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 subsequent onset of ideation or attempt. Survival models also examined whether individual early substance use was related to subsequent onset of ideation or 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
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; Rimokh, 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 assessment, 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 Figs. 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
Table 1
Demographics and Rates of Suicidal Ideation, Suicide Attempt, and Substance Use and Dependence, across all interviews (N=3277).

<table>
<thead>
<tr>
<th>Race</th>
<th>Gender</th>
<th>All Subjects (N=3277)</th>
<th>European-American (N=2296)</th>
<th>African-American (N=981)</th>
<th>p</th>
<th>Male (N=1615)</th>
<th>Female (N=1662)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline, mean (SD)</td>
<td>Age at last assessment, mean (SD)</td>
<td>16.1 (3.3)</td>
<td>21.7 (5.0)</td>
<td>16.0 (3.3)</td>
<td>21.6 (4.8)</td>
<td>0.1510</td>
<td>16.0 (3.3)</td>
<td>21.3 (4.9)</td>
</tr>
<tr>
<td>Male, %</td>
<td>49.3</td>
<td>49.1</td>
<td>49.7</td>
<td>0.7293</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>African-American, %</td>
<td>29.9</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>30.2</td>
<td>29.7</td>
<td>0.7293</td>
<td>–</td>
</tr>
<tr>
<td>Hispanic, %</td>
<td>6.7</td>
<td>5.7</td>
<td>9.2</td>
<td>0.0002</td>
<td>7.9</td>
<td>5.6</td>
<td>0.0090</td>
<td>–</td>
</tr>
<tr>
<td>Lifetime suicidal thoughts and behaviors</td>
<td>Suicidal ideation, %</td>
<td>30.2</td>
<td>31.6</td>
<td>27.1</td>
<td>0.0104</td>
<td>25.9</td>
<td>34.4</td>
<td>0.0001</td>
</tr>
<tr>
<td>Suicide attempt, %</td>
<td>5.8</td>
<td>5.6</td>
<td>6.3</td>
<td>0.4278</td>
<td>4.0</td>
<td>7.6</td>
<td>0.0001</td>
<td>–</td>
</tr>
<tr>
<td>Lifetime substance use and use disorders</td>
<td>Alcohol use, %</td>
<td>80.3</td>
<td>81.2</td>
<td>78.3</td>
<td>0.0561</td>
<td>79.8</td>
<td>80.8</td>
<td>0.4752</td>
</tr>
<tr>
<td>Alcohol dependence, %</td>
<td>13.3</td>
<td>15.2</td>
<td>8.9</td>
<td>&lt; 0.0001</td>
<td>14.6</td>
<td>12.1</td>
<td>0.0339</td>
<td>–</td>
</tr>
<tr>
<td>Nicotine use, %</td>
<td>46.6</td>
<td>50.3</td>
<td>37.7</td>
<td>&lt; 0.0001</td>
<td>51.1</td>
<td>42.2</td>
<td>&lt; 0.0001</td>
<td>–</td>
</tr>
<tr>
<td>Early nicotine use, %</td>
<td>14.7</td>
<td>16.6</td>
<td>10.5</td>
<td>&lt; 0.0001</td>
<td>14.8</td>
<td>14.7</td>
<td>0.9243</td>
<td>–</td>
</tr>
<tr>
<td>Nicotine dependence, %</td>
<td>20.0</td>
<td>22.0</td>
<td>15.3</td>
<td>&lt; 0.0001</td>
<td>22.9</td>
<td>17.2</td>
<td>&lt; 0.0001</td>
<td>–</td>
</tr>
<tr>
<td>Cannabis use, %</td>
<td>62.9</td>
<td>61.0</td>
<td>67.4</td>
<td>&lt; 0.0006</td>
<td>66.3</td>
<td>59.7</td>
<td>&lt; 0.0001</td>
<td>–</td>
</tr>
<tr>
<td>Early cannabis use, %</td>
<td>17.3</td>
<td>15.4</td>
<td>21.8</td>
<td>&lt; 0.0001</td>
<td>20.4</td>
<td>14.3</td>
<td>&lt; 0.0001</td>
<td>–</td>
</tr>
<tr>
<td>Cannabis dependence, %</td>
<td>17.4</td>
<td>16.9</td>
<td>18.8</td>
<td>0.1889</td>
<td>23.1</td>
<td>11.9</td>
<td>&lt; 0.0001</td>
<td>–</td>
</tr>
<tr>
<td>Other lifetime characteristics</td>
<td>Parental alcohol use disorder</td>
<td>&lt; 0.0001</td>
<td>–</td>
<td>38.8</td>
<td>38.6</td>
<td>38.0</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Neither parent AUD, %</td>
<td>38.3</td>
<td>36.8</td>
<td>41.9</td>
<td>–</td>
<td>38.6</td>
<td>38.0</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Maternal-only AUD, %</td>
<td>17.4</td>
<td>15.0</td>
<td>23.0</td>
<td>–</td>
<td>16.2</td>
<td>18.7</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Paternal-only AUD, %</td>
<td>27.2</td>
<td>27.7</td>
<td>26.0</td>
<td>–</td>
<td>27.6</td>
<td>26.8</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Both parents AUD, %</td>
<td>17.1</td>
<td>20.6</td>
<td>9.1</td>
<td>–</td>
<td>17.7</td>
<td>16.6</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>22.9</td>
<td>24.7</td>
<td>18.6</td>
<td>–</td>
<td>16.9</td>
<td>28.7</td>
<td>&lt; 0.0001</td>
<td>–</td>
</tr>
<tr>
<td>Externalizing disordersa</td>
<td>20.1</td>
<td>17.7</td>
<td>25.6</td>
<td>&lt; 0.0001</td>
<td>25.2</td>
<td>15.1</td>
<td>&lt; 0.0001</td>
<td>–</td>
</tr>
<tr>
<td>Internalizing disordersb</td>
<td>7.0</td>
<td>8.0</td>
<td>4.8</td>
<td>0.0011</td>
<td>5.0</td>
<td>9.0</td>
<td>&lt; 0.0001</td>
<td>–</td>
</tr>
<tr>
<td>Number of assessment waves</td>
<td>0.0306</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

a Conduct, oppositional defiant, hyperactivity-impulsivity component of attention-deficit hyperactivity-impulsivity disorder;  
b Panic, social phobia.

2.7. Data analysis

We took a lifetime perspective for all analyses. Data across all reports made by an individual were included, spanning the baseline through 10-year follow-up period and positive endorsement of a behavior, at any wave, was considered as lifetime history for that behavior. Thus, any individual (N=3277) who had participated in the baseline interview was included.

First, we examined the cross-sectional relationship between substance use, dependence, SI and SA, while accounting for covariates, using logistic regression. For these analyses, there was no requirement for independent variables to have occurred prior to the onset of the dependent measure.

Second, to examine reciprocal and time-varying relationships between substance involvement and suicidal thoughts and behaviors, we adopted a survival analytic approach. Because onset of substance use and SI and SA temporally clustered around age 13–16 years, a time-varying approach was adopted whereby an independent variable was considered a “predictor” only if it had an onset age prior to the age of onset of the dependent variable. For instance, in order for SI to be a predictor for onset of alcohol use, age at onset of SI was required to be less than the age at onset of alcohol use (Supplemental Table S1 provides proportions of individuals reporting substance involvement prior to SI/SA and vice versa). There were multiple reports of age of onset; for the current analyses, the report that was closest in age to the age at interview was taken, assuming that it would minimize recall bias. All covariates were also coded to precede the onset of the dependent measure as well.

Person-year data were fitted to discrete time logistic regression models using PROC SURVEYLOGISTIC (SAS v9), which adjusts for complex survey designs, such as data clustered in families, by using a robust variance estimator. After an initial analysis that only included gender, AA race/ethnicity, Hispanic status and age at last interview as covariates, a model that included all covariates was fitted to the data to obtain an adjusted odds-ratio. In addition, we tested for interactions with sex (female as reference group) and race (European-American as reference group) in separate models that only accounted for demographic variables. Significant interaction terms were further adjusted for other covariates. The models fitted to the data are described below.

For Model 1, SI and SA were the dependent variables and early substance use was the independent variable; in other words, we examined whether early substance use “predicted” onset of SI and SA, as has been frequently done in prior longitudinal studies. We elected to focus on early substance use for Model 1 because, as shown in Supplemental Figures, the median age of onset of SI and SA preceded the typical median age of onset of alcohol, nicotine and cannabis use. In contrast, in Models 2–3, substance involvement provides proportions of individuals reporting substance involvement prior to SI/SA and vice versa. There were multiple reports of age of onset; for the current analyses, the report that was closest in age to the age at interview was taken, assuming that it would minimize recall bias. All covariates were also coded to precede the onset of the dependent measure as well.
3. Results

3.1. Sample characteristics

Substance use (46.6–80.3%), including early use (onset ages 14 years: 14.7–22.2%) was common by the most recent interview (Table 1). African-American participants were less likely to report early alcohol and nicotine use but more likely to report early cannabis use. Males were more likely to report early cannabis use. Combining data across the six assessments, 13.3%, 20.0% and 17.4% of the respondents met criteria for a lifetime history of alcohol, nicotine and cannabis dependence respectively. Correlations across the substance use measures ranged from 0.77 to 0.88 and from 0.61 to 0.67 across the substance dependence measures. SI was reported by 30.2% while SA was reported by 5.8% of respondents. Despite the items being non-nested, no one reported SA without also reporting SI. Both SI and SA had a median onset age of 15 years and were more commonly reported by females than males; SI was significantly less frequently reported by African-American participants, but no significant ethnic differences emerged for SA. Overall, SI and SA were considerably more common in those reporting early substance use (Supplemental Table S2), while substance use and dependence were more common in those with a prior history of SI and SA (Supplemental Table S3). A matrix of the tetrachoric correlations between all measures is presented in Supplemental Table S4.

3.2. Cross-sectional logistic regression

Even after adjustment for covariates, a history of SI was associated with 1.42–2.22 odds of use and dependence of alcohol, nicotine and cannabis (Table 2). Associations with SA were even stronger, with odds-ratios ranging from 1.47 to 4.42. Early substance use was also associated with both SI and SA, even after adjustment for covariates (Odds Ratio – OR - ranging from 1.80 to 2.71).

3.3. Discrete time logistic regression

Is early substance use associated with onset of suicidal ideation and attempt?

Model 1: As shown in Table 3, early alcohol and nicotine use respectively were associated with 1.49 and 1.66 increased odds of SA (when adjusting for demographic covariates alone), although these associations were no longer significant after adjustment for the full set measures were the dependent variables, and we examined the reciprocal pathway from SI and SA to onset of substance use and dependence.

Model 1: Whether early onset (<14 years) of alcohol, nicotine and cannabis use is associated with onset of (a) SI and (b) SA;

Model 2: Whether SI is associated with onset of (a) alcohol, (b) nicotine and (c) cannabis use and dependence;

Model 3: Whether SA is associated with onset of (a) alcohol, (b) nicotine and (c) cannabis use and dependence.

Table 2
Odds-ratios with their 95% confidence intervals from logistic regression documenting cross-sectional association between a lifetime history of suicidal ideation, suicide attempt and use and dependence of alcohol, nicotine and cannabis (N=3277).

<table>
<thead>
<tr>
<th></th>
<th>Adjusted for gender, race, Hispanic, age</th>
<th>Adjusted for all covariates*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Suicidal ideation (SI)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td>2.14 (1.67, 2.74)</td>
<td>1.42 (1.05, 1.93)</td>
</tr>
<tr>
<td>Early alcohol use</td>
<td>2.22 (1.86, 2.64)</td>
<td>1.80 (1.45, 2.24)</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>2.91 (2.35, 3.61)</td>
<td>2.03 (1.56, 2.64)</td>
</tr>
<tr>
<td>Nicotine use</td>
<td>2.50 (2.12, 2.95)</td>
<td>1.81 (1.48, 2.21)</td>
</tr>
<tr>
<td>Early nicotine use</td>
<td>2.08 (1.63, 2.44)</td>
<td>1.83 (1.43, 2.34)</td>
</tr>
<tr>
<td>Nicotine dependence</td>
<td>2.79 (2.32, 3.36)</td>
<td>2.10 (1.67, 2.64)</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>2.34 (1.95, 2.80)</td>
<td>1.74 (1.40, 2.16)</td>
</tr>
<tr>
<td>Early cannabis use</td>
<td>2.22 (1.83, 2.69)</td>
<td>2.07 (1.64, 2.62)</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>3.25 (2.67, 3.96)</td>
<td>2.22 (1.74, 2.82)</td>
</tr>
</tbody>
</table>

* Covariates: AA: race is African-American; H: Hispanic; EDx: Externalizing disorders (conduct, oppositional defiant); IDx: Internalizing disorders (panic, social phobia); MDD: Major depressive disorder; M-AUD: Maternal-only history of alcohol use disorder; P-AUD: Paternal-only history of alcohol use disorder; B-AUD: Both maternal and paternal history of alcohol use disorder; 22-yrs: aged < 22 at current last assessment; 2, 4, 6, 8, 10-yr FU: participation in follow-up assessments; S: Male sex.

Table 3
Early alcohol, nicotine, and cannabis use (independent variables) and onset of suicidal ideation and attempt (dependent) – odds-ratios and 95% confidence intervals from discrete-time hazard analyses (N=3277).

<table>
<thead>
<tr>
<th></th>
<th>Onset of Suicidal Ideation</th>
<th>Onset of Suicide Attempt</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early Alcohol Use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted for gender, race, Hispanic, age</td>
<td>1.09 (0.93, 1.28)</td>
<td>1.49 (1.07, 2.07)</td>
</tr>
<tr>
<td>Adjusted for all covariates*</td>
<td>0.99 (0.84, 1.17)</td>
<td>1.29 (0.90, 1.84)</td>
</tr>
<tr>
<td>not S, not AA, H, 22-yr, M-AUD, P-AUD, B-AUD, 8-yr FU, no MDD, EDx, ED</td>
<td>not S, H, not 22-yr, M-AUD, B-AUD, no MDD, EDx</td>
<td></td>
</tr>
<tr>
<td><strong>Early Nicotine Use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted for gender, race, Hispanic, age</td>
<td>1.10 (0.91, 1.33)</td>
<td>1.66 (1.17, 2.37)</td>
</tr>
<tr>
<td>Adjusted for all covariates*</td>
<td>0.99 (0.81, 1.20)</td>
<td>1.33 (0.91, 1.95)</td>
</tr>
<tr>
<td>not S, not AA, H, 22-yr, M-AUD, P-AUD, B-AUD, 8-yr FU, no MDD, EDx, EDx</td>
<td>not S, H, M-AUD, B-AUD, no MDD, EDx</td>
<td></td>
</tr>
<tr>
<td><strong>Early Cannabis Use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted for gender, race, Hispanic, age</td>
<td>1.06 (0.88, 1.27)</td>
<td>1.45 (1.00, 2.12)</td>
</tr>
<tr>
<td>Adjusted for all covariates*</td>
<td>0.94 (0.77, 1.13)</td>
<td>1.13 (0.76, 1.67)</td>
</tr>
<tr>
<td>not S, not AA, H, 22-yr, M-AUD, P-AUD, B-AUD, 8-yr FU, no MDD, EDx, ED</td>
<td>not S, H, M-AUD, B-AUD, no MDD, EDx</td>
<td></td>
</tr>
</tbody>
</table>

* Only significant covariates are listed: AA: race is African-American; H: Hispanic; EDx: Externalizing disorders (conduct, oppositional defiant, hyperactivity-impulsivity component of attention-deficit hyperactivity-impulsivity disorder); IDx: Internalizing disorders (panic, social phobia); MDD: Major depressive disorder; M-AUD: Maternal-only history of alcohol use disorder; P-AUD: Paternal-only history of alcohol use disorder; B-AUD: Both maternal and paternal history of alcohol use disorder; 22-yrs: aged < 22 at current last assessment; 2, 4, 6, 8, 10-yr FU: participation in follow-up assessments; S: Male sex.
of SI or SA, males with a history of early substance use that preceded the main event of SI or SA, males with a history of early substance use that preceded SI or SA) resulted in the onset of SI or SA with a lifetime history of MDD (i.e. Major depressive disorder; M-AUD: Maternal-only history of alcohol use disorder; P-AUD: Paternal-only history of alcohol use disorder; B-AUD: Both maternal and paternal history of alcohol use disorder; 22-yrs: aged < 22 at current last assessment; 2, 4, 6, 8, 10-yr FU: participation in follow-up assessments; S: Male sex.

### Table 4

The role of race and gender on the relationship between suicidal ideation and attempt and use as well as dependence of alcohol, nicotine and cannabis, adjusted for main effects of gender, race, Hispanic, and age (N=3277). Results represent odds ratios (95% confidence intervals).

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Predictor x Male</th>
<th>Predictor x Male (adj.)</th>
<th>Predictor x AA</th>
<th>Predictor x AA (adj.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use</td>
<td>0.61 (0.50, 0.75)</td>
<td>0.94 (0.63, 1.42)</td>
<td>0.77 (0.48, 1.25)</td>
<td>0.70 (0.49, 1.00)</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>1.17 (0.95, 1.44)</td>
<td>1.09 (0.78, 1.53)</td>
<td>0.52 (0.34, 0.80)</td>
<td>0.49 (0.32, 0.77)</td>
</tr>
<tr>
<td>Nicotine use</td>
<td>0.66 (0.57, 0.77)</td>
<td>1.33 (1.01, 1.74)</td>
<td>0.69 (0.50, 0.94)</td>
<td>0.69 (0.50, 0.95)</td>
</tr>
<tr>
<td>Nicotine dependence</td>
<td>1.15 (0.97, 1.36)</td>
<td>1.38 (1.04, 1.84)</td>
<td>0.69 (0.49, 0.98)</td>
<td>0.68 (0.47, 0.97)</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>0.68 (0.58, 0.79)</td>
<td>1.14 (0.84, 1.55)</td>
<td>1.20 (0.85, 1.71)</td>
<td>0.85 (0.59, 1.22)</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>1.17 (0.97, 1.41)</td>
<td>2.04 (1.50, 2.78)</td>
<td>2.02 (1.47, 2.78)</td>
<td>0.85 (0.59, 1.22)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.94 (0.72, 1.25)</td>
<td>0.95 (0.52, 1.71)</td>
<td>0.69 (0.40, 1.19)</td>
<td>0.70 (0.40, 1.19)</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>1.68 (1.21, 2.34)</td>
<td>0.99 (0.53, 1.85)</td>
<td>0.45 (0.22, 0.92)</td>
<td>0.40 (0.19, 0.84)</td>
</tr>
<tr>
<td>Nicotine use</td>
<td>1.02 (0.76, 1.37)</td>
<td>1.26 (0.92, 1.70)</td>
<td>0.67 (0.37, 1.21)</td>
<td>0.67 (0.37, 1.21)</td>
</tr>
<tr>
<td>Nicotine dependence</td>
<td>1.68 (1.28, 2.22)</td>
<td>1.08 (0.61, 1.91)</td>
<td>0.60 (0.34, 1.07)</td>
<td>0.60 (0.34, 1.07)</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>0.94 (0.70, 1.26)</td>
<td>1.13 (0.60, 2.13)</td>
<td>1.40 (0.79, 2.46)</td>
<td>0.59 (0.31, 1.09)</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>1.61 (1.21, 2.16)</td>
<td>2.06 (1.19, 3.56)</td>
<td>2.43 (1.41, 4.17)</td>
<td>0.59 (0.31, 1.09)</td>
</tr>
</tbody>
</table>

* Adjusted for: AA: race is African-American; H: Hispanic; EDx: Externalizing disorders (conduct, oppositional defiant, hyperactivity-impulsivity component of attention-deficit hyperactivity-impulsivity disorder); IDx: Internalizing disorders (panic, social phobia); MDD: Major depressive disorder; M-AUD: Maternal-only history of alcohol use disorder; P-AUD: Paternal-only history of alcohol use disorder; B-AUD: Both maternal and paternal history of alcohol use disorder; 22-yrs: aged < 22 at current last assessment; 2, 4, 6, 8, 10-yr FU: participation in follow-up assessments; S: Male sex.

### Table 5

Lifetime history of suicide ideation (SI - independent) and onset of alcohol, nicotine and cannabis use and dependence (dependent) - odds ratios with their 95% Confidence Intervals from discrete-time hazard analyses (N=3277). Models "adjusted for all covariates" report multivariate (i.e., adjusted odds – ratios; Supplemental Table S5 for covariate odds ratios).

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Predictor x Male</th>
<th>Predictor x Male (adj.)</th>
<th>Predictor x AA</th>
<th>Predictor x AA (adj.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use</td>
<td>0.61 (0.50, 0.75)</td>
<td>0.67 (0.51, 0.88)</td>
<td>0.63 (0.48, 0.84)</td>
<td>0.72 (0.49, 1.04)</td>
</tr>
<tr>
<td>Alcohol attempt</td>
<td>1.49 (1.07, 2.07)</td>
<td>0.54 (0.31, 0.93)</td>
<td>0.43 (0.24, 0.75)</td>
<td>0.76 (0.36, 1.61)</td>
</tr>
<tr>
<td>Early Nicotine use</td>
<td>1.10 (0.91, 1.33)</td>
<td>0.74 (0.53, 1.04)</td>
<td>0.50 (0.30, 0.82)</td>
<td>0.52 (0.32, 0.86)</td>
</tr>
<tr>
<td>Early Alcohol use</td>
<td>1.66 (1.17, 2.37)</td>
<td>0.37 (0.19, 0.71)</td>
<td>0.33 (0.17, 0.64)</td>
<td>0.29 (0.09, 0.94)</td>
</tr>
<tr>
<td>SI - &gt; substance use/dependence</td>
<td>1.06 (0.88, 1.27)</td>
<td>0.79 (0.58, 1.10)</td>
<td>0.64 (0.45, 0.92)</td>
<td>0.70 (0.49, 1.00)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.45 (1.00, 2.12)</td>
<td>0.42 (0.23, 0.77)</td>
<td>0.37 (0.20, 0.69)</td>
<td>0.34 (0.15, 0.77)</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>0.61 (0.50, 0.75)</td>
<td>0.94 (0.63, 1.42)</td>
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<tr>
<td>Nicotine use</td>
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<tr>
<td>Nicotine dependence</td>
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<td>1.33 (1.01, 1.74)</td>
<td>0.69 (0.50, 0.94)</td>
<td>0.69 (0.50, 0.95)</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>1.15 (0.97, 1.36)</td>
<td>1.38 (1.04, 1.84)</td>
<td>0.69 (0.49, 0.98)</td>
<td>0.68 (0.47, 0.97)</td>
</tr>
<tr>
<td>Cannabis dependence</td>
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<td>1.20 (0.85, 1.71)</td>
<td>0.85 (0.59, 1.22)</td>
</tr>
<tr>
<td>Alcohol use</td>
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<tr>
<td>Nicotine use</td>
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<td>1.26 (0.92, 1.70)</td>
<td>0.67 (0.37, 1.21)</td>
<td>0.67 (0.37, 1.21)</td>
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<tr>
<td>Nicotine dependence</td>
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<td>0.59 (0.31, 1.09)</td>
</tr>
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<td>Cannabis dependence</td>
<td>1.61 (1.21, 2.16)</td>
<td>2.06 (1.19, 3.56)</td>
<td>2.43 (1.41, 4.17)</td>
<td>0.59 (0.31, 1.09)</td>
</tr>
</tbody>
</table>

* Only significant covariates are listed: AA: race is African-American; H: Hispanic; EDx: Externalizing disorders (conduct, oppositional defiant, hyperactivity-impulsivity component of attention-deficit hyperactivity-impulsivity disorder); IDx: Internalizing disorders (panic, social phobia); MDD: Major depressive disorder; M-AUD: Maternal-only history of alcohol use disorder; P-AUD: Paternal-only history of alcohol use disorder; B-AUD: Both maternal and paternal history of alcohol use disorder; 22-yrs: aged < 22 at current last assessment; 2, 4, 6, 8, 10-yr FU: participation in follow-up assessments; S: Male sex.
and both parents; OR = 1.57–2.21; Supplemental Table S6). When examining interactions between SI and sex and race, several additional significant findings emerged. Even though there was no main effect of SI on the onset of cannabis dependence, males with SI were more likely than females with SI to meet criteria for cannabis dependence. Likewise, despite an absence of main effects, African-Americans with SI were less likely than their European-American counterparts to meet criteria for alcohol dependence (Table 4). Also, males with SI were more likely than females with SI to meet criteria for both nicotine use and dependence, although these results did not hold after accounting for covariates. Finally, African-Americans with SI were less likely than European-Americans with SI to meet criteria for nicotine use and dependence.

**Model 3:** A prior history of SA was not associated with onset of alcohol, nicotine or cannabis use (OR = 1.04–1.19; Table 6). However, a prior history of SA was associated with 1.44–1.61 adjusted odds of onset of alcohol, nicotine and cannabis dependence. Similar to results for Model 2, males with SA were more likely than their female counterparts to meet criteria for cannabis dependence (Table 4). Also, like in Model 2, MDD (OR = 0.47–0.70), externalizing disorders (OR = 1.30–2.30) and family history of alcohol use disorders, particularly having two parents with alcohol use disorder (OR = 1.73–2.32), were the strongest correlates of onset of substance use and dependence (Supplemental Table S7).

**4. Discussion**

In a sample enriched for familial liability to substance use, particularly alcohol dependence, we find support for associations between substance involvement, SI and SA. When examined using cross-sectional approaches, these associations were significant and positive, ranging from 1.42 (SI and alcohol use) to 4.42 (SA and alcohol use), and were robust to the inclusion of covariates. These findings suggest that, across the lifetime, substance involvement and suicidal thoughts and behaviors are, somewhat independently, associated. These results are highly consistent with several studies, and in particular, with two recent meta-analyses for alcohol use disorders and tobacco smoking. The first meta-analysis (Darvishi et al., 2015) of 420,732 participants concluded that alcohol use disorders were associated with suicidal ideation (OR = 1.86), attempt (OR = 3.13) and completion (OR = 2.59). The second (Poorolajal and Darvishi, 2016) identified 63 studies on the relationship between current smoking and suicide (N = 8,063,634) and found significant associations for suicidal ideation, plan, attempt and completion (OR > 2.0). These findings also support results from another meta-analysis which suggests that chronic, but not acute, cannabis use is associated with suicidal ideation and attempt (Borges et al., 2016).

Next, we examined whether prior early substance use increases the likelihood of onset of SI and SA. In our data, evidence for this hypothesis was limited and most associations, which were with SA, were explained by comorbid factors, such as MDD, family history and externalizing disorders. Evidence that males with early substance use were less likely than females with early substance use to report SA is also consistent with the notion that early substance use in women might be indicative of a liability to both internalizing and externalizing problems (Brady et al., 1999; Kessler et al., 1997). Males with early substance use may be more likely to progress to other externalizing behaviors while females with early substance use may be vulnerable to future problems with depressed mood and suicidal thoughts as well (Kandel et al., 1991). Similarly, early substance use was less likely to be related to SI and SA in African-Americans relative to their European-American counterparts. Future studies with larger sample sizes for African-American participants might be better suited to the identification of aspects of substance use and misuse that relate to SI and SA in this population. Importantly, MDD diagnosis that preceded early substance use and SI as well as SA exerted a protective influence (OR = 0.33–0.59; Table S5). We attribute this negative association (i.e. OR < 1) to the time-varying nature of MDD because analyses in which MDD was not required to have occurred prior to the onset of the dependent variable showed OR > 5. Thus, the OR associated with MDD reflects meeting criteria for a diagnosis at a fairly young age, which may be related to even earlier, but not subsequent, onsets of SI and SA. We, unfortunately, did not have age of onset data on first dysphoric or anhedonic symptom to be able to evaluate their time-varying effect on SI and SA.

We also examined whether a history of SI or SA was associated with onset of substance use and dependence. Here, an interesting divergence between SI and SA was noted. Unlike the cross-sectional findings, a prior history of SI was associated with a reduced likelihood of the onset of alcohol, nicotine and cannabis use (OR = 0.71–0.77). This was not the case for SA. Because onset of SI and substance use tend to cluster around similar ages (Supplemental Figs. S1A, S1B, S1C, S2A and S2B), we presume that these "protective" effects might reflect a trajectory indicative of escalating problems with internalizing beha-

**Table 6**

Lifet ime history of suicide attempt (SA - independent) and onset of alcohol, nicotine and cannabis use and dependence (dependent) - odds ratios with their 95% Confidence Intervals from discrete-time hazard analyses (N = 3277). Models adjusted for all covariates report multivariate (i.e., adjusted odds – ratios; Supplemental Table S5 for covariate odds – ratios).

<table>
<thead>
<tr>
<th>Suicide Attempt</th>
<th>Onset of Alcohol Use</th>
<th>Onset of Alcohol Dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted for gender, race, Hispanic and age</td>
<td>0.94 (0.72, 1.25)</td>
<td>1.68 (1.21, 2.34)</td>
</tr>
<tr>
<td>Adjusted for all covariates*</td>
<td>1.17 (0.88, 1.55)</td>
<td>1.60 (1.12, 2.28)</td>
</tr>
<tr>
<td>not AA, M-AUD, P-AUD, B-AUD, no MDD, EDx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted for gender, race, Hispanic and age</td>
<td>1.02 (0.76, 1.37)</td>
<td>1.68 (1.28, 2.22)</td>
</tr>
<tr>
<td>Adjusted for all covariates*</td>
<td>1.19 (0.88, 1.61)</td>
<td>1.61 (1.19, 2.17)</td>
</tr>
<tr>
<td>S, not AA, not 22-ys, M-AUD, P-AUD, B-AUD, not 6, 8, 10-yr FU, no MDD, EDx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted for gender, race, Hispanic and age</td>
<td>0.94 (0.70, 1.26)</td>
<td>1.61 (1.21, 2.16)</td>
</tr>
<tr>
<td>Adjusted for all covariates*</td>
<td>1.04 (0.79, 1.38)</td>
<td>1.44 (1.06, 1.96)</td>
</tr>
<tr>
<td>S, AA, M-AUD, P-AUD, B-AUD, not 10-yr FU, no MDD, EDx</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Only significant covariates are listed: AA: race is African-American; H: Hispanic; EDx: Externalizing disorders (conduct, oppositional defiant, hyperactivity-impulsivity component of attention-deficit hyperactivity-impulsivity disorder); IDx: Internalizing disorders (panic, social phobia); MDD: Major depressive disorder; M-AUD: Maternal-only history of alcohol use disorder; P-AUD: Paternal only history of alcohol use disorder; B-AUD: Both maternal and paternal history of alcohol use disorder; 22-ys: aged < 22 at current last assessment; 2, 4, 6, 8, 10-yr FU: participation in follow-up assessments; S: Male sex.
vior(s) (e.g., MDD) that are independent of experimentation or self-
medication with substances. Early SI might represent significant 
depressed mood which may also reduce the chance that individuals 
will interface with delinquent peer groups (potentially, due to peer 
rejection) who might have otherwise promoted substance use (Hussong 
et al., 2011). In fact, a prior study of these data show similar protective 
effects of a score assessing difficulties with family and peers on age of 
onset of alcohol use (Kupferman et al., 2013). This hypothesis is also 
supported by the stronger correlation between MDD and SI (r=0.74) 

rather than SA (r=0.52). Alternatively, those with early SI (or MDD, 
OR=0.47–0.71; Tables S6 and S7) may be at greater risk for very early, 
but not later, onset of substance use. In other words, these findings 
may support the idea that early SI is preceded by even earlier substance 
use and is unlikely to be a “predictor” of it. In addition, this finding may 
also be sample-specific. Individuals in COGA are at high genetic 
and environmental liability for onset of substance use; thus, if SI precedes 
this expected behavior of substance use, it may reflect a developmental 
pattern of psychopathology that does not increase risk for substance-
related onsets.

SA was associated with onset of alcohol, nicotine and cannabis 
dependence, even after accounting for comorbid psychiatric diagnoses 
and family history of alcohol use disorder, with the effects on cannabis 
dependence being stronger in males. This finding is largely, but not 
entirely, inconsistent with several prior studies that have examined this 
reciprocal path. For instance, one large-scale longitudinal study found 
a dose-dependent relationship between frequent cannabis use and SI 
(van Ours et al., 2013) in males but did not find evidence for prior SI 
predicting increases in cannabis use. Similarly, while numerous studies 
have reported that ever and current smoking (Lucas et al., 2013) are 
prospectively associated with suicide, at least one study found that 

prior suicide-related outcomes were not associated with subsequent 
current smoking (Covey et al., 2012). Despite this, increases in smoking 
subsequent to SA might reflect self-medication for depressed mood 
(Hughes, 2008). Finally, the role of both acute and chronic alcohol use 

in SA has also been closely studied (Bagge et al., 2008; Conner et al., 
2014). Within this literature, there are several proposed pathways that 
support our finding. For instance, escalation in alcohol use, subsequent 
to ideation, may reflect changes in drinking expectancies or motives 

or to facilitate SA. Distal effects have also been proposed — for instance, 
alterations in the residential, educational or vocational environment 

subsequent to SA, as well as other profound environmental changes 
(e.g., hospitalization) might result in escalations in problematic alcohol 
use (Bagge and Sher, 2008).

Our finding that SA is associated with onset of alcohol, nicotine and 
cannabis dependence might be interpreted in several ways. First, 
increased likelihood of substance use disorders, particularly in those 
with SA, might reflect escalations in substance use for negative affect 
regulation (i.e. self-medication: Khantzian, 1997; or coping: Esposito-
Smythers et al., 2004), as has been noted for mood and anxiety 
disorders (e.g. Bolton et al., 2009; Crum et al., 2013; Dawes et al., 
2008; Robinson et al., 2011). Psychiatric disorders such as MDD, 
even in their active form (Breslau et al., 2004), predict nicotine 
dependence (e.g. Breslau et al., 1993). Alternatively, this association 
may reflect a shared liability to behaviors that include negative affect as 
a component. Negative affect, including depressed mood (e.g. with-
drawal) are hallmark features of substance use disorders (Brady et al., 
2005) as well as SI and SA. Studies have also suggested that shared 
genetic influences may be responsible for the comorbidity across MDD 
and alcohol (Kendler et al., 1993) and nicotine dependence (Edwards 
et al., 2011; Thornton et al., 2016). However, adjustment for MDD did 
not abolish our association suggesting that this shared liability may be 
more general than MDD (e.g. Ellingson et al., 2016). Third, increased 
likelihood of substance use disorders in those with a prior history of SA 
may reflect a general predisposition towards impulsive and aggressive 
behaviors (Turecki, 2005). It is noteworthy that despite all individuals 
who reported SA also reporting SI (i.e., no attempts without ideation), 
results differed for the two outcomes. This finding might indicate that 
SA represents an escalation in severity of suicidal thoughts and 
behaviors and that new risk and protective influences might come into 
play at this more severe stage. Also, that significant effects in our data 
might relate to ascertainment and individuals being at higher familial 
liability for substance use and misuse cannot be discounted as such 
internalizing pathways are commonly noted in offspring of individuals 
with alcoholism (e.g., Hussong et al., 2011).

Several limitations of the current study are noteworthy. First, the 
generalizability of our findings, especially the observation of null 
associations, should be viewed in the context of ascertainment. The 

sample recruited offspring, many of whom were at high familial liability 
to alcohol use disorders. Consequently, only 38.3% of the offspring 
report that neither of their parents had an alcohol use disorder. Given 
the co-aggregation of other substance use and suicidal thoughts and 
behaviors with alcohol use disorders, it is not surprising that the 

prevalence of substance involvement in this sample is higher than 
estimates from the general U.S. population (e.g. 44.8% in the National 
Household Survey of Drug Use and Health versus 63% in COGA; U.S. 
Department of Heath and Human Services, 2014). Similarly, our 
estimate of SI (30.2%) is considerably higher than that for similarly 
aged individuals in the National Comorbidity Survey – Replication 
(18%; (Kessler and Merikangas, 2004)). Even though we control for 

family history, and it exerts significant effect, it is possible that our 
study design influenced the pattern of our results. It is also noteworthy 
that rates of cigarette smoking exceed those of cannabis use in this 

sample, however, this observation is consistent with estimates from the 
recent Monitoring the Future Survey (Johnston et al., 2016). Second, 
even though the study was designed to be longitudinal, it is ongoing, 
and not all participants have had the opportunity to participate in later 
follow-ups. Thus, younger participants may have had fewer opportu-
nities to report their substance use behavior and may not have passed 
the age of risk for onset of cannabis use or of developing substance 
dependence. To leverage this study design, we employed survival 
models which allowed for such right censored data and we included 

age at last interview as a covariate. A related concern is attrition – as 
the study is ongoing, non-participation in subsequent waves is not 
necessarily indicative of attrition. However, analyses of those who were 
eligible to have participated in the 6 year follow-up found no significant 
differences related to substance use behaviors or psychiatric character-
istics. We also adjusted for number of follow-ups in all analyses. Third, 
recall bias may have influenced reports of all variables, particularly age 
of onset. We attempted to ameliorate this concern by using multiple 
reports of age of onset and selecting the one that was closest in age to 
the age of the respondent at the time of the interview. This may have 
resulted in higher ages being ascribed to onset. On average, the 
difference between first, earliest and the age of onset selected by us, 
for any variable, was 1 year. Fourth, as we required independent 
variables (and covariates) to be time-varying, we were only able to 
focus on early substance use as “predictors” of SI and SA, as the onset 
age for SI and SA was fairly low and typically preceded the onset of 
substance use and dependence. That is, in many instances, the typical 

age of onset of substance use and dependence occurred after the onset 
of SI and SA. Despite this, caution is needed in deriving any causal 
inference, as recall bias and other unmeasured confounders may be 
responsible for observed patterns of results. Fifth, due to their low 
prevalence, particularly at earlier ages, we did not examine illicit drugs 
other than cannabis. Sixth, when examining early use and dependence, 
never users were treated the same as late and non-dependent users 
(i.e., coded as “0”) respectively. This creates a confound, in that 
associations that are specific to early onset of use or onset of 
dependence cannot be disentangled for associations with onset of any 
use. Future studies should study substance involvement as a multi-
stage process. Seventh, despite the longitudinal design, we did not 
study whether substance involvement was associated with new onsets 
of SI and SA, nor do we have data to examine completed suicides. Such
an analysis will be more feasible when greater numbers of participants complete further follow-up assessments. Similarly, we did not examine measures of frequent, chronic or heavy substance use, which have been implicated as risk factors for the onset of SI and SA.

Our analyses call for further studies that outline the nature of these associations – for instance, to what extent are these associations representative of causal pathways or indicative of shared predispositions? Importantly, future efforts should be targeted at understanding the role of both depression and impulsivity (Turecki, 2005), especially when considering the relationship between SA and substance involvement. For instance, studies have reported stronger associations between unplanned SA and substance involvement (Borges et al., 2010; Delforterie et al., 2015) indicating the potential role of impulsivity but a when considering the relationship between SA and substance involve-

References


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Appendix A. Supporting information

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