Comorbid trajectories of substance use as predictors of Antisocial Personality Disorder, Major Depressive Episode, and Generalized Anxiety Disorder

Judith S. Brook a,⁎, Chenshu Zhang a, Elizabeth Rubenstone a, Brian A. Primack b, David W. Brook a

a New York University School of Medicine, Department of Psychiatry, 215 Lexington Ave., 15th Floor, New York, NY 10016, USA
b University of Pittsburgh School of Medicine, Department of Medicine, Division of General Internal Medicine, 230 McKee Place, Suite 600, Pittsburgh, PA 15213-2582, USA

HIGHLIGHTS

• We examined comorbid trajectories of substance use from adolescence to adulthood.
• 4 trajectory groups of comorbid substance use and one non-use group were extracted.
• The 4 groups were more likely than non-users to have psychiatric disorders at age 37.
• The most severe substance-using group had the highest risk for psychiatric disorders.
• Treatment programs for community adults may need to address comorbid conditions.

ABSTRACT

Objective: To determine longitudinal associations between patterns of comorbid cigarette, alcohol, and marijuana use and Antisocial Personality Disorder (ASPD), Major Depressive Episode (MDE), and Generalized Anxiety Disorder (GAD) in adulthood.

Method: A random community-based sample [n = 36.6 (SD = 2.8)] from the Children and Adults in the Community Study, an ongoing investigation of substance use and psychiatric disorders. Data were collected at six time waves. Conjoint trajectories of cigarette, alcohol, and marijuana use spanning adolescence to adulthood were determined; multivariable logistic regression analyses assessed associations between trajectory group membership and having ASPD, MDE, or GAD in adulthood.

Results: Five conjoint trajectory groups were obtained: HHH (chronic cigarette, alcohol, and marijuana use), DDD (delayed/late-starting cigarette, alcohol, and marijuana use), LML (low/no smoking, moderate alcohol use, occasional marijuana use), HMN (chronic smoking, moderate alcohol use, no marijuana use), and NON (occasional alcohol use only). Compared with members of the NON group, those in the HHH group had significantly greater odds for having ASPD (Adjusted Odds Ratio [AOR] = 28.52, 95% Confidence Interval [CI] = 9.44–86.17), MDE (AOR = 2.67, 95% CI = 1.14–6.26), and GAD (AOR = 6.39, 95% CI = 2.62–15.56). Members of the DDD, LML, and HMN groups had weaker and less consistent associations with the three psychiatric outcomes.

Conclusions: In a large, community-based sample, long-term concurrent use of more than one substance was associated with both externalizing and internalizing psychiatric disorders in adulthood. Prevention and treatment programs might target individuals in the community and general clinical populations with comorbid substance use, even if they haven’t been identified as having a substance use disorder.

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Comorbid substance use and Antisocial Personality Disorder
Comorbid substance use and Major Depressive Episode
Comorbid substance use and Generalized Anxiety Disorder

1. Introduction

1.1. Comorbid substance use

Substance use is often comorbid with psychopathology (Agrawal, Budney, & Lynskey, 2012; Chen, Wagner, & Anthony, 2002; Degenhardt & Hall, 2003; Degenhardt, Hall, & Lynskey, 2001; Hämäläinen, Kaprio, Isometsä, et al., 2001; Jackson, Sher, &
Schulenberg, 2008). According to the National Survey on Drug Use and Health, the use of individual substances—such as cigarettes, alcohol, or marijuana—among persons aged 18 years or older was associated with about twice the odds of having reported a Major Depressive Episode (MDE) (SAMHSA, 2014). However, while the concurrent use of more than one substance (e.g., tobacco and alcohol) is common (Degenhardt & Hall, 2003; Jackson et al., 2008; Witkiewitz, Desai, Steckler, et al., 2012), there has been less empirical research on associations between comorbid substance use and psychopathology. Comorbid substance use may stem from both genetic and psychosocial factors (Agrawal et al., 2012; Palmer, Young, Hopper, et al., 2009; Young, Rhee, Stallings, Corley, & Hewitt, 2006). Increasing evidence points to a genetic overlap in the propensity to use tobacco, alcohol, and marijuana (Young et al., 2006; Sartor, Grant, Bucholz, et al., 2010), factors such as behavioral undercontrol, poor familial relationships, affiliation with deviant peers, and drug accessibility may also predispose the individual to heterogeneous substance use (Agrawal et al., 2012; Brook, Rubenstone, Zhang, & Brook, 2012a; Van Ryzin, Fosco, & Dishion, 2012). Therefore, a better understanding of distinct patterns of comorbid substance use may be more practically relevant to prevention and treatment programming than focusing on the use of an individual substance, e.g., marijuana.

1.2. Substance use and psychopathology

In addition, most studies on substance use and psychopathology have examined individuals already in treatment for substance use disorders (SUDs). These investigations have shown that individual use of cigarettes, alcohol, or marijuana is associated with conditions such as Antisocial Personality Disorder (ASPD), Major Depressive Episode (MDE), and Generalized Anxiety Disorder (GAD) (Chen et al., 2002; Kedzior & Laeber, 2014). However, such studies do not take into account the large number of adults in the community who have engaged in long-term substance use that does not meet the threshold of a disorder. More work in this area may illuminate the potential value of addressing comorbid substance use in community-based populations and/or clinical populations of individuals who have not yet been identified as having SUDs.

Another important gap in the literature is that most investigations on associations between substance use and psychopathology have employed cross-sectional designs and/or measured substance use during a narrowly circumscribed period—typically adolescence and/or young adulthood. These approaches, while valuable, do not address the extent to which persistent substance use may affect individuals’ lives over time or its impact during adulthood. Substance use may be associated with later psychopathology due to shared underlying psychosocial and genetic factors (Malone, Taylor, Marmorstein, McGu, & Iacono, 2004) or due to the adverse physiological and psychological effects of the substance(s) on the individual, such as dysregulated stress reactivity (Lovallo, 2006). A greater understanding of long-term comorbid substance use and its association with later psychopathology among a community sample will be valuable to the design and improvement of treatment programs for such comorbidity.

1.3. Hypotheses

The present study extends prior research by addressing the preceding voids in the research literature. In particular, we examine patterns of the comorbid use of three substances of abuse (tobacco, alcohol, and marijuana) among a community-based sample across a span of 23 years. Further, we determine associations between these patterns and psychopathology (ASPD, MDE, and GAD) in adulthood. Our hypotheses are based on the few studies on comorbid tobacco, alcohol, and marijuana use and on trajectory analyses of the use of one or two of these substances (Brook, Lee, Brown, & Finch, 2012b; Caldeira, O’Grady, Vincent, & Arria, 2012). Specifically, we hypothesized approximately seven trajectory groups of substance use, consisting of: 1) chronic, heavy users of all three substances (tobacco, alcohol and marijuana); 2) a delayed/late-starting group, in which members used all three substances; 3) an alcohol and marijuana use only group; 4) a cigarette and alcohol use group; 5) a cigarette and marijuana use group; 6) a declining or “maturing out” group that used cigarettes, alcohol and/or marijuana at rates that started to decline in the late 20s; and 7) a group that used no substances at all or engaged in occasional alcohol use only. We hypothesized that, compared with membership in the low/non-use trajectory group, membership in each of the trajectory groups of comorbid substance use would be associated with ASPD, MDE, and GAD in adulthood (H1). Additionally, we expected that membership in the heaviest use groups would be more highly related to ASPD, MDE, and GAD than membership in the lower use groups (H2). Finally, we hypothesized that trajectory groups in which members used marijuana (an illicit substance) would be more highly associated with ASPD than membership in trajectory groups that used cigarettes and/or alcohol only (H3).

2. Methods

2.1. Participants and procedure

The present study comprises the seventh wave of data collection of the Children and Adults in the Community study, an on-going psychosocial investigation of substance use and psychiatric disorders. Families were randomly selected in 1975 (Time 1; T1) from one of two upstate New York counties, Albany and Saratoga. Participants were representative of the northeast U.S. at that time as there was a close match between their families and the results of the 1980 U.S. Census with respect to several demographic variables, such as racial distribution, family income, maternal education, and family structure.

Only mothers of the participants in the current study were interviewed at T1 (N = 973). (The participants in the current study were X age = 5 years at that time.) Participant data, on which the present study is based, were collected at six subsequent waves: 1983 (Time 2; T2, N = 756), 1985–1986 (Time 3; T3, N = 739), 1992 (Time 4; T4, N = 750), 1997 (Time 5; T5, N = 749), 2002 (Time 6; T6, N = 673), and 2005–2006 (Time 7; T7, N = 607). The mean ages (SD) of the participants were 14.1 (2.8) at T2, 16.3 (2.8) at T3, 22.3 (2.8) at T4, 27.0 (2.8) at T5, 31.9 (2.8) at T6, and 36.6 (2.8) at T7 (age range 32–42 years). The ethnic distribution of participants at T1 was 90% White, 8% African American, and 2% Other. 50% of the sample was female.

Structured interviews were conducted by trained lay interviewers at T2-T4. Questionnaires were self-administered at T5-T7. Interviews and questionnaires took approximately 2 h to complete. After complete description of the study to the subjects, written informed consent was obtained from participants and their mothers at T2-T4, and from participants only at T5-T7. The Institutional Review Board of the New York University School of Medicine approved the procedures used in this research study. Additional details regarding the overall study methodology are available from a prior publication (see Brook, Whitteman, Gordon, & Cohen, 1986).

2.2. Measures

2.2.1. The independent variables

Substance Use. At each wave (T2-T7), participants were asked about the frequencies of their cigarette, alcohol (beer, wine, or hard liquor), and marijuana use during the period from the last time wave through the current time wave. Specific items were adapted from the Monitoring the Future study (Johnston, O’Malley, Bachman, et al., 2006). The measures of cigarette, alcohol, and marijuana use have been found to predict young adult and adult health problems (Brook, Saar, Zhang, & Brook, 2009) and psychiatric disorders (Brook et al., 2012b; Brook,
Mum, and maximum BPPs. For each group, we also reported the corresponding mean, minimum, and maximum BPPs. In one of these groups, there was a pattern of little substance use at each point in time for participants assigned to the group (see Fig. 1). The observed trajectory polynomial to be cubic. The full information maximum likelihood (FIML) approach was used for missing data (Schafer & Graham, 2002), and fifty random sets of starting values were used to optimize the likelihood function. The minimum Bayesian Information Criterion (BIC) was used to determine the number of substance use trajectory groups (G). After extracting latent classes, we assigned each participant the likelihood function. The minimum Bayesian Information Criterion (Wittchen & Kessler, 1994), as has our adaptation. (See supplemental Tables S2–S4 for the ASPD, MDE, and GAD diagnostic criteria.)

2.2.2. The dependent variables

Mental Health Outcomes. Antisocial Personality Disorder (ASPD), Major Depressive Episode (MDE), and Generalized Anxiety Disorder (GAD) were each assessed using an adaptation of the respective measure from the University of Michigan Composite International Diagnostic Interview (UM-CIDI) (Kessler, McGonagle, Zhao, et al., 1994). The UM-CIDI, which we adapted for consistency with the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (American Psychiatric Association, 1994), has demonstrated good validity and reliability (Wittchen & Kessler, 1994), as has our adaptation. (See supplemental Tables S2–S4 for the ASPD, MDE, and GAD diagnostic criteria.)

2.2.3. Covariates

Socio-demographic Covariates. We captured several socio-demographic variables for use as covariates in multivariable models, including sex, age, and county residency. We also assessed parental educational level and family income at baseline (T2) for the current study. Both scales were continuous and their respective response ranges were first grade through ≥ college senior for parental education level, and $4000–$5999 to ≥$50,000 for baseline family income.

2.3. Data analysis

We used Growth Mixture Modeling (GMM) in Mplus version 6© (Muthén & Muthén, 2010) to partition the sample according to underlying substance use trajectory patterns involving cigarette, alcohol, and marijuana use (N = 806). We treated cigarette, alcohol, and marijuana use at each point in time as censored normal variables. We set each trajectory polynomial to be cubic. The full information maximum likelihood (FIML) approach was used for missing data (Schafer & Graham, 2002), and fifty random sets of starting values were used to optimize the likelihood function. The minimum Bayesian Information Criterion (BIC) was used to determine the number of substance use trajectory groups (G). After extracting latent classes, we assigned each participant to the substance use trajectory group with the largest Bayesian posterior probability (BPP). For each of the substance use trajectory groups, we created an indicator variable that had a value of 1 if the participant had the largest BPP for that group and 0 otherwise. The observed trajectories for a group were the averages of cigarette, alcohol, and marijuana use at each point in time for participants assigned to the group (see Fig. 1). For each group, we also reported the corresponding mean, minimum, and maximum BPPs.

Next, we conducted logistic regressions using SAS (SAS Institute Inc., 2014) to assess the associations of the substance use trajectory groups with ASPD, MDE, and GAD. The analyses were conducted separately for each dependent variable. Our primary multivariable models controlled for all potentially confounding socio-demographic variables described above: sex, age, county residency, parental education level, and family income, each at T2. Each model compared participants in the G-1 (number of trajectory groups minus 1) at-risk groups (e.g., the group of chronic cigarette, alcohol, and marijuana use) to members of the low-risk group (i.e., the occasional alcohol use only group). We used the G-1 BPPs of the at-risk groups as independent variables and the BPP of the low-risk group as the reference group. For each BPP variable, we reported the adjusted odds ratio (AOR) and corresponding 95% Confidence Interval (CI).

3. Results

3.1. Attrition analysis

There were no statistically significant differences between participants included in the analyses of ASPD, MDE, and GAD at T7 (N = 607) and those who did not participate (N = 199) with respect to age (t = −0.74, p-value = 0.46) and earlier internalizing behavior (t = 0.14, p-value = 0.89). However, there was a greater percentage of female participants (χ²(1) = 28.24, p-value < 0.001) and trends towards less earlier delinquency (t = 1.92, p-value = 0.06) and higher parental educational level (t = 1.66, p-value = 0.10) among participants who were included in the T7 analyses, as compared to those who were excluded.

3.2. Substance use scores

The mean cigarette smoking score and marijuana use score peaked at T4 (mean = 1.38 and 1.00, respectively) when the participants were in their early twenties, and declined from T4–T7. The mean alcohol use scores also peaked at T4 (mean = 1.46), but remained relatively stable from T4–T7 (Table S5).

3.3. Trajectory groups

We calculated GMM solutions for two trajectory groups (BIC = 31,858; entropy = 0.906), three trajectory groups (BIC = 31,142; entropy = 0.892), four trajectory groups (BIC = 30,526; entropy = 0.888), and five trajectory groups (BIC = 30,323; entropy = 0.875). We were unable to attain convergence for a six-group solution. Based on these BIC criteria and on face validity of the resulting groups, a five-group model was selected (Fig. 1). There were two trajectory groups in which members used all three substances (tobacco, alcohol, and marijuana). One group, which showed a pattern of chronic, moderate-to-heavy cigarette, alcohol, and marijuana use, was labeled HHH (high levels of each of the three substances: 13.0%; mean BPP = 90%, min BPP = 43%, max BPP = 100%). The other trajectory group in which members used all three substances displayed a pattern of delayed or late-starting moderate cigarette, alcohol, and marijuana use (labeled DDD for delayed onset of all three substances: 23.5%; mean BPP = 91%, min BPP = 49%, max BPP = 100%). There were two trajectory groups in which members used two substances. In one of these groups, there was a pattern of little to no tobacco use, moderate alcohol use, and occasional marijuana use (LML for low tobacco use, moderate alcohol use, and low marijuana use; 17.7%; mean BPP = 92%, min BPP = 40%, max BPP = 100%). The other trajectory group in which members used two substances showed a pattern of chronic, heavy smoking, moderate alcohol use, but no marijuana use. This group was labeled HMM (15.0%; mean BPP = 89%, min BPP = 38%, max BPP = 100%). Finally, the group characterized by a pattern of occasional alcohol use only was named NON (i.e., no smoking, occasional alcohol use, and no marijuana use; 30.8%; mean BPP = 5%, min BPP = 49%, max
1. HHH (Chronic, moderate-to-heavy cigarette smoking, alcohol use, and marijuana use)

![Graphs showing smoking, alcohol use, and marijuana use trajectories for Group 1]

2. DDD (Late-starting, moderate cigarette smoking, alcohol use, and marijuana use)

![Graphs showing smoking, alcohol use, and marijuana use trajectories for Group 2]

3. LML (Little to no tobacco use, moderate alcohol use, and occasional marijuana use)

![Graphs showing smoking, alcohol use, and marijuana use trajectories for Group 3]

4. HMN (Chronic heavy smoking, moderate alcohol use but no marijuana use)

![Graphs showing smoking, alcohol use, and marijuana use trajectories for Group 4]

5. NON (Occasional alcohol use only)

![Graphs showing smoking, alcohol use, and marijuana use trajectories for Group 5]
BPP = 100%). Contrary to expectation, our results did not obtain a co-morbid tobacco and marijuana use group or a “maturing out” trajectory group. The size and percentage of participants in each trajectory group appear in Table 1.

3.4. Multivariate logistic regression analyses

We conducted multivariate logistic regression analyses for the BPPs of the comorbid trajectory groups as predictors of adult antisocial personality disorder, major depressive episode, and generalized anxiety disorder (N = 607) (see Table 2).

Compared to the BPP of the low-risk group, NON (occasional drinking only), the BPP of the chronic triple substance use group (HHH) had a greater probability of ASPD (Adjusted Odds Ratio [AOR] = 28.52), MDE (AOR = 2.67), and GAD (AOR = 6.39). The BPP of the group of delayed-starting moderate cigarette, alcohol, and marijuana use (DDD), compared to the BPP of the occasional drinking only group (NON), had a greater likelihood of ASPD (AOR = 2.89; a statistical trend) and GAD (AOR = 2.64). In addition, the BPP of the group of little to no smoking, chronic moderate drinking, and occasional marijuana use (LML), compared to the BPP of the occasional drinking only group (NON), had a greater likelihood of exhibiting ASPD (AOR = 5.61) and GAD (AOR = 3.71). Finally, the BPP of the group of chronic heavy smoking and occasional to moderate drinking but no marijuana use (HMN), compared to the BPP of the group of occasional drinking only (NON), had a greater likelihood of exhibiting ASPD (AOR = 4.25).

4. Discussion

4.1. Support for the hypotheses

As hypothesized (H1), membership in each of the comorbid substance use groups (HHH, DDD, LML, and HMN) was associated with a greater likelihood of psychiatric disorders, as compared with membership in the occasional drinking only (NON) group. However, there were weaker and less consistent associations between membership in each of the intermediate substance using groups: DDD (delayed/late-starting moderate cigarette, alcohol, and marijuana use), LML (little to no smoking, chronic, moderate drinking, and occasional marijuana use), and HMN (chronic, heavy smoking, occasional to moderate drinking, and no marijuana use) and psychiatric outcomes than between membership in the chronic triple substance use group (HHH) and these outcomes. Among the intermediate groups, none was associated with MDE, and only membership in DDD (the delayed/late-starting triple substance use group) and the LML group (little/no smoking, moderate drinking, and occasional marijuana use) was associated with GAD. Membership in DDD, LML and HMN were each associated with ASPD (although there was a statistical trend for the DDD group). H2 was upheld, therefore, because membership in HHH (the chronic triple substance use trajectory group) was more strongly associated with each of the clinical outcomes than any of the intermediate substance use categories. Finally, H3 was supported because both of the trajectory groups featuring persistent marijuana use over time, HHH and LML, were more strongly related to ASPD than the DDD (delayed/late-starting use of all three substances) or the HMN (heavy smoking, occasional to moderate drinking, and no marijuana use) groups.

The fact that membership in the HHH group (chronic smoking, drinking, and marijuana use) was associated with such strong odds for the development of psychopathology suggests that it would be valuable to target these individuals in prevention and treatment programming. This is notable especially because these were individuals recruited in the community who had not necessarily been identified previously as having SUDs. Especially considering budgetary concerns facing many community-based prevention organizations, it is valuable to know that focusing on this particular group may represent an optimization of resources.

4.2. The effect of delayed-onset substance use

It is interesting that those in the delayed/late-starting triple substance use group (DDD) had substantially lower risk of progressing to psychopathology compared with those in the chronic triple substance use group (HHH). This highlights the importance of taking into account trajectories over time instead of simple point estimates of substance use. While members of both groups used all three substances, the critical difference was that HHH individuals had early and then sustained use, while DDD individuals progressed later. It would be valuable for future research to address more deeply what it is about delaying substance use that may provide a protective benefit with regard to psychopathology in adulthood. One possibility is that social and environmental protective factors, such as strong familial bonds and less neighborhood deterioration, might both delay substance use and lessen the possibility of depression in adulthood (Buu et al., 2009; Brook et al., 2013; Choi, Harachi, & Catalano, 2006). Another possibility is that it is early substance use in particular that may exert neurobiological effects which increase predisposition to conditions such as ASPD, MDE, and GAD.

4.3. Trajectories of substance use and Antisocial Personality Disorder (ASPD)

Members of all four of the comorbid substance-using trajectory groups, HHH, DDD, LML, and HMN, were more likely to report ASPD in adulthood than were members of the NON group. These results are commensurate with prior research (Goldstein, Chou, Saha, et al., 2016), and demonstrate that long-term substance use among a non-clinical sample is highly comorbid with ASPD even in the case of legal substance use or if a substance use disorder has not been diagnosed. Of particular interest is the increased likelihood of ASPD among members of the HMN group, which used only comorbid legal substances (tobacco and alcohol). These findings suggest that the chronic comorbid use of any substances (legal or illegal) may alienate the individual from pro-social activities and individuals, especially as cigarette smokers become increasingly marginalized (Christakis & Fowler, 2008). Additionally, legal substances may share genetic risk factors with ASPD (Kendler, Prescott, Myers, & Neale, 2003). The co-occurrence of substance use and antisocial behaviors may reflect a common underlying liability or shared risk markers for externalizing behaviors (Palmer et al., 2009; Kendler et al., 2003). One trait that may link substance use and antisocial behavior is sensation seeking, which is believed to have both a biological and a social basis (Harden, Quinn, & Tucker-Drob, 2012; Roberti, 2004). Sensation seeking, characterized by a willingness to undertake risks to obtain novel experience regardless of the consequences (Zuckerman, 1994), is commensurate with both deviant and substance use behaviors, and is highly prevalent among substance users (Mahoney et al., 2015 Jan; Quinn & Harden, 2013) and antisocial individuals (DeShong & Kurtz, 2013; Wagner, 2001).

### Table 1

<table>
<thead>
<tr>
<th>Triple trajectory group</th>
<th>N</th>
<th>Proportion of the sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>HHH (chronic, moderate-to-heavy cigarette, alcohol, and marijuana use)</td>
<td>105</td>
<td>13.0%</td>
</tr>
<tr>
<td>DDD (delayed/late-starting moderate cigarette, alcohol, and marijuana use)</td>
<td>189</td>
<td>23.5%</td>
</tr>
<tr>
<td>LML (little to no tobacco use, moderate alcohol use, and occasional marijuana use)</td>
<td>143</td>
<td>17.7%</td>
</tr>
<tr>
<td>HMN (chronic heavy smoking, moderate alcohol use but no marijuana use)</td>
<td>121</td>
<td>15.0%</td>
</tr>
<tr>
<td>NON (occasional alcohol use only)</td>
<td>248</td>
<td>30.8%</td>
</tr>
</tbody>
</table>
4.4. Trajectories of substance use and Major Depressive Episode

Compared to the NON group, only membership in the HHH group predicted MDE. These findings were somewhat surprising given that prior research has demonstrated a link between the independent use of each substance and depression (Chen et al., 2002; Hamalainen et al., 2001). One possible explanation is that there is known to be a dose-response association between substance use and MDE (Hamalainen et al., 2001; Lev-Ran et al., 2014), and perhaps only members of the HHH group reached a quantitative threshold that predicted greater odds of MDE.

4.5. Trajectories of substance use and Generalized Anxiety Disorder (GAD)

Our findings are consistent with prior investigations which have shown that the independent use of tobacco, alcohol or marijuana predicts later anxiety disorders, including GAD (Degenhardt, Coffey, Romaniuk, et al., 2013; Moylan, Jacka, Pasco, & Berk, 2012). In the present study, however, only membership in the groups that used comorbid marijuana (HHH, DDD and LML)—and not the group that used legal substances only (HMN)—was associated with a greater likelihood of GAD. This finding implies that the psychosocial and/or biological effects of marijuana, in concert with the use of other substances, increase the risk of GAD. For example, individuals who use marijuana may experience greater functional impairment (e.g., poorer interpersonal relationships, less educational achievement, lower socioeconomic status) which mediates the link with GAD in adulthood. In addition, there is clinical evidence that the active ingredient in marijuana, Δ9-tetrahydrocannabinol (THC), can induce anxiety (Freeman, Dunn, Murray, et al., 2014). These findings are also supported by other emerging research connecting marijuana use with more substantial psychiatric risk than has been noted in the past (Gibbs et al., 2015; Lubman, Cheetham, & Vücel, 2014).

4.6. Limitations and suggestions for future research

Because our sample consisted of primarily White participants from upstate New York, results cannot be generalized to other racial/ethnic groups or to individuals living outside of this geographic area. It is also important to note that we did not examine factors (e.g., social, environmental) that may help to explain associations between substance use and psychiatric disorders, and which might be considered for inclusion in future research. For example, youth who are exposed to adverse family situations may be at elevated risk for both substance use and psychopathology in later life (Pilowsky, Wickramaratne, Nomura, & Weissman, 2006; Green, Zebrik, Fothergill, Robertson, & Ensminger, 2012). Furthermore, it is possible that psychopathology is a covariate of long-term substance use or that early antecedents of adult psychopathology (e.g., childhood conduct disorder) may precede the onset of substance use.

Although our study did not assess opioids (the non-medical use of prescription drugs or heroin), given the current pandemic, we strongly encourage future research to examine the trajectories, comorbidities and psychiatric sequelae of these drugs among an adult population. It is estimated that opioids are used by 3.4 million persons worldwide (United Nations Office on Drugs and Crime, 2015). In the U.S., almost 2 million persons have an opioid substance use disorder (Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality, 2015), and the mortality rate due to opioids (9% per 100,000) has increased 200% over the course of approximately fifteen years (Centers for Disease Control and Prevention, 2015). Therefore, a better understanding of the relationship of opioid use to other substance use and to psychopathology could inform both clinicians and policy makers. Among adolescents, for instance, Ali et al. (2015) demonstrated an association between prescription drug misuse and depression.

4.7. Clinical implications

Despite these limitations, the present study adds to the literature by elucidating longitudinal patterns of comorbid substance use and their associations with adult psychopathology. Findings suggest that individuals presenting with substance use should be screened for the use of other substances, and assessed for psychiatric disorders in adulthood. Additionally, results suggest that clinicians diagnose and adapt treatment to the full scope of problems which may affect adults presenting with either substance use, ASPD, MDE, or GAD. Optimally, the early identification and treatment of substance use may forestall its long-term use and potential for later psychopathology. This may be especially important as several studies have found that individuals who use more than one psychotropic substance and/or who have comorbid psychopathology are more likely to experience poorer outcomes (Nunes, Selzer, Levounis, & Davies, 2010).

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The sponsors had no role in the study design, the collection, analyses, or interpretation of the data, drafting of the manuscript, or the decision to submit the paper for publication.
Contributors

All authors substantially contributed to the present work: Dr. Judith S. Brook is the Principal Investigator of the study of which the data were used in this paper. Dr. Brook also was involved in the research design, data analysis, writing, and editing of the manuscript. Elizabeth Rubenstone conducted the literature review, and contributed to the writing and editing. Chenshu Zhang conducted all statistical analyses. Dr. Brian A. Primack assisted with writing of the manuscript and editing it for important intellectual content. Dr. David Brook took part in the writing and editing of the work. All authors were involved in data interpretation, and all approved the final submitted version of the manuscript.

Conflict of interest statement

All authors declare that they have no conflicts of interest.

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None of the authors has any conflict of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.addbeh.2016.06.003.

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