%	4.9%
Bipolar disorder	2.1%	2.4%	3.0%	3.5%
Conduct disorder	20.2%	22.2%	23.8%	23.9%
Generalized anxiety disorder	1.3%	0.9%	0.4%	0.6%
Major depressive disorder	6.6%	7.4%	4.4%	7.9%
Obsessive compulsive disorder	1.8%	2.5%	1.8%	2.6%
Panic disorder	6.3%	6.1%	4.7%	7.3%
Posttraumatic stress disorder	13.8%	13.4%	11.4%	14.0%
Social phobia	5.5%	4.3%	5.2%	5.5%
<i>Substance use disorders</i>				
Alcohol dependence *	39.3%	35.2%	43.8%	60.2%
Cannabis dependence	35.9%	37.3%	41.9%	41.0%
Nicotine dependence	38.4%	36.3%	39.8%	52.8%
Cocaine dependence *	32.3%	28.8%	33.3%	55.6%
Childhood Risk Factors Experienced Prior to OD Onset				
Death of a parent < age 6	4.8%	3.9%	4.6%	4.5%
Witnessed violent crime < age 14	22.7%	22.4%	21.0%	23.0%
Victim of violent crime < age 14	8.7%	9.1%	7.5%	7.5%
Sexually abused < age 14	17.4%	20.5%	17.4%	19.1%
Severely physically abused < age 14	13.9%	12.9%	8.8%	12.4%
Cocaine use in household < age 14	11.1%	13.3%	12.6%	8.6%

	Years from First Use to Onset of Dependence			
	<1	1–2	3–6	>6
	n=695	n=493	n=510	n=460
Heroin use in household < age 14	7.1%	7.3%	7.3%	5.4%

*
p < 0.002 (critical value after Bonferroni correction)

Table 3

Results of ordinal logistic regression analysis predicting transition time from first cocaine use to dependence onset^a

	Odds Ratio (95% CI)
Female sex	0.86 (0.72–1.02)
Race/ethnicity ^b	
Black/African-American	1.18 (0.95–1.47)
Other non-European-American	1.21 (0.92–1.60)
Conduct disorder	1.56 (1.28–1.90) [*]
Generalized anxiety disorder	2.98 (0.90–9.91)
Major depressive disorder	0.78 (0.55–1.12)
Alcohol dependence	0.53 (0.44–0.64) [*]
Nicotine dependence	0.63 (0.53–0.76) [*]
Opioid dependence	0.27 (0.22–0.32) [*]
Severely physically abused < age 14	1.32 (1.02–1.70) [*]

^{*} p < 0.05;

^a adjusted for age and age at first use;

^b reference group= European-American; 95% CI = 95% confidence intervals

Table 4

Results of ordinal logistic regression analysis predicting transition time from first opioid use to dependence onset^a

	Odds Ratio (95% CI)
Female sex	1.17 (0.99–1.39)
Race/ethnicity ^b	
Black/African-American	1.31 (1.07–1.61) [*]
Other non-European-American	1.22 (0.95–1.58)
Conduct disorder	1.22 (1.02–1.46) [*]
Alcohol dependence	0.54 (0.46–0.65) [*]
Nicotine dependence	0.64 (0.54–0.77) [*]
Cocaine dependence	0.50 (0.42–0.60) [*]
Severely physically abused < age 14	1.50 (1.17–1.91) [*]

^{*} p < 0.05;

^a adjusted for age and age at first use;

^b reference group= European-American; 95% CI = 95% confidence intervals