



Research paper

Reciprocal relationships between substance use and disorders and suicidal ideation and suicide attempts in the Collaborative Study of the Genetics of Alcoholism



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ABSTRACT

Background: Substance use and misuse and suicidal thoughts and behaviors tend to co-occur. The purpose of this study was to examine whether (a) suicidal ideation and attempt are related to onset of alcohol, nicotine and cannabis use and dependence; (b) early use of alcohol, nicotine and cannabis is associated with onset of suicidal ideation and attempt; and (c) whether these associations persist while controlling for covariates, such as family history of alcohol problems, major depression and other internalizing and externalizing disorders.

Methods: The prospective cohort of the Collaborative Study of the Genetics of Alcoholism (COGA; N=3277) was used. Cross-sectional and discrete time logistic regression (i.e. survival) analyses examined associations between suicidal ideation and attempt and onset of alcohol, nicotine and cannabis use and dependence. Survival models also examined whether individual early substance use was related to onset of ideation and attempt.

Results: Ideation was related to 0.71–0.77 odds of onset of subsequent alcohol, nicotine and cannabis use. Attempt was associated with 1.44–1.61 odds of later alcohol, nicotine and cannabis dependence, even after accounting for covariates. Evidence for early substance use being related to subsequent onset of ideation or attempt was limited. Several sex and race differences emerged.

Limitations: The sample was ascertained for family history of alcoholism; not all participants had been followed up allowing for censored observations; reporting bias.

Conclusion: Suicide attempts are associated with increased likelihood of onset of substance dependence.

1. Introduction

Suicide is the second leading cause of death in individuals aged 15–29 years (World Health Organization, 2016). In the United States, rates of documented suicide have increased by 24% between 1999 and 2014

(Curtin et al., 2016). A history of past suicide attempts (SA) are among the most prominent risk factors leading to suicide death and, in and of themselves, contribute to approximately \$33,000 in health care and disability costs per attempt (Palmer et al., 1995; Shepard et al., 2015). According to data from the National Comorbidity Survey, about 4.6% of

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U.S. adults report SA (Kessler et al., 1999); however, a more considerable proportion, 13.5%, report a lifetime history of suicidal ideation (SI; Nock et al., 2008). SI often precedes SA. However, many SAs occur in the absence of significant SI and indeed, the etiology of SI and SA have been characterized to be partially distinct (Nock et al., 2016). Some have posited that SA, in the absence of SI, may reflect a liability to impulsive behaviors (Conner et al., 2006; Rimkeviciene et al., 2015; Turecki, 2005), risk for which may be exacerbated in those with a family history of substance use.

Alcohol, nicotine and cannabis use and use disorders have been inconsistently linked to both SI (Nock et al., 2008) and SA (Borges and Loera, 2010). For instance, alcohol use and related problems during adolescence and early adulthood have been prospectively linked to SI (Fergusson et al., 2013) and, cross-sectionally, to SI and SA (Darvishi et al., 2015). Current smoking is associated with SI and SA as well (Poorolajal et al., 2016). Studies have also found that smokers with severe nicotine dependence are more likely than non-smokers to report more frequent and serious SA (Berlin et al., 2015; Lopez-Castroman et al., 2016). Some longitudinal studies have found profound elevations in risk for SI and SA in chronic, heavy and early-onset cannabis users (Delforterie et al., 2015; Silins et al., 2014; van Ours et al., 2013) while other studies have attributed these associations to confounding measures (Price et al., 2009), thus the evidence is inconclusive (Borges et al., 2016). In contrast to this literature, little is known about whether SI and SA are themselves associated with the onset of substance use and substance use disorders. While rates of substance use and use disorders are typically elevated in individuals reporting suicidal thoughts and behaviors, such associations have been primarily attributed to possible pathways that lead from substance use to SI and SA, and evidence for reverse “causality” (i.e. SI/SA leading to increased substance involvement) has not been supported by a limited longitudinal literature (e.g. Covey et al., 2012; van Ours et al., 2013).

The present study examines reciprocal associations between substance involvement (alcohol, nicotine and cannabis use and dependence) and SI and SA in a longitudinal cohort which was partially derived from families at high genetic risk for alcohol use disorders. In a sample of 3277 participants, we examined the extent to which early substance use was associated with subsequent onset of SI and SA, and conversely, whether SI and SA that preceded onset of substance involvement was associated with alcohol, nicotine and cannabis use and dependence.

2. Methods and materials

2.1. Sample

Data were drawn from the baseline through 10-year follow-up data collection conducted with the prospective cohort of the Collaborative Study of the Genetics of Alcoholism (COGA), which is characterized in detail elsewhere (Bucholz et al., 2017). Briefly, the parent COGA study (Begleiter et al., 1995; Reich, 1996) aimed to delineate the genetic and environmental underpinnings of alcoholism and comorbid psychiatric disorders. High risk families were identified through probands who were in inpatient or outpatient clinics for alcohol problems; families with 2 additional relatives with alcoholism were further prioritized. Control families were ascertained from a variety of sources (e.g., driver's license records) and alcoholism was not an exclusion criterion. First degree relatives and, in some cases, members from the extended pedigree, were interviewed. The prospective component of COGA is an ongoing data collection project that aims to understand the impact of genes and environment on substance use and related milestones in youth and young adults, most of whom (86.7%) are at high familial risk for alcoholism. In 2005, adolescent and young adult offspring born from 1982 onwards were recruited from alcoholic and control COGA families described above. The prospective study was designed to be conducted on offspring of ages 12–22 years at their baseline assess-

ment, with at least one parent who was interviewed in the first phases of the parent COGA study. Subsequent assessments occur every two years with data available on 3277 participants (aged 12–26 years; there were some offspring who required repeat tracking and multiple invitations over several years to participate in the baseline interview and as a result 1.3% of offspring were older than age 22 at their first interview). Currently, 2759, 2238, 1733, 1093 and 409 individuals have participated in the 2, 4, 6, 8 and 10 year follow-ups respectively, reflecting data collected between January 2005 and June 2016. For the present study, we used all available data, across all interviews, such that as long as individuals had participated in the baseline, their data were included.

2.2. Measures

Substance use, DSM-IV (American Psychiatric Association, 1994) diagnosis of alcohol, nicotine and cannabis dependence and of other psychiatric disorders (as well as covariates) and measures of suicidal thoughts and behaviors were assessed using the child and adult versions of the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA; Bucholz et al., 1994; Hesselbrock et al., 1999). The assessment is available at: (https://zork.wustl.edu/niaaa/coga_instruments/resources.html).

2.3. Substance use

Respondents were queried about whether they had ever used alcohol, tobacco cigarettes (i.e. nicotine) or cannabis. Those who had used each substance were further asked to recall the age at which they had first used the substance. For all three substances, the median age of onset was 16 years. For analyses (i.e. model 1) in which SI or SA were the dependent variables, early substance use was defined as onset of each substance prior to age 15, based on the bottom quartile of the distribution of ages of onset. Supplemental Fig. S1A–S1C show the distribution of ages of onset for each substance.

2.4. Substance dependence

DSM-IV criteria, assessed with the SSAGA, were used to ascertain lifetime history of alcohol, nicotine and cannabis dependence.

2.5. Suicidal ideation and attempt

All participants were queried about (a) whether they had “ever thought about taking their own life” (ideation: SI) and (b) whether they had “ever tried to kill” themselves (attempt: SA). SA was queried regardless of a history of SI. Importantly, SI and SA items were not nested within the diagnostic section for major depressive disorder (MDD) although individuals who reported SI and SA in that section were coded accordingly as having reported the behavior. For the current analyses, individuals reporting any SA (e.g. even those reporting drug-related SA, 14%) were included. The distribution of ages of onset for SI and SA are shown in Supplemental Figs. S2A and S2B respectively.

2.6. Other covariates

Several additional variables were included to adjust the association between substance use, dependence, SI and SA. These included (a) demographic factors (self-reported sex, African-American ancestry (race), Hispanic ethnicity, and age at last assessment wave (range 12 – 33 years, coded as a median split at 22 years); (b) family history of alcohol use disorder (neither parent, mother only, father only, or both parents); (c) psychiatric disorders, including those broadly defined as externalizing (meeting criteria for any one of the following: conduct, oppositional defiant, or the hyperactivity-impulsivity component of

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