Published in final edited form as:

J Addict Med. 2014 ; 8(4): 241–248. doi:10.1097/ADM.0000000000000039.

Stimulant Dependence and Stimulant Associated Psychosis: Clinical Characteristics and Age of Onset in a Native American Community Sample

David A. Gilder, MD¹, Ian R. Gizer, PhD², Philip Lau, MA¹, and Cindy L. Ehlers, PhD^{1,3}

¹Molecular and Cellular Neuroscience Department, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037

²Department of Psychological Sciences, University of Missouri, Columbia, MO 65211

³Department of Molecular and Experimental Medicine, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037

Abstract

Objectives—Native Americans experience some of the highest rates of DSM-IV stimulant dependence (SD) of all US ethnic groups. The present report examined the clinical characteristics and age of onset of stimulant use, SD, remission from SD, and stimulant associated psychosis (SAP) in a Native American community sample.

Methods—Demographic information, stimulant (methamphetamine or cocaine) use, and lifetime DSM-IV psychiatric disorder diagnoses were assessed in 858 Native Americans. Logistic regression was used to assess the associations of demographic, stimulant use, and psychiatric disorder variables with SD, remission from SD, and stimulant associated psychosis (SAP). Kaplan-Meier survival analyses were used to assess time from first use to the onset of stimulant dependence.

Results—The overall rate of SD was 33%, of remission from SD 73%, and of SAP 17%. SD was associated with: older age, less current annual household income, fewer lifetime years of education, intravenous stimulant use, and earlier age of first stimulant use. Remission from SD was associated with: older age, currently being married, and never having used stimulants intravenously. ADHD (assessed as a lifetime disorder), increased number of years of daily stimulant use, and intravenous use, were independently associated with SAP. Younger age at first use was significantly associated with shorter survival to the onset of stimulant dependence.

Conclusions—SD is prevalent in this population and is associated with less income and education and an earlier age at first use. Intravenous stimulant use adds additional risk for SD, non-remission, and psychosis.

Corresponding Author: Dr. Cindy L. Ehlers, TSRI, 10550 North Torrey Pines Road SP30-1501, La Jolla, CA 92037 USA, Telephone: (858) 784-7058; Fax: (858) 784-7409; cindye@scripps.edu.

Conflicts of Interest

Dr. David Gilder, Dr. Ian R. Gizer, and Mr. Philip Lau declare no potential conflicts of interest.

Keywords

Stimulant Dependence; Psychosis; Risk Factors; Native Americans

INTRODUCTION

National surveys suggest that rates of stimulant dependence (SD) differ among ethnic groups with Native Americans having among the highest rates of all groups evaluated (Substance Abuse and Mental Health Services Administration [SAMHSA], 2005a,b). Among Native Americans in drug treatment, the rate of primary amphetamine use has been shown to be higher than that for other illicit drugs (Evans et al., 2006). From 1997 to 2004, the number of Indian Health Service outpatient treatment visits attributed to stimulants increased by 30 times (Indian Health Service, 2005). Thus, focusing efforts on understanding the causes of SD in this minority population is critically needed in order to address health disparities.

One factor that appears to influence the development of SD is early age of first use. In the National Household Survey of Drug Abuse, stimulant users who had early onset of use had increased odds of progressing to dependence (Wu and Schlenger, 2003). In addition to early age of first use, other factors, including male gender, Native American ethnicity, being unmarried, low annual household income, and affective, anxiety, and personality disorders, have been shown to be associated with the stimulant dependence and with the transition from first use to dependence (Lopez-Quintero et al., 2011a; Lev-Ran et al., 2013a,b). Further understanding of the role these factors play in the trajectory from first stimulant use to SD and with remission from SD are needed in order to uncover unique genetic and environmental risk factors for the development of and remission from SD.

SD is also frequently accompanied by psychosis (stimulant associated psychosis, (SAP)). It is characterized by paranoid delusional ideation, ideas of reference, and auditory hallucinations (Brady et al., 1991; Grant et al., 2012; Roncero et al., 2012). In clinical samples, the frequency of methamphetamine psychosis ranges from 8–46% (Bramness et al., 2012; Grant et al., 2012) and of cocaine psychosis from 12–100% (Roncero et al., 2012). Greater amounts of cocaine use and intravenous use have been associated with cocaine induced psychosis (Brady et al., 1991; Roncero et al., 2012), but the same relationship is not as clear for methamphetamine associated psychosis (Grant et al., 2012). The rates of and factors associated with SAP in Native American users are unknown.

The present report is part of a larger study exploring risk factors for substance dependence in a Native American community in the west (Ehlers et al., 2004, 2008; Gilder et al., 2007, 2008). The aims of the present study were to: (1) assess the prevalence of SD and demographic, stimulant use, and psychiatric disorder risk factors associated with SD; (2) assess the impact of earlier age of first use on survival from first use to dependence; (3) determine the rate of remission from SD and factors associated with remission; and (4) determine the prevalence of and risk factors for SAP in this high risk Native American sample.

METHODS

Participants

Participants were recruited from eight geographically contiguous reservations with a total population of about 3,000 individuals. Participants were recruited using a combination of a venue-based method for sampling hard-to-reach populations (Kalton and Anderson, 1986; Muhib et al., 2001) as well as a respondent-driven procedure (Heckathorn, 1997). The venues included: tribal halls, health clinics, tribal libraries, and stores on the reservations. Fliers advertising the study were placed in each venue with the telephone number of the tribal recruitment coordinator. The venues were also regularly visited by the tribal recruitment coordinator who approached potential participants to offer information about enrollment in the study. Approximately half of the participants were recruited using each method. A 10–25% rate of refusal using the venue method occurred depending on the venue. The refusal rate in the respondent-driven procedure is not known. Potential participants contacted the tribal recruitment coordinator or the study coordinator at the research facility. At the time, interested participants were given a brief description of the study, were told that transportation would be provided, and were informed as to the amount they would be paid for participation. Individuals who elected to participate by the venue method were encouraged to inform other eligible participants about the study (respondent-driven procedure). Transportation from their home to The Scripps Research Institute was provided by the study. Participants were paid \$100 for their participation.

To be included in the study, participants had to be at least 1/16th Native American Heritage, be between the ages of 18 and 85 years, and be mobile enough to be transported from his or her home to The Scripps Research Institute (TSRI). The protocol for the study was approved by the Institutional Review Board of TSRI, the Scientific Advisory Committee of the General Clinical Research Center, and the Indian Health Council, a tribal review group overseeing health issues for the reservations where recruitment was undertaken. Written informed consent was obtained from each participant after the study was fully explained.

Measures

Each participant completed an interview with the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) (Bucholz et al., 1994), in order to generate Diagnostic and Statistical Manual (DSM) IV diagnoses. The SSAGA has undergone both reliability and validity testing (Bucholz et al., 1994; Hesselbrock et al., 1999) and has been used in another Native American sample (Hesselbrock et al., 2000, 2003). All interviews were reviewed and all best final diagnoses (lifetime prevalence) were made by a research psychiatrist/addiction specialist (DAG).

Demographic information was used construct variables to be used in data analysis. A participant's Native American Heritage (NAH) was calculated from the reported ethnicity of the biological grandparents as 50% vs. < 50%. Years of education was total lifetime years of school attained. Current annual household income was determined as < \$20K vs. \$20K per year, current marital status as married vs. not married, and current employment as employed vs. not employed.

A participant with ≥ 3 SD criteria which occurred in the same 12 month period was diagnosed as having SD. Onset of SD was considered that age at which the participant first had ≥ 3 SD criteria in the same 12 month period. Participants were considered to have remitted from SD if, at the time of assessment, they had ≥ 12 months with no SD criteria (full sustained remission). One year partial sustained remission was also assessed. Participants were considered to have partially remitted if, at the time of assessment, they had ≥ 12 months with one or two SD criteria. Determination was made whether or not the participant had used cocaine and never used methamphetamine, had SD associated with cocaine and not methamphetamine, and had ever used a stimulant intravenously.

The diagnostic category “any affective disorder” was considered positive if a participant had a lifetime history of one or more of the following: major depressive disorder, bipolar I, bipolar II, or dysthymia. The diagnostic category “any anxiety disorder” was considered positive if a participant had a lifetime history of one or more of the following: panic disorder, agoraphobia, social phobia, or obsessive compulsive disorder. The category “any psychotic disorder” was positive if the participant had a lifetime history of one or more of the following: schizophrenia, schizoaffective disorder, brief reactive psychosis, or psychosis not otherwise specified. The category “any potentially psychotic disorder” was positive if the participant had a lifetime history of major depression with psychosis or bipolar I illness. The category “ASPD/CD” was positive if the participant had a history of Antisocial Personality Disorder or Conduct Disorder prior to age 15 years. The category “ADHD” was positive if the participant had Attention Deficit Hyperactivity Disorder prior to age 7 years. These psychiatric disorders were assessed as independent of substance use. Psychotic symptoms induced by stimulant use were also assessed and if they persisted for ≥ 1 month following discontinuation of stimulant use.

Data Analysis

In the entire community sample of 858 individuals, demographic and clinical variables assessing putative risk for SD were compared in the SD and the non-SD groups using the analysis of variance (ANOVA) for continuous variables and 2×2 contingency tables and Fisher’s Exact Test for dichotomous variables. Logistic regression was used to assess the association with SD of age, male gender, NAH $\geq 50\%$, intravenous use, and variables significantly associated with SD in the bivariate comparisons, which were: annual income $< \$20K$, years of education, ASPD/CD, ADHD, and age of first use. In the subsample of individuals who had used a stimulant one or more times in their lives and for whom an age of first use was known ($n=499$), Kaplan-Meier survival analyses were undertaken to assess survival from first use to onset of SD by age of first use groups dichotomized by <13 , 15, 17, 19, and 21 years vs. 13, 15, 17, 19, and 21 years, respectively.

In the sub-sample of individuals who had developed SD ($n=286$), the frequency of one year sustained full remission from SD was assessed. Demographic, substance use, and psychiatric disorder risk variables were compared in the non-remitted vs. remitted groups using the ANOVA for continuous variables and 2×2 contingency tables and Fisher’s Exact Test for dichotomous variables. These variables included those assessed for association with SD and, in addition, whether the participant had received treatment; and the longest period of daily

use in years of stimulants, cannabis, sedatives, opioids, and other drugs, whether the participant had drunk alcohol daily for 1 month. The frequency of partial sustained remission was also assessed.

Finally, the frequency of SAP and demographic, substance use, and psychiatric disorder risk variables potentially associated with SAP were assessed in the subsample of participants who had used stimulants (n=499). The variables included the same demographic and clinical variables assessed for remission. The SAP and non-SAP groups were compared using ANOVA for continuous variables and 2×2 contingency tables and Fisher's Exact Test for dichotomous variables. Age, male gender, NAH $\geq 50\%$, intravenous use, and risk variables found to be associated with SAP in bivariate comparisons (except treatment) were examined using logistic regression for their association with SAP in the presence of covariates. Frequencies of types of psychotic symptoms and whether psychotic symptoms persisted for 1 month following discontinuation of stimulant use were recorded. Demographic, psychiatric and drug use variables that were associated with individual types of psychotic symptoms were analyzed using logistic regression for those symptoms with a sufficient number of endorsers.

All analyses were carried out using SPSS software (version 16, SPSS Inc., Chicago). In all analyses the alpha level (2-tailed) was set at 0.05 and p-values were considered significant if < 0.05 .

RESULTS

The rate of SD in the entire sample of 858 participants was 33.3% (33.1% in men and 33.5% in women). The demographics of the sample are similar to what has been described for these tribes in the 2000–2012 census (US Census Bureau). The stimulant used in this population was primarily methamphetamine and secondarily cocaine. Only 10.6% of stimulant users reported using only cocaine, and only 5.2% of stimulant dependent participants had only cocaine dependence. Most stimulant users reported a nasal route of administration with only 16% of users reporting an intravenous route of administration. Ninety-one percent of those who used stimulants intravenously had SD. Demographic, stimulant use, and psychiatric disorder variables for the entire sample and comparing subgroups with SD vs. without SD are shown in Table 1. As compared to non-SD participants, SD participants had: fewer years of education, lower annual household income, higher NAH, and were more likely to have ASPD/CD and ADHD at an earlier age of stimulant initiation, and were more likely to use stimulants intravenously. Having “any affective disorder” or “any anxiety disorder” was not significantly more frequent in those with SD as compared to those without SD.

Logistic regression was used to assess for associations between SD and: age, gender, age of first use, and other demographic, and psychiatric disorder variables that were significantly associated with SD in the bivariate comparisons. In the entire sample (n=858), older age, lower annual household income, fewer years of education, and earlier age of first use were associated with SD, as seen in Table 2. In the subsample of participants who had used stimulants and for whom an age of first use was known (n=499), Kaplan-Meier survival analyses demonstrated that each earlier age at first use was associated ($p<0.001$) with

shortened survival time to onset of DSM-IV SD, in the presence of censored cases. The survival curves are presented in Figure 1.

The overall rate of one year full sustained remission from SD was 73.4% (70.3% in men; 73.8% in women). Thirteen of the “cocaine only” dependent participants remitted from dependence. Demographic, stimulant use, and psychiatric disorder variables associated (p-value) with remission in bivariate comparisons were: age (0.011), higher annual income (0.030), more years of education (0.023), being married (0.001), and being employed (0.006). Twenty-five percent of users and 41% of those with SD sought treatment. The types of treatment reported were: Narcotics Anonymous or other self-help group, outpatient drug free program, other outpatient program, inpatient drug-free program, inpatient admission for medical complications, and other programs. Those who sought treatment were not more likely to remit than those who did not seek treatment. The results of logistic analyses of the association of remission with age, gender, NAH, intravenous use and variables associated with remission in the bivariate analyses can be seen in Table 3. Older age, being married, and not having used intravenously were associated with remission. Only 6 participants experienced partial sustained remission.

The rate of SAP in the subsample of those who had used stimulants (n=499) was 16.6%. Of the “cocaine only” stimulant users, 2 (13%) experienced cocaine associated psychotic symptoms. Of those participants who used intravenously, 30 (36.6%) developed SAP. A comparison of the group of participants with SAP to the group without SAP, within the subsample of those participants who had ever used stimulants was conducted. These analyses used the same demographic, stimulant use, and psychiatric disorder variables used for remission as well as additional substance use variables, including the largest number of years of daily use of stimulants, sedatives, opioids, other drugs, cannabis, and alcohol. As compared to stimulant users who did not develop SAP, those who did (p-value) were more likely to be male (0.015); to have fewer years of education (< 0.001); to have ASPD/CD (0.001) and ADHD (0.001); to have a longer duration of total years of daily use of stimulants (0.001), sedatives (0.009), and “other” drugs (0.028), to have used intravenously (p<0.001), and to have undergone treatment (p<0.001). Any psychotic illness, any potentially psychotic illness, and any psychotic or potentially psychotic illness, and larger number of total years of daily use of opioids, cannabis, and alcohol were not associated with SAP. When age, gender, NAH, intravenous use, and those variables significantly associated with SAP in the bivariate comparisons were assessed for association with SAP in the presence of covariates using logistic regression, intravenous use, ADHD, and total years of daily use of stimulants remained significantly associated with SAP, as seen in Table 4.

Eighty-three participants experienced 1 stimulant associated psychotic symptom, the criterion for diagnosing SAP. Thus, 16.6% of those who had used stimulants and 29% of those with SD experienced SAP. Frequencies of types of psychotic symptoms in the 83 participants who experienced SAP were as follows: auditory hallucinations, 77%; 2 voices talking to each other, 69%; visual hallucinations, 67%; tactile hallucinations, 14%; olfactory hallucinations, 6%; receiving special messages, 16%; delusions of reference, 56%; delusions of grandiosity, 16%; somatic delusions, 6%; persecutory delusions, 36%; delusions of guilt, 13%; delusions of thought control, 11%; delusions of thought insertion, 11%; delusions of

thought withdrawal, 1%; and delusions of thought broadcasting, 10%. Using intravenously ($p<0.03$) was significantly associated with a higher likelihood of having persecutory delusions. Having ASPD/CD ($p<0.024$) increased the likelihood of experiencing delusions of reference. More years of daily cannabis use ($p<0.01$) was associated with less likelihood of reporting that 2 or more voices were talking to each other.

Sixty-three cases of SAP had sufficient data to assess whether or not their SAP persisted for 1 month following discontinuation of stimulants; of these, four (7%) of cases persisted for one month or more after stopping stimulants. None of the four had an independent psychotic or potentially psychotic diagnosis.

DISCUSSION

The lifetime rate of SD of 33.0% in this Native American community sample is higher than that found for stimulants in an epidemiologic study (Compton et al., 2005). The higher rate in this sample is consistent with data from epidemiologic and survey sources that methamphetamine use has impacted Native American, western U.S., and rural dwelling peoples at rates higher than most other ethnicities, U.S. locations, and metropolitan areas of the country (SAMHSA, 2005b, 2011; Indian Health Services, 2009; Forcehimes et al., 2011; Johnston et al., 2011).

The results of this study are also consistent with Compton et al. (2005) findings from the NESARC that amphetamine (though not cocaine) dependence is equally common in men and women. In this community sample, older age was associated with SD, which may represent a cohort effect, i.e. that the older participants in this study were in the young adult age of risk during a time period when methamphetamine manufacture, availability, and use was higher than it is today in the areas from which this sample was drawn. SD was associated with lower annual household income and fewer years of education. Low household income and less education may be associated with SD because it disrupts work and school performance. In this Native American sample, SD was not associated with having ASPD/CD, which is inconsistent with findings from the NESARC, in which both cocaine and amphetamine dependence were associated with ASPD, though neither was associated with CD considered separately from ASPD (Compton et al., 2005). In this sample, affective and anxiety disorders were not associated with SD. This is in contrast to epidemiologic findings in the NESARC (Conway et al., 2006) that affective and anxiety disorders are comorbid with both amphetamine and cocaine dependence. However, we have demonstrated previously that this sample of Native Americans has low base rates of anxiety and affective disorders despite having high rates of substance use. We also have suggested previously that this population may have protective factors for these disorders.

In this sample, earlier age of first stimulant use was associated with SD. The mean age of first stimulant use was 18.9 years, younger than ages of first use for cocaine (20.3 years) and amphetamine (23.0 years) reported in the 2006 NSDUH (SAMHSA, 2007). In a study of findings from three Los Angeles area high risk programs (Dickerson et al., 2012), the mean age of first amphetamine use in Native Americans was 19.7 years, younger than all other racial and ethnic groups, and closer to the age of first stimulant use found in this sample.

The rate of sustained full remission from SD in this sample (73% in the total sample; 70.3% in men; 73.8% in women) was substantial. This rate is consistent with a reported epidemiological rate of 84.6% for remission from cocaine dependence in Native Americans (Lopez-Quintero, 2011b) and 74% from a North American high income methamphetamine sample (Calabria et al., 2010). History of treatment for a drug problem was not associated with remission, which is consistent with previous studies of remission from alcohol (Gilder et al., 2008) and cannabis (Gilder et al., 2007) in samples from the same population from which the current study sample was drawn. ASPD/CD was not associated with remission in this study, suggesting that the risk factors for SD represented by antisocial disorders do not militate against remission.

Seventeen percent of those who had used stimulants and 29.0% of those with SD experienced SAP. These rates are similar to the range of rates 8–46% reported in non-Native American methamphetamine using and dependent individuals (Smith et al., 2009; Grant et al., 2012) and cocaine using and dependent individuals (Smith et al., 2009; Roncero et al., 2012). In previous studies, SAP is associated with several putative risk factors: gender, early use, quantity of use, severity of dependence, other substance use and dependence, ASPD, major depression, other psychiatric illness, ADHD, premorbid schizoid or schizotypal traits, and a family history positive for psychiatric illness (Chen et al., 2003; McKetin et al., 2006; Salo et al., 2008, 2011; Smith et al., 2009; Grant et al., 2012; Roncero et al., 2012). In the present study, ADHD, more years of daily use of stimulants, and intravenous use were associated with SAP. Unlike an Australian urban community study of methamphetamine users (McKetin et al., 2006), there was no association of an independent psychotic disorder diagnosis with SAP in this study. The association of SAP with ADHD may result from individuals with ADHD being more likely to self-medicate with illicit stimulants or higher doses of illicit stimulants and/or may result from a pre-existing vulnerability to SAP represented by childhood ADHD, as suggested by Salo et al. (2008). In this study, SAP appears to be specifically associated with stimulant use and not other substance, including cannabis, use. The rates of individual stimulant associated psychotic symptoms seen in this population appear to be similar to the rates in reported in community (McKetin et al., 2006) and treatment studies of non-Native American methamphetamine (Iwanami et al., 1994; Chen et al., 2003) and cocaine (Brady et al., 1991) users and dependent individuals.

CONCLUSIONS

SD is prevalent in this population and is associated with older age, less income, less education, and earlier age of first use. High rates of spontaneous remission are seen. Remission is associated with being older, being married, and not having used stimulants intravenously. SAP is associated with ADHD, greater years of continuous daily use, and intravenous use. Individual, family, and community prevention efforts aimed at reducing and delaying use of stimulants by youth and intravenous use in all age groups are rational strategies to decrease stimulant addiction and psychosis in this, and perhaps other, populations. Risk factors for SD, remission, and SAP appear to be similar to those that have been reported for the general population. Further efforts that focus on understanding the causes of SD in this minority population are critically needed in order to address the health disparities seen in this high-risk population. However, the results of this study should be

interpreted in light of several limitations. First, our findings may not generalize to other Native Americans in the population from which the sample was drawn. The selection process was not random, and we have no information on those who refused to participate. For the same reason our findings may not generalize to other tribes living in the general geographic area from where the current sample was drawn or to other Native American tribes. In addition, comparison of our findings with those of NESARC is for reference only as our study is not matched to those studies for region, urbanicity, age, or socioeconomic status. Secondly, we used cross-sectional and retrospective data, and longitudinal studies may identify different risk variables for the disorder. Third, we acknowledge that a judgment about the real-world, as opposed to the purely statistical, significance of any variable associated with SD, remission, or SAP is important, particular when using these or any research findings to design intervention and prevention strategies.

Acknowledgments

The authors thank Greta Berg, Linda Corey, Anita Desikan, Susan Lopez, Evelyn Phillips, Shirley Sanchez, Gina Stouffer, and Derek Wills for assistance in data collection and analysis.

Sources of Funding

Dr. Ehlers work has been funded by the NIH. She has received compensation as a consultant from Neurocrine Biosciences and Raptor Pharmaceutical Corp. in capacities not related to the subject of the report. National Institutes of Health (NIH) funding for this study was provided by the National Institute on Alcoholism and Alcohol Abuse (NIAAA) AA010201 and the National Institute of Drug Abuse (NIDA) DA030976

REFERENCES

- Brady KT, Lydiard RB, Malcolm R, Ballenger JC. Cocaine-induced psychosis. *J Clin Psychiatry*. 1991; 52:509–512. [PubMed: 1752853]
- Bramness JG, Gundersen OH, Guterstam J, et al. Amphetamine-induced psychosis--a separate diagnostic entity or primary psychosis triggered in the vulnerable? *BMC Psychiatry*. 2012; 12:221. [PubMed: 23216941]
- Bucholz KK, Cadoret R, Cloninger CR, et al. A new, semi-structured psychiatric interview for use in genetic linkage studies: a report on the reliability of the SSAGA. *J Stud Alcohol*. 1994; 55:149–158. [PubMed: 8189735]
- Calabria B, Degenhardt L, Briegleb C, et al. Systematic review of prospective studies investigating "remission" from amphetamine, cannabis, cocaine or opioid dependence. *Addict Behav*. 2010; 35:741–749. [PubMed: 20444552]
- Chen CK, Lin SK, Sham PC, et al. Pre-morbid characteristics and co-morbidity of methamphetamine users with and without psychosis. *Psychol Med*. 2003; 33:1407–1414. [PubMed: 14672249]
- Compton WM, Conway KP, Stinson FS, Colliver JD, Grant BF. Prevalence, correlates, and comorbidity of DSM-IV antisocial personality syndromes and alcohol and specific drug use disorders in the United States: results from the national epidemiologic survey on alcohol and related conditions. *J Clin Psychiatry*. 2005; 66:677–685. [PubMed: 15960559]
- Conway KP, Compton W, Stinson FS, Grant BF. Lifetime comorbidity of DSM-IV mood and anxiety disorders and specific drug use disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry*. 2006; 67:247–257. [PubMed: 16566620]
- Dickerson DL, Fisher DG, Reynolds GL, Baig S, Napper LE, Anglin MD. Substance use patterns among high-risk American Indians/Alaska Natives in Los Angeles County. *Am J Addict*. 2012; 21:445–452. [PubMed: 22882395]
- Ehlers CL, Wall TL, Betancourt M, Gilder DA. The clinical course of alcoholism in 243 Mission Indians. *Am J Psychiatry*. 2004; 161:1204–1210. [PubMed: 15229052]

- Ehlers CL, Gilder DA, Phillips E. P3 components of the event-related potential and marijuana dependence in Southwest California Indians. *Addict Biol.* 2008; 13:130–142. [PubMed: 18201292]
- Evans E, Spear SE, Huang YC, Hser YI. Outcomes of drug and alcohol treatment programs among American Indians in California. *Am J Public Health.* 2006; 96:889–896. [PubMed: 16571710]
- Forcehimes AA, Venner KL, Bogenschutz MP, et al. American Indian methamphetamine and other drug use in the Southwestern United States. *Cultur Divers Ethnic Minor Psychol.* 2011; 17:366–376. [PubMed: 21988577]
- Gilder DA, Lau P, Corey L, Ehlers CL. Factors associated with remission from cannabis dependence in southwest California Indians. *J Addict Dis.* 2007; 26:23–30. [PubMed: 18032229]
- Gilder DA, Lau P, Corey L, Ehlers CL. Factors associated with remission from alcohol dependence in an American Indian community group. *Am J Psychiatry.* 2008; 165:1172–1178. [PubMed: 18519526]
- Grant KM, LeVan TD, Wells SM, et al. Methamphetamine-associated psychosis. *J Neuroimmune Pharmacol.* 2012; 7:113–139. [PubMed: 21728034]
- Heckathorn DD. Respondent-driven sampling: a new approach to the study of hidden populations. *Soc Probl.* 1997; 44:174–199.
- Hesselbrock M, Easton C, Bucholz KK, Schuckit M, Hesselbrock V. A validity study of the SSAGA--a comparison with the SCAN. *Addiction.* 1999; 94:1361–1370. [PubMed: 10615721]
- Hesselbrock MN, Hesselbrock VM, Segal B, Schuckit MA, Bucholz K. Ethnicity and psychiatric comorbidity among alcohol-dependent persons who receive inpatient treatment: African Americans, Alaska Natives, Caucasians, and Hispanics. *Alcohol Clin Exp Res.* 2003; 27:1368–1373. [PubMed: 12966342]
- Hesselbrock VM, Segal B, Hesselbrock MN. Alcohol dependence among Alaska Natives entering alcoholism treatment: a gender comparison. *J Stud Alcohol.* 2000; 61:150–156. [PubMed: 10627109]
- Indian Health Services. Rockville, MD: U.S. Department of Health and Human Services; 2005. Resources and Patient Management System. Retrieved from: <http://www.ihs.gov/RPMS/index.cfm?module=home&option=otherdocuments> [Accessed 02/19/14]
- Indian Health Service. Rockville, MD: U.S. Department of Health and Human Services; 2009. Trends in Indian Health 2002–2003 Edition. Retrieved from: http://www.ihs.gov/dps/files/Trends_02-03_Brochure.pdf [Accessed 02/19/14]
- Iwanami A, Sugiyama A, Kuroki N, et al. Patients with methamphetamine psychosis admitted to a psychiatric hospital in Japan. A preliminary report. *Acta Psychiatr Scand.* 1994; 89:428–432. [PubMed: 8085475]
- Johnston, LD.; O'Malley, PM.; Bachman, JG. Ann Arbor, MI: Institute for Social Research, The University of Michigan; 2011. Monitoring the Future National Survey Results on Drug Use, 1975–2002: Volume II, College Students and Adults 19–40. (NIH Publication No. 03-5376). Supported by NIDA. Retrieved from: http://www.monitoringthefuture.org/pubs/monographs/mtf-vol2_2010.pdf [Accessed 02/19/14]
- Kalton G, Anderson DW. Sampling rare populations. *J Roy Stat Soc.* 1986; 149:65–82.
- Lev-Ran S, Imtiaz S, Rehm J, Le FB. Exploring the association between lifetime prevalence of mental illness and transition from substance use to substance use disorders: results from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC). *Am J Addict.* 2013a; 22:93–98. [PubMed: 23414492]
- Lev-Ran S, Le SY, Imtiaz S, Rehm J, Le FB. Gender differences in prevalence of substance use disorders among individuals with lifetime exposure to substances: results from a large representative sample. *Am J Addict.* 2013b; 22:7–13. [PubMed: 23398220]
- Lopez-Quintero C, Hasin DS, de Los Cobos JP, et al. Probability and predictors of remission from lifetime nicotine, alcohol, cannabis or cocaine dependence: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Addiction.* 2011b; 106:657–669. [PubMed: 21077975]
- Lopez-Quintero C, Perez de Los CJ, Hasin DS, et al. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National

- Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Drug Alcohol Depend. 2011a; 115:120–130. [PubMed: 21145178]
- McKetin R, McLaren J, Lubman DI, Hides L. The prevalence of psychotic symptoms among methamphetamine users. Addiction. 2006; 101:1473–1478. [PubMed: 16968349]
- Muhib FB, Lin LS, Stueve A, et al. A venue-based method for sampling hard-to-reach populations. Public Health Rep. 2001; 116(Suppl 1):216–222. [PubMed: 11889287]
- Roncero C, Ros-Cucurull E, Daigre C, Casas M. Prevalence and risk factors of psychotic symptoms in cocaine-dependent patients. Actas Esp Psiquiatr. 2012; 40:187–197. [PubMed: 22851479]
- Salo R, Nordahl TE, Leamon MH, et al. Preliminary evidence of behavioral predictors of recurrent drug-induced psychosis in methamphetamine abuse. Psychiatry Res. 2008; 157:273–277. [PubMed: 17928066]
- Salo R, Flower K, Kielstein A, Leamon MH, Nordahl TE, Galloway GP. Psychiatric comorbidity in methamphetamine dependence. Psychiatry Res. 2011; 186:356–361. [PubMed: 21055832]
- Smith MJ, Thirithalli J, Abdallah AB, Murray RM, Cottler LB. Prevalence of psychotic symptoms in substance users: a comparison across substances. Compr Psychiatry. 2009; 50:245–250. [PubMed: 19374969]
- Substance Abuse and Mental Health Services Administration (SAMHSA). Rockville, MD: Office of Applied Studies, U.S. Department of Health and Human Services; 2005a. DASIS Report: Substance Abuse Treatment Admissions among American Indians and Alaska Natives: 2002. Retrieved from: <http://www.drugabusestatistics.samhsa.gov/2k5/IndianTX/IndianTX.pdf> [Accessed 02/19/14]
- Substance Abuse and Mental Health Services Administration (SAMHSA). Rockville, MD: Office of Applied Studies, SAMHSA, U.S. Department of Health and Human Services; 2005b. The NSDUH Report: Methamphetamine Use, Abuse and Dependence: 2002, 2003, and 2004. Retrieved from: <http://oas.samhsa.gov/2k5/meth/meth.pdf> [Accessed 02/19/14]
- Substance Abuse and Mental Health Services Administration (SAMHSA). Rockville, MD: Office of Applied Studies, U.S. Department of Health and Human Services; 2007. Results from the 2006 National Survey on Drug Use and Health: National Findings. NSDUH Series H-32, DHHS Publication No. SMA-07-4293. Retrieved from: <http://www.samhsa.gov/data/nsduh/2k6nsduh/2k6results.pdf> [Accessed 02/19/14]
- Substance Abuse and Mental Health Services Administration (SAMHSA). Rockville, MD: Office of Applied Studies, U.S. Department of Health and Human Services; 2011. Substance Use among American Indian or Alaska Native Adolescents. Retrieved from: http://www.samhsa.gov/data/2k11/WEB_SR_005/SubsUse_Among_AmInd_NatAlsk_Adlscent.pdf [Accessed 02/19/14]
- U.S. Census Bureau. [Accessed 02/19/14] 2000 and 2010 Censuses and the 2005 – 2009 and 2008 – 2012 American Community Survey 5-Year Estimates. Retrieved from: <http://www.census.gov/>
- Wu LT, Schlenger WE. Psychostimulant dependence in a community sample. Subst Use Misuse. 2003; 38:221–248. [PubMed: 12625429]

Survival analysis of age onset stimulant use to the development of stimulant dependence

Figure. 1.

The graphs exhibit the cumulative survival rates between 2 groups of subjects: those who first used stimulants before the age 13, 15, 17, 19, and 21 years versus those who first stimulants after age 13, 15, 17, 19, 21 years, respectively. The cumulative survival rate is the proportion of subjects within the group who survive (i.e. have not developed stimulant dependence) at different points in time after the subjects' first exposure to stimulants. The survival curves of the older stimulant consumption group are consistently above ($p < 0.001$) those of the younger group, and their survival curves diverge farther and farther as time progresses. These graphs clearly indicate that subjects who consume stimulants at a later age are more likely to survive without stimulant dependence than those who consume stimulants at an earlier age.

Table 1
Demographic, stimulant use, and psychiatric disorder variables in an American Indian community sample comparing those with and those without DSM-IV stimulant dependence (n = 858)

Demographic or Clinical Variable	Total Sample n = 858	Stimulant Dependent n = 286	Non- Stimulant Dependent n = 572	p-value
	mean (SD)	mean (SE)	mean (SE)	
Age range = 18–82 years (n = 858)	31.2 (13.2)	32.2 (0.6)	30.7 (0.6)	0.112
Years of education range = 3–17 years (n=857)	11.6 (1.6)	11.2 (0.1)	11.8 (0.1)	<0.001
Age of first use range = 9–55 years (n = 499)	18.9 (6.0)	18.1 (0.4)	19.9 (0.4)	0.001
	n (%)	n (%)	n (%)	Fisher Exact Test p-value
Gender (n = 858)				
Male	357 (41.6)	118 (41.3)	239 (41.8)	0.941
Annual income (n = 795)				
< \$20,000/year	362 (45.5)	147 (54.6)	215 (40.9)	<0.001
Any employment (n = 832)				
Yes	319 (38.3)	93 (34.7)	226 (40.1)	0.147
Married (n = 856)				
Yes	141 (16.5)	56 (19.6)	85 (14.9)	0.079
NAH 50% or greater (n = 858)				
Yes	355 (41.4)	132 (46.2)	223 (39.0)	0.047
ASPD/CD (n = 858)				
Yes	152 (17.8)	78 (27.3)	74 (12.9)	<0.001
ADHD (n = 858)				
Yes	88 (10.3)	38 (13.3)	50 (8.7)	0.043
Any Affective Disorder (n = 858)				
Yes	198 (23.1)	72 (25.2)	126 (22.0)	0.304
Any Anxiety Disorder (n = 858)				
Yes	116 (13.5)	41 (14.3)	75 (13.1)	0.672
Any Affective or Anxiety Disorder (n = 858)				

Demographic or Clinical Variable	Total Sample n = 858	Stimulant Dependent n = 286	Non- Stimulant Dependent n = 572		
Yes	262 (30.5)	92 (32.2)	170 (29.7)	0.7–1.6	0.480
Intravenous Stimulant Use (n = 499)					
Yes	82 (16.4)	75 (26.2)	7 (1.2)	4.7–23.2	<0.001

NAH = Native American Heritage, which is calculated from reported ethnicity of paternal and maternal biological grandparents. ASPD/CD = having a history of either Adult Antisocial Personality Disorder or Conduct Disorder with onset prior to 15 years of age. ADHD = having a history of Attention-Deficit/Hyperactivity Disorder with onset prior to 7 years of age.

Table 2

Logistic regression (n=858) analysis of demographic, stimulant use, and psychiatric disorder variables associated with DSM-IV stimulant dependence in an American Indian community sample.

Independent Variable/Factor	B	S.E.	Odds Ratio	p-value
Age	0.03	0.01	1.03	0.01
Male Gender	-0.22	0.21	0.81	0.30
NAH 50% or greater	0.14	0.20	1.15	0.48
Annual Income < \$20K	0.49	0.20	1.64	0.01
Fewer years of education	0.16	0.07	1.18	0.01
ASPD/CD	0.41	0.26	1.51	0.11
ADHD	0.22	0.36	1.25	0.54
Earlier age of first use (as a continuous variable)	0.08	0.02	1.08	<0.001

Multivariate logistic regression was used to assess the association of stimulant dependence (as the outcome variable) with the following independent variables or factors entered into the initial model: age, male gender, Native American Heritage (NAH) 50%, annual income < \$20K, fewer years of education, ASPD/CD, ADHD, and earlier age of first use as a continuous variable (as independent variables). Significance was set at $p < 0.05$.

Table 3

Logistic regression analyses of demographic, stimulant use, and psychiatric disorder variables associated with one year full sustained remission from DSM-IV stimulant dependence in an American Indian community sample (n = 286).

Independent Variable/Factor	B	S.E.	Odds Ratio	p-value
Age	0.04	0.02	1.04	0.01
Male Gender	-0.01	0.31	0.99	0.98
NAH 50% or greater	0.12	0.31	1.13	0.69
Annual Income < \$20K	-0.34	0.32	0.71	0.28
Fewer years of education	-0.15	0.09	0.11	0.86
Married	1.45	0.54	4.27	0.01
Employed	0.58	0.35	1.79	0.09
Intravenous use	-1.01	0.36	0.36	0.01

Multivariate logistic regression was used to assess the association of remission from stimulant dependence (as the outcome variable) with the following independent variables or factors entered into the initial model: age, male gender, Native American Heritage (NAH) 50%, annual income < \$20K, fewer years of education, being married, being employed, and intravenous use as independent variables. Significance was set at $p < 0.05$.

Table 4

Logistic regression analyses of demographic, stimulant use, and psychiatric disorder variables associated with stimulant associated psychosis in an American Indian community sample (n = 499).

Independent Variable/Factor	B	S.E.	Odds Ratio	p-value
Age	−0.01	0.02	0.99	0.71
Male Gender	0.27	0.27	1.31	0.32
NAH 50% or greater	−0.15	0.26	0.86	0.58
ADHD	1.08	0.35	2.93	<0.01
Earlier age of first use	−0.01	0.03	1.01	0.85
Years of continuous daily stimulant use	0.07	0.03	1.07	0.03
Intravenous use	1.21	0.31	3.35	<0.001

Multivariate logistic regression was used to assess the association of stimulant associated psychosis (as the outcome variable) with the following independent variables or factors entered into the initial model: age, male gender, Native American Heritage (NAH) 50%, ADHD, earlier age of first use, years of continuous daily stimulant use, and intravenous use as independent variables. Significance was set at $p < 0.05$.