Drug Use and the Risk of Major Depressive Disorder, Alcohol Dependence, and Substance Use Disorders

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Background: The Children in the Community Study is a prospective longitudinal study investigating the association between early drug use (childhood, adolescence, and early 20s) and later psychiatric disorders (in the late 20s).

Methods: Using data from a community-based sample of 736 adults (50% female) from upstate New York, the subjects were interviewed at the mean ages of 14, 16, 22, and 27 years. Psychiatric disorders, measured by age-appropriate versions of the University of Michigan Composite International Diagnostic Interview, and participant’s drug use were assessed.

Results: Adolescent and young adult tobacco use was significantly associated with an increased risk of alcohol dependence and substance use disorders at a mean age of 27 years, but not with new episodes of major depressive disorder. Earlier alcohol use significantly predicted later major depressive disorder, alcohol dependence, and substance use disorders in the late 20s, as did early marijuana use and other illicit drug use. Except for the effect of tobacco use on major depressive disorder, early drug use was significantly related to later psychiatric disorders, even after statistically controlling for age, sex, parental educational level, family income, and prior episodes of major depressive disorder and substance use disorders.

Conclusions: Our results suggest that early drug use is associated with and predicts later psychiatric disorders. Preventive implications stem from the importance of studying a range of psychiatric disorders in the context of substance use assessed over a wide age range.

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MANY CLINICAL and community studies have confirmed that there is a significant link between legal and illegal drug use and psychopathology.1-24 Drug use itself has been found to be significantly related to substance use disorders (SUDs).3-8,11,13-15,25 Including nicotine dependence,1,3 anxiety, and affective disturbances,1,5,9,13,15,19,25 In fact, in general, drug users have both higher rates and more severe levels of psychological impairments than do individuals who do not use drugs.1,4,7,17 Yet, despite the finding that drug use is related to psychiatric disorders, it has been unclear whether drug use precedes the development of psychiatric disorders.2,15 A more complete delineation of the relationship between earlier drug use and later psychiatric disorders will contribute information for prevention and intervention.

Our focus in the current longitudinal study is whether drug use in childhood, adolescence, and/or early adulthood predicts episodes of psychiatric disorders in the late 20s. Our rationale for assuming such influences is based on findings that indicate that drug use is associated with effects on psychosocial, physical, and cognitive functioning that, in turn, predict major depressive disorder (MDD), alcohol dependence, and SUDs.10 The overwhelming number of studies, whether of treatment4-8,13,16,17,23 or community samples,1,3,11,12,19,20,22,25-27 are cross-sectional. In contrast, the present study of a community sample has a longitudinal design. Herein we investigate changes that occur over a long span of time (eg, 14 years). More specifically, adult psychopathology is assessed in relation to drug behavior present during childhood through early adulthood. While there are a few existing studies that have used a longitudinal design,9,14,28-30 the relationship between drug use and psychiatric symptoms has only been investigated in a time-limited manner. For example, McGee et al31 reported that tobacco, alcohol, and cannabis use at the age of 18 years is associated with an elevated risk of later substance dependence and antisocial behavior among 21-year-old men. Hansell and White29 found that drug use in early adolescence was associated with psychological distress (ie, depression, anxiety, and phobic anxiety) in later adolescence. Although not using clinical diagnostic criteria, Newcomb and Bentler32 showed independent effects of drug use in early and
late adolescence on psychosomatic complaints and emotional distress in the early 20s.

In a previous analysis of this sample, we examined the relationship between substance use in adolescence and psychiatric disorders in the early 20s. The findings indicated that tobacco and illicit drug use in adolescence were related to MDD in the early 20s. In the present study, we extend this analysis to consider the cumulative effect of substance use (as well as drug use during specific developmental periods) on episodes of MDD in the late 20s. In addition, we test the association between prior substance use and later alcohol dependence and substance dependence.

In contrast to other investigators who examined the relationship of drug use and SUDs during adolescence alone, we examine the effects of drug use (tobacco, alcohol, marijuana, and other illicit drugs) during childhood, adolescence, and the early 20s on the development of episodes of MDD, alcohol dependence, and SUDs in the late 20s. Our hypothesis is that earlier drug use is associated with later psychiatric disorders.

METHODS

PARTICIPANTS

Participation was based on a randomly selected cohort (n = 975) studied prospectively since 1975. Population data from the 1970 census (updated for 1975) for sampling units in Albany and Saratoga (New York) counties were obtained. A systematic sample of primary sampling units (areas) in each county was then drawn with probability proportional to the number of households. Blocks were selected with probability proportional to size (number of households). Address lists were compiled. Households with at least 1 child between 1 and 10 years of age were qualified to participate. In each household 1 child was randomly selected. The original sample was representative of the population of children in upstate New York for sex, family intactness, family income, and parental educational level, according to the 1980 Survey of the US Bureau of the Census. Eighty-five percent of the original sample agreed to participate. Data on the participants were collected in their homes in 1975 (time 1 [T1]; mean [SD] age, 5.57 [2.85] years), 1983 (time 2 [T2]; mean [SD] age, 14.05 [2.80] years), 1986 (time 3 [T3]; mean [SD] age, 16.26 [2.81] years), 1992 (time 4 [T4]; mean [SD] age, 22.28 [2.82] years), and in 1997 (time 5 [T5]; mean [SD] age, 26.99 [2.80] years). At T1, the participant’s age range was between 1 and 10 years, with equal numbers of participants at each age. Written informed consent was obtained from the mothers of the participants in 1975; from the participants and their mothers in 1983, 1986, and 1992; and from the participants only in 1997. The sample for the analyses in this study was the 1997 sample (T5; n = 736), which had the following distribution: 92% white, 50% female, 38% married, and 93% with at least a 12th grade education. There was a 2% attrition rate from the 1992 sample (T4).

Data were collected using structured interviews of the participants. The participants were seen in their homes by lay interviewers who were extensively trained and supervised. Participants who moved outside the United States were interviewed by telephone or mailed questionnaires. There were no differences between those whom we interviewed in person, by telephone, or by mailed questionnaires. Brook et al33 discuss in detail the sampling procedures and the composition of the original sample.

MEASUREMENT OF PRIOR EPISODES OF MDD AND SUDS DURING CHILDHOOD AND ADOLESCENCE

For the current study, prior episodes of MDD during childhood, early adolescence (T2), and middle and/or late adolescence (T3) were used as control variables. Prior MDD and SUDs were assessed by a supplemented version of the Diagnostic Interview Schedule for Children, using computer algorithms designed to match DSM-III-R criteria, to combine information collected from mothers and youths.33 Further details are presented in Brook et al.33 We combined the 2 wave measures to create a dichotomous scale for prior MDD and/or prior SUDs. The percentage of subjects who qualified for the diagnoses of prior episodes of MDD and SUDs (T2 and T3) was 5.21% and 9.59%, respectively.

MEASUREMENT OF SUBSTANCE USE

In addition to the assessment of alcohol dependence and SUDs in 1997 (T5) described earlier, we included questions on the use of drugs (tobacco, alcohol, marijuana, and other illicit drugs). These questions asked about the frequency of ever using drugs in childhood and early adolescence (1983 [T2]), use during the last 2 years of middle and late adolescence (1986 [T3]), and using during the last 5 years in the early 20s (1992 [T4]). The cigarette measure at each point in time had a 6-point rating scale ranging from never smoking (0) to smoking 1½ packs daily (5). The alcohol measure at each time had a 5-point rating scale ranging from never (0) to 3 or more drinks daily (4). The marijuana use measure at each time had an 8-point rating scale ranging from never (0) to daily use (7). Finally, the other illicit drug use (eg, cocaine, heroin, amphetamines, and others) measures had an 8-point scale ranging from never (0) to daily use (7). We regrouped these items into 4-point scales to create consistent measures for each drug: never (0), light use (1), moderate use (2), and heavy use (3). Frequency of use was added across all time points to provide a separate cumulative measure for each of the drugs considered. Thus, higher scores were obtained by more frequent users, that is, individuals who used illicit drugs more frequently when considering their drug use at all points in time. The percentages of children, early adolescents, middle adolescents, late adolescents, and young adults in their early 20s who smoked cigarettes, drank alcohol, smoked marijuana, and used illegal drugs other than marijuana are listed in Table 1. The definitions of the levels of the use of cigarettes, alcohol, marijuana, and other illicit drugs are consistent with those reported by O’Malley et al36 and Wallace et al.28

MEASUREMENT OF PSYCHIATRIC DISORDERS

Major depressive disorder, alcohol dependence, and SUDs were assessed in 1997 (T5) using a modified version of the University of Michigan Composite International Diagnostic Interview.25,26 The University of Michigan Composite International Diagnostic Interview is a highly structured research diagnostic instrument developed for use by trained lay interviewers to assess the most common diagnoses among children, adolescents, and young adults as described in the DSM-III-R.33 Reliability and validity measures for the instrument are described by Wittchen et al.25,26 In the present study, we updated the University of Michigan Composite International Diagnostic Interview so that MDD, alcohol dependence, and SUDs were considered present only if they met modified DSM-IV criteria.38 Major depressive disorder was diagnosed if subjects had a change in functioning reflected by 5 or more of the following criteria during the same 2-week period: (1) depressed mood most of the day, nearly every day, or (2) markedly diminished interest or pleasure in all, or almost all, activities (1 must be present);
The following findings based on the Pearson product-moment correlations indicated that (1) chronological age was unrelated to any of the disorders; (2) sex (males higher than females) was only related to SUDs \( r = 0.12, P < .001 \); (3) higher family income was negatively related to MDD \( r = -0.08, P < .05 \) and positively related to alcohol dependence \( r = 0.08, P < .05 \); (4) higher parental educational levels were negatively related to MDD \( r = -0.09, P < .05 \) and positively related to alcohol dependence and to SUDs \( r = 0.09, P < .05 \); (5) prior episodes of MDD were positively related to later MDD \( r = 0.16, P < .001 \) and alcohol dependence \( r = 0.08, P < .05 \); and (6) prior episodes of SUDs were positively related to later SUDs \( r = 0.11, P < .01 \).

**Table 2** gives the results of the logistic regression analyses. The dependent variables were psychiatric disorders (MDD, alcohol dependence, and SUDs) and the independent variables were earlier drug use (tobacco, alcohol, marijuana, and other illicit drugs). Sociodemographic characteristics and prior episodes of MDD and SUDs as well as childhood aggression were used as statistical controls.

Frequency of tobacco use over the childhood and early adolescent, middle and later adolescent, and young adult periods (T2, T3, and T4, respectively) was associated with an increased risk for alcohol dependence and SUDs, but not with the risk for episodes of MDD in the late 20s (T5). Individuals who had smoked tobacco more frequently (T2-T4) were more likely to have alcohol dependence (OR, 1.42; 95% CI, 1.17-1.72, \( P < .001 \)) and SUDs (OR, 1.16; 95% CI, 1.0-1.33, \( P < .05 \)). Heavier alcohol use during childhood and early adolescence (OR, 1.42; 95% CI, 1.17-1.72, \( P < .001 \)) and SUDs (OR, 1.16; 95% CI, 1.0-1.33, \( P < .05 \)).

**STATISTICAL ANALYSIS**

Data were rarely missing for the participants. There were a few cases in which the participants did not know the answer or refused to respond (no more than 1%-2%). Separate logistic regression analyses were conducted for the independent variables of tobacco, alcohol, marijuana, and other illicit drug use (during childhood and early adolescence, middle and late adolescence, and/or the early 20s) and the dependent variables of episodes of MDD, alcohol dependence, and SUDs (in the late 20s). We obtained adjusted odds ratios (ORs) and 95% confidence intervals (CIs). Given the small number of youth with psychiatric diagnoses, we were unable to do the analyses for the different subgroups (eg, parental educational level, family income, age, and sex). Therefore, these variables were statistically controlled for in the logistic regression analyses. In a second series of logistic regression analyses, we examined the relation of the independent drug use variables and the psychiatric disorders (MDD, alcohol dependence, and SUDs) controlling for episodes of appropriate psychiatric disorders (MDD or SUDs) during childhood, early adolescence, and middle and late adolescence. The analyses were also done with control for childhood aggression; the findings were not significantly altered.

### Table 1. Substance Use at Time 2 Through Time 4*

<table>
<thead>
<tr>
<th>Degree of Substance Use</th>
<th>Tobacco</th>
<th>Alcohol</th>
<th>Marijuana</th>
<th>Other Illicit Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>T2</td>
<td>T2-T3</td>
<td>T3-T4</td>
<td>T2</td>
</tr>
<tr>
<td>Light</td>
<td>17.6</td>
<td>16.7</td>
<td>16.9</td>
<td>16.9</td>
</tr>
<tr>
<td>Moderate</td>
<td>13.4</td>
<td>14.4</td>
<td>13.4</td>
<td>13.4</td>
</tr>
<tr>
<td>Heavy</td>
<td>3.7</td>
<td>6.1</td>
<td>15.1</td>
<td>0.1</td>
</tr>
</tbody>
</table>

*Data are given as percentages. T2 indicates time 2: data collected in 1983; T3, time 3: data collected in 1986; and T4, time 4: data collected in 1992 as part of the Children in the Community Study.
had a significant effect on later MDD, alcohol dependence, and SUDs. Overall, except for the effect of tobacco use on MDD, drug use during the early years was significantly related to later psychiatric disorders, even after statistically controlling for age, sex, parental educational level, family income, and episodes of prior psychiatric symptoms.

We also examined the results of the logistic regression analysis for each of the periods (T2, T3, and T4). The independent variables were tobacco, alcohol, marijuana, and other illicit drugs. The dependent variables were MDD, alcohol dependence, and SUDs.

As given in Table 3, there was a relationship between T2 marijuana use and MDD. The use of tobacco, alcohol, marijuana, and other illicit drugs at T2 and T4 were related to alcohol dependence and SUDs at T5. Tobacco use at T2 and alcohol and other illicit drugs used at T4 were related to MDD at T5.

We compared the consistent users at T2 through T4 and later users of drugs at T3 through T4 with respect to MDD, alcohol use, and SUDs. Insufficient total numbers of the population in the early user group did not allow for statistical comparisons. Although there was no overall statistical significance in the comparison between the later users vs the consistent users, a trend did emerge on the measure of SUDs. The consistent group, whether for tobacco, alcohol, marijuana, or other illicit drugs, showed more evidence of SUDs than the later users (9% vs 6% for tobacco use; 12% vs 4% for alcohol dependence; 13% vs 8% for marijuana use; and 19% vs 11% for other illicit drug use).

**COMMENT**

As predicted, our results demonstrate that the cumulative frequency of drug use (alcohol, marijuana, and other illegal drugs) covering the period of childhood and early adolescence, middle and late adolescence, and/or early adulthood (T2-T4) was associated with episodes of MDD, alcohol dependence, and SUDs in the late 20s (T5). This finding supports and further extends the literature in a number of ways. First, the study provides evidence that drug use precedes MDD and alcohol dependence, and is not merely a consequence of these disorders. Related to this, the study demonstrates that certain types of drug use (eg, marijuana) during childhood and adolescence should not necessarily be treated as benign conditions that the youth may outgrow. Second, unlike other studies, our data demonstrate that the relationship between drug use and psychiatric disorders can hold across a large span of time (eg, 14 years). Moreover, for the most part, our results indicate that the relationships between our independent variables and alcohol dependence and SUDs stem from drug use at both T2 and T3 as well as T4. Major depressive disorder has the strongest relationship with the recent use of alcohol and illegal drugs other than marijuana. Third, the link between drug use in childhood and early adolescence, middle and late adolescence, and/or the early 20s and MDD, alcohol dependence, and SUDs in the late 20s appears even after controlling for the effects of sex, age, prior episodes of MDD, and socioeconomic status.
With the exception of tobacco use, our results extend the findings of cross-sectional studies to our longitudinal sample and show that earlier drug use is associated with the occurrence of several psychiatric disorders at a later time. More specifically, alcohol use increases the risk of later MDD, alcohol dependence, and SUDs. Marijuana use and the use of other illicit drugs also increase the risk of later drug dependence. The present study examines the use of tobacco, alcohol, and other illicit drugs, in addition to the use of marijuana. Although we cannot assert that our study indicates a causal relationship between drug use and the later occurrence of psychiatric disorders, substance use appears at least to contribute to the occurrence of some psychiatric disorders.

There may be a variety of mechanisms underlying the linkage between the use of alcohol, marijuana, or other illicit drugs and later psychiatric disorders, associated with different causes. In line with a psychopharmacological interpretation, it may be that different neurobiological and behavioral changes occur with multiple exposures to different drugs. However, despite the different pharmacological properties of the various substances, the similarity of the ORs between drug use and psychiatric disorders (1.2-1.4) suggests the homogeneity of their mechanisms, which may arise from unmeasured common underlying factors such as family conflict, drug-using peers, or genetic factors. Such underlying common factors may have an effect at some time during development on the onset of marijuana use which, in turn, may be related to mental illnesses. Therefore, limitation of drug use may lessen the adverse effect of earlier family or genetic factors on the development of later psychiatric disorders.

In our earlier work, we found that tobacco use in late adolescence did predict MDD in the early 20s. In this analysis, our results extend these findings by demonstrating that tobacco use in late adolescence predicts MDD in the late 20s. However, contrary to expectation, tobacco use in the early 20s does not predict MDD in the late 20s. This finding may point to a critical period for the noxious influence of tobacco use on the later development of MDD.

The study has several limitations. The sample we used was predominantly white; therefore, we can only generalize to a population of white youth. However, the study is based on an epidemiological sample of the northeast, and the rates of drug use were not too different from those found elsewhere in the United States at each point in time. We were able to make comparisons of individual changes in addition to the cohort changes noted previously. There was a trend for consistent users to report greater SUDs than later users on each of the 4 drug conditions. This type of focus on individual patterns may not be evident in a cohort analysis. Such individual analyses would be important to pursue in the future. Although some researchers have noted the relative validity of self-reports of drug use, we were unable to include external validation of the psychiatric disorders or drug use to confirm our self-report measures. More detailed reporting of psychiatric disorders may appear in adulthood compared with adolescence, and, thus, may contribute to the statistical significance of the young adult findings, specifically, a higher prevalence of psychiatric disorders.

### Table 3. Childhood, Adolescent, and/or Early 20s Drug Use as Related to Risks of Major Depressive Disorder, Alcohol Dependence, and Substance Use Disorders in the Late 20s*

<table>
<thead>
<tr>
<th>Substance Use Net of Covariates</th>
<th>Disorder in Late 20s</th>
<th>MDD†</th>
<th>95% CI</th>
<th>Alcohol Dependence†</th>
<th>95% CI</th>
<th>Substance Use Disorders‡</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior to T2</td>
<td>1.461‡</td>
<td>1.041-2.050</td>
<td>1.636‡</td>
<td>1.087-2.460</td>
<td>1.742</td>
<td>1.156-2.264</td>
<td></td>
</tr>
<tr>
<td>T2-T3</td>
<td>1.422‡</td>
<td>1.079-1.875</td>
<td>1.765‡</td>
<td>1.241-2.510</td>
<td>1.303</td>
<td>0.912-1.862</td>
<td></td>
</tr>
<tr>
<td>T3-T4</td>
<td>0.920</td>
<td>0.722-1.171</td>
<td>1.772‡</td>
<td>1.316-2.385</td>
<td>1.351</td>
<td>1.027-1.775</td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior to T2</td>
<td>1.589</td>
<td>0.956-2.642</td>
<td>1.978‡</td>
<td>1.087-3.601</td>
<td>2.354</td>
<td>1.294-4.282</td>
<td></td>
</tr>
<tr>
<td>T2-T3</td>
<td>1.484</td>
<td>0.997-2.211</td>
<td>1.651‡</td>
<td>1.012-2.695</td>
<td>1.358</td>
<td>0.831-2.219</td>
<td></td>
</tr>
<tr>
<td>T3-T4</td>
<td>2.085§</td>
<td>1.408-3.085</td>
<td>2.191‡</td>
<td>1.329-3.813</td>
<td>2.015</td>
<td>1.233-3.243</td>
<td></td>
</tr>
<tr>
<td>Marijuana use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior to T2</td>
<td>1.565‡</td>
<td>1.102-2.222</td>
<td>1.659‡</td>
<td>1.097-2.507</td>
<td>1.649</td>
<td>1.607-2.548</td>
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</tr>
<tr>
<td>T2-T3</td>
<td>1.438§</td>
<td>1.081-1.912</td>
<td>1.303</td>
<td>0.907-1.873</td>
<td>1.632</td>
<td>1.143-2.330</td>
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<tr>
<td>T3-T4</td>
<td>1.175</td>
<td>0.887-1.555</td>
<td>1.575 §</td>
<td>1.143-2.170</td>
<td>2.056§</td>
<td>1.510-2.799</td>
<td></td>
</tr>
<tr>
<td>Other illicit drug use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior to T2</td>
<td>1.482</td>
<td>0.901-2.439</td>
<td>2.581§</td>
<td>1.279-3.571</td>
<td>1.926</td>
<td>1.150-3.227</td>
<td></td>
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<tr>
<td>T2-T3</td>
<td>1.160</td>
<td>0.733-1.838</td>
<td>1.818§</td>
<td>1.136-2.389</td>
<td>1.517</td>
<td>0.927-2.482</td>
<td></td>
</tr>
<tr>
<td>T3-T4</td>
<td>2.194§</td>
<td>1.509-3.086</td>
<td>2.635§</td>
<td>1.730-4.006</td>
<td>2.897§</td>
<td>1.935-4.334</td>
<td></td>
</tr>
</tbody>
</table>

*Net of covariates indicates statistical control on sex, age, parental educational level, family income, and appropriate prior episodes of psychiatric disorders. OR indicates odds ratio; CI, confidence interval; T2, time 2: data collected in 1983; T3, time 3: data collected in 1986; T4, time 4: data collected in 1992 as part of the Children in the Community Study; and MDD, major depressive disorder.
†These analyses were also controlled for prior episodes of MDD during childhood and adolescence.
‡These analyses were also controlled for prior episodes of substance use disorders during childhood and adolescence.
¶P<.05.
||P<.01.
disorders. For example, adolescents have an easier time reporting concrete events like drug use than internal processes such as mood symptoms. Furthermore, we did not include some DSM-IV disorders (eg, antisocial personality disorder); thus, we may have underestimated the extent to which earlier drug use is related to such later psychiatric disorders. There may be some underreporting of alcohol use by the participants. Perhaps this accounts for the fact that the relationship between alcohol use and later alcohol dependence was not higher than the relationship between alcohol use and later SUDs.

Despite these caveats, the study has implications for the prevention of MDD, alcohol dependence, SUDs, and possibly other psychiatric disorders. The results indicate that to the extent that substance use is implicated in psychiatric disorders, a decrease in youth substance use may be accompanied by a corresponding decrease in later psychiatric disorders. Thus, from a treatment perspective, early detection of drug use will be facilitated if physicians are aware that drug use in children, adolescents, and young adults may signal the development of later MDD, alcohol dependence, and SUDs. Well-coordinated interventions against the early use of drugs may act to alleviate physiological or psychosocial problems that are related to adult psychiatric disorders.

The study indicates the importance of examining a range of psychiatric disorders in conjunction with many kinds of earlier substance use over a wide age range to afford a more complete picture of how these complex factors are developmentally related. Physicians may derive benefit from such an approach in planning prevention and treatment interventions.

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