Associations between anhedonia and marijuana use escalation across mid-adolescence

Adam M. Leventhal1,2, Junhan Cho1, Matthew D. Stone1, Jessica L. Barrington-Trimis1, Chih-Ping Chou1,3, Steven Y. Sussman1,2,3, Nathaniel R. Riggs4, Jennifer B. Unger1, Janet Audrain-McGovern5 & David R. Strong6

Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA1, Department of Psychology, University of Southern California, Los Angeles, CA, USA2, School of Social Work, University of Southern California, Los Angeles, CA, USA3, Department of Human Development and Family Studies, Colorado State University, Fort Collins, CO, USA4, Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA5 and Department of Family Medicine and Public Health, School of Medicine, University of California, San Diego, La Jolla, CA, USA6

ABSTRACT

Background and aims Anhedonia—a transdiagnostic psychopathological trait indicative of inability to experience pleasure—could lead to and result from adolescent marijuana use, yet this notion has not been tested. This study aimed to estimate the association of: (1) anhedonia at age 14 with rate of change in marijuana use over an 18-month follow-up, and (2) marijuana use at age 14 with rate of change in anhedonia over follow-up. Secondary aims were to test whether gender, baseline marijuana use history and peer marijuana use moderated these associations.

Design Observational longitudinal cohort repeated-measures design, with baseline (age 14 years), 6-month, 12-month and 18-month follow-up assessments.


Participants Students [n = 3394; 53.5% female, mean (standard deviation) age at baseline = 14.1 (0.42)].

Measurements Self-report level of anhedonia on the Snaith–Hamilton Pleasure Scale and frequency of marijuana use in the past 30 days.

Findings Parallel process latent growth curve models adjusting for confounders showed that baseline anhedonia level was associated positively with the rate of increase in marijuana use frequency across follow-ups [β, 95% confidence interval (CI) = 0.115 (0.022, 0.252), P = 0.03]. Baseline marijuana use frequency was not related significantly to the rate of change in anhedonia across follow-ups [β, 95% CI = −0.015 (−0.350, 0.321), P = 0.93]. The association of baseline anhedonia with faster marijuana use escalation was amplified among adolescents with (versus without) friends who used marijuana at baseline [β, 95% CI = 0.179 (0.043, 0.334) versus 0.064 (−0.071, 0.187), interaction P = 0.04], but did not differ by gender or baseline ever marijuana use.

Conclusions In mid-adolescence, anhedonia is associated with subsequent marijuana use escalation, but marijuana use escalation does not appear to be associated with subsequent anhedonia.

Keywords Adolescents, anhedonia, longitudinal research, marijuana use, policy, prevention.

INTRODUCTION

Marijuana is one of the most widely used illicit substances world-wide [1,2]. Although it has been reported that marijuana use rate has stabilized or even decreased in recent years in most high-income countries, the continuing high prevalence of use among adolescents and young adults [1,2] is a cause for concern. Such emerging trends have heightened interest in the link between mental health problems and adolescent marijuana use to inform policy and prevention efforts.

Understanding the comorbidity between psychopathology and marijuana use is complicated. Marijuana use is associated with numerous different psychiatric disorders [3,4], each of which tend to co-occur with one another [5]. Additionally complicating matters is the potential bidirectional nature of this association, with evidence that marijuana use may both predict and result from poor mental health [6]. A parsimonious explanation of this comorbidity may be that a small set of transdiagnostic psychopathological vulnerabilities that give rise to numerous mental health conditions may also contribute to and
result from marijuana use [7]. Such transdiagnostic vulnerabilities may account for the pervasive patterns of psychiatric comorbidity with use of marijuana and other substances [8–10].

One such transdiagnostic vulnerability is anhedonia—diminished capacity to experience pleasure in response to rewards. As a subjective manifestation of deficient reward processing capabilities, anhedonia is believed to result from hypoactive brain reward circuitry [11]. While anhedonia is a core feature in a DSM-defined major depressive episode [12], it has also been linked to other psychopathologies comorbid with drug use, including psychosis [13], borderline personality disorder [14], social anxiety [15], attention deficit hyperactivity disorder [16] and post-traumatic stress disorder [17] and has therefore been proposed to be a transdiagnostic process [7]. Departing from its consideration as a ‘symptom’ of a disease state as in DSM-defined major depression, anhedonia has also been conceptualized as a continuous dimension, upon which there are substantial interindividual differences [18]. Individuals at the lower end of the anhedonic spectrum experience high levels of pleasure and experience robust affective responses to pleasurable events, whereas those at the upper end of this spectrum exhibit more prominent deficits in their pleasure experience [18,19]. Anhedonia operates as a ‘trait-like’ dimension that is stable yet malleable [20], which is empirically and conceptually distinct from other emotional constructs, such as reward sensitivity (i.e. extraversion and positive emotionality), alexithymia and emotional numbing (i.e. dampened positive and negative emotions), sadness and negative affect [21–23].

Recent literature documents a consistent association between anhedonia and substance use in adults [7]. To the best of our knowledge, there has been only prior study of the association between anhedonia and marijuana use in youth, which found higher anhedonia levels among treatment-seeking marijuana users than healthy controls in a cross-sectional analysis of 62 French adolescents and young adults [24]. Given the absence of longitudinal data, it is unclear whether anhedonia is a risk factor for or consequence of adolescent marijuana use. Because youth with higher anhedonia levels experience little pleasure from routine rewards (e.g. food, social interaction) they may seek out drugs of abuse, such as marijuana, which stimulate neural circuitry that underlie pleasure pharmacologically [25]. Alternatively, repeated tetrahydrocannabinol (THC) exposure during adolescence produces enduring deficits in brain reward system function and anhedonia-like behavior in rodent models [26]. In observational studies of adults, heavy or problematic marijuana use is associated with subsequent anhedonia [6] and diminished brain reward region activity during reward anticipation [27]. Consequently, it is plausible that anhedonia may both increase risk of marijuana use and result from marijuana use.

Because early adolescence is a period in which risk of marijuana use uptake is high [28] and the developing brain may be vulnerable to cannabinoid-induced neuroadaptations [29], this study estimated the strength of bidirectional longitudinal associations between anhedonia and marijuana use among adolescents during the first 2 years of high school. The primary aim was to test the following hypotheses: (1) greater baseline anhedonia would be associated with a faster rate of escalation in marijuana use across follow-up periods; and (2) more frequent use of marijuana at baseline would be associated with increases in anhedonia across follow-ups.

A secondary aim was to test whether these putative risk pathways were amplified or suppressed among pertinent subpopulations and contexts. Associations of affective disturbance and other risk factors with adolescent substance use escalation have been reported to be amplified among girls (versus boys) [30,31], early- (versus late-) onset substance users [32] and those with substance-using peers [33]. We therefore tested whether associations between anhedonia and marijuana use were moderated by gender, history of marijuana use prior to the study surveillance period at baseline and peer marijuana use at baseline.

METHODS

Design

This study used an observational longitudinal cohort repeated measures design, involving assessments at baseline (age 14 years), 6-month, 12-month and 18-month follow-ups.

Participants and procedures

Data were drawn from the Happiness & Health Study, a longitudinal cohort survey of substance use and mental health among high school students in Los Angeles, CA, USA. Among 40 public high schools approached to participate in the study because of their diverse demographic characteristics and proximity, 10 participated in this study (characteristics of participating schools in reference to Los Angeles county public schools appear in the online Supporting information, Table S1). Of the 4100 eligible 9th grade students, 3396 students and their parents provided active written or verbal assent and consent, respectively, and enrolled. Data collection involved four semi-annual assessments: baseline (wave 1: fall 9th grade, 2013; n surveyed = 3383, 99.6%) and 6-month (wave 2: spring 9th grade, 2014; n = 3293, 97.0%), 12-month (wave 3: fall 10th grade, 2014; n = 3288, 96.8%) and 18-month (wave 4: spring 10th grade, 2015; n = 3262, 96.1%) follow-ups. At each wave, paper-and-pencil surveys were administered in students’ classrooms on site. Students not in class during data collections completed...
surveys by telephone, internet or mail (6-month follow-up: \( n = 51 \), 12-month follow-up: \( n = 153 \), 18-month follow-up: \( n = 215 \)). The University of Southern California institutional review board approved the study.

**Measures**

**Anhedonia**

At each time-point, anhedonia was assessed by the Snaith–Hamilton Pleasure Scale (SHAPS) [34], which includes 14 self-statements of pleasure response to rewarding sensory stimuli, social activities and hobbies (e.g. ‘I would be able to enjoy a beautiful landscape or view’). Responses to each item [rated 0 (strongly agree), 1 (agree), 2 (disagree), 3 (strongly disagree)] are summed, with a higher score indicating greater anhedonia level. Among adolescents, the SHAPS has exhibited a unidimensional factor structure and strong convergent and discriminant validity [23]. Internal consistency in this sample was adequate (\( \alpha \) across waves > 0.89). The proportion surpassing a recommended cut-off indicating possible clinically significant anhedonia [34] is reported (i.e. disagree or strongly disagree ≥ 3 Items).

**Marijuana use**

At each time-point, marijuana use was measured using well-validated items based on the Monitoring the Future [35] surveys assessing past 6-month use (yes/no) and days used in past 30 days (forced choice with nine options, ranging from 0 to 30 days). To ensure adequate frequency across each level of marijuana use, responses were coded ordinaly for the primary outcome [0 (no use in the past 6 months), 1 (used in the past 6 months, but not in last 30 days), 2 (1–2 days in last 30), 3 (3–5 days), 4 (6–14 days) and 5 (≥ 15 days)].

**Moderators**

Gender, baseline ever use of marijuana (yes/no; to distinguish youth whose use trajectories reflected new onset versus carry-over of use patterns that predated the assessment period), and number of five closest friends who had used marijuana in the past 30 days (≥ 1 versus 0) were assessed via self-report.

**Covariates**

A priori covariates were selected based on their association with anhedonia or marijuana use in the extant literature [16,36,37]. Time-invariant socio-demographic covariates included youth age, gender, race/ethnicity and highest parental education level based on responses to investigator-defined forced-choice items at baseline (see response categories in Table 1). To rule out that that associations occur because anhedonia is merely a proxy for psychopathologies that couple directly with marijuana use, well-established self-report scales which have shown strong psychometric properties in adolescent samples were administered and applied as time-invariant covariates. These measures included the Center for Epidemiologic Studies Depression Scale (CESD; \( \alpha = 0.81 \)) [38] measure of past week depressive symptom frequency, Revised Child Anxiety and Depression Scale–Social Phobia subscale (RCADS-SP; \( \alpha = 0.92 \)) [39,40], and the Current Symptoms Scale–Self Report Form [41] measure of DSM-IV attention deficit/hyperactivity disorder (ADHD) symptoms during the past 6 months (\( \alpha = 0.92 \)). The CESD and RCADS-SP values at the baseline wave were used. Because ADHD measures were not added to the assessment battery until wave 2, wave 2 ADHD scores were used in the analysis. Alcohol and cigarette use frequencies, which were each measured and coded in the same fashion as marijuana use, well-established self-report scales which have shown strong psychometric properties in adolescent samples were administered and applied as time-invariant covariates.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>( n ) (%) or mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex ((n = 3369),^a)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1801 (53.5%)</td>
</tr>
<tr>
<td>Male</td>
<td>1568 (46.2%)</td>
</tr>
<tr>
<td>Age ((n = 3360),^a)</td>
<td>14.08 (0.42)</td>
</tr>
<tr>
<td>Race/ethnicity ((n = 3311),^b)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>520 (15.7%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1557 (47.0%)</td>
</tr>
<tr>
<td>Black</td>
<td>166 (5.0%)</td>
</tr>
<tr>
<td>Asian</td>
<td>535 (16.2%)</td>
</tr>
<tr>
<td>Multi-ethnic/Other</td>
<td>533 (16.1%)</td>
</tr>
<tr>
<td>Highest parental education level ((n = 2931),^c,^b)</td>
<td></td>
</tr>
<tr>
<td>≤8th grade</td>
<td>117 (4.0%)</td>
</tr>
<tr>
<td>Some high school</td>
<td>266 (9.1%)</td>
</tr>
<tr>
<td>High school graduate</td>
<td>493 (16.8%)</td>
</tr>
<tr>
<td>Some college</td>
<td>573 (19.5%)</td>
</tr>
<tr>
<td>College graduate</td>
<td>927 (31.6%)</td>
</tr>
<tr>
<td>Graduate degree</td>
<td>555 (18.9%)</td>
</tr>
<tr>
<td>Depressive symptom level(^e) ((n = 3349),^b,^a)</td>
<td>14.43 (11.76)</td>
</tr>
<tr>
<td>Social phobia level(^d) ((n = 3206),^b,^a)</td>
<td>11.84 (7.29)</td>
</tr>
<tr>
<td>ADHD(^d) ((n = 3170),^b,^a)</td>
<td>12.78 (9.95)</td>
</tr>
<tr>
<td>Has a friend who uses marijuana ((n = 3305),^b,^a)</td>
<td>1178 (35.6)</td>
</tr>
<tr>
<td>Baseline ever use of marijuana ((n = 3329),^b,^a)</td>
<td>503 (15.1)</td>
</tr>
<tr>
<td>Marijuana use onset before age 14 years ((n = 3329),^b,^a)</td>
<td>475 (14.3)</td>
</tr>
</tbody>
</table>

\(^a\)Available (non-missing) data for respective variable and, for categorical variables, denominator for within-column percentages. \(^b\)Participants who marked ‘do not know’ response \((n = 422)\) recoded as missing. \(^c\)Center for Epidemiologic Studies Depression Scale total score. \(^d\)Revised Children’s Anxiety and Depression Scale – Social phobia subscale score. \(^e\)The Attention/Deficit Hyperactivity Disorder (ADHD) Self-Rating Scale total sum score. SD = standard deviation.
use, were included as a time-varying covariate at each wave to disentangle anhedonia’s relation with marijuana use from other drug use.

**Statistical analysis**

To characterize trajectories of anhedonia and marijuana use across time, latent growth curve modeling was applied to estimate a baseline level (based on intercept) and linear slope (rate of change across the four time-points) for both anhedonia and marijuana use. Univariate latent growth curve models were first fitted for marijuana use and anhedonia separately to determine the shape and variance of trajectories. A two-process parallel latent growth curve model (see Fig. 1) was then fitted, which simultaneously included growth factors for anhedonia and marijuana use after adjusting for covariates listed above and including within-construct level-to-slope associations [42]. The parallel process model was constructed to test: (1) bidirectional longitudinal associations by including directional paths from baseline anhedonia level to marijuana use slope as well as baseline marijuana use level to anhedonia slope; and (2) non-directional correlations between baseline levels of anhedonia and marijuana use and between anhedonia slope and marijuana use slope. Significant directional longitudinal paths between anhedonia and marijuana use in the overall sample were tested subsequently in moderation analyses of differences in the strength of paths across subsamples stratified by moderator status using a multi-group analysis [43]. Analyses were performed using Mplus [44] with the complex analysis function to adjust parameter standard errors due to clustering of the data by school. To address item- and wave-level missing data, full information maximum likelihood estimation with robust standard errors was applied. Continuous and categorical ordinal scaled outcomes were applied for anhedonia and marijuana use, respectively. The Akaike information criterion (AIC) and the Bayesian information criterion (BIC) were used to gauge model fit in which lower values represent better-fitting models [45]. For moderator analyses, $\chi^2$ differences were calculated using log-likelihood values and the number of free parameters contrasting the model fit with (versus without) equality constraints on the anhedonia–marijuana use path of interest across groups stratified by the moderator variable. Standardized parameter estimates and 95% confidence intervals (CI) are reported. Significance was set at $\alpha = 0.05$ (two-tailed).

**RESULTS**

**Preliminary analyses**

Among study enrollees, 3394 [99.9%; 53.5% female, M (SD) age at baseline = 14.1 (0.42)] provided at least one data point for the variables in primary models and

![Parallel latent growth curve model of anhedonia and marijuana use.](image-url)
Table 2 Descriptive statistics for repeated measures of substance use and anhedonia.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Wave 1 (n = 3383)</th>
<th>Wave 2 (n = 3293)</th>
<th>Wave 3 (n = 3288)</th>
<th>Wave 4 (n = 3262)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana use, n (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No use in the past 6 months</td>
<td>2983 (89.8%)</td>
<td>2730 (84.6%)</td>
<td>2709 (83.9%)</td>
<td>2577 (80.9%)</td>
</tr>
<tr>
<td>Past 6-month use without use in last 30 days</td>
<td>76 (2.3%)</td>
<td>152 (4.7%)</td>
<td>132 (4.1%)</td>
<td>176 (5.5%)</td>
</tr>
<tr>
<td>1–2 days in the last 30 days</td>
<td>98 (3.0%)</td>
<td>125 (3.9%)</td>
<td>141 (4.4%)</td>
<td>154 (4.8%)</td>
</tr>
<tr>
<td>3–5 days in the last 30 days</td>
<td>44 (1.3%)</td>
<td>76 (2.4%)</td>
<td>75 (2.3%)</td>
<td>82 (2.6%)</td>
</tr>
<tr>
<td>6–14 days in the last 30 days</td>
<td>48 (1.4%)</td>
<td>62 (1.9%)</td>
<td>73 (2.3%)</td>
<td>82 (2.6%)</td>
</tr>
<tr>
<td>≥15 days in the last 30 days</td>
<td>73 (2.2%)</td>
<td>82 (2.5%)</td>
<td>97 (3.0%)</td>
<td>113 (3.5%)</td>
</tr>
<tr>
<td>Available data, n&lt;sup&gt;b&lt;/sup&gt;</td>
<td>n = 3322</td>
<td>n = 3227</td>
<td>n = 3227</td>
<td>n = 3184</td>
</tr>
<tr>
<td>Alcohol use, n (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No use in the past 6 months</td>
<td>2729 (83.2%)</td>
<td>2372 (73.5%)</td>
<td>2311 (71.6%)</td>
<td>2266 (71.3%)</td>
</tr>
<tr>
<td>Past 6-month use without use in last 30 days</td>
<td>160 (4.9%)</td>
<td>249 (7.7%)</td>
<td>240 (7.4%)</td>
<td>231 (7.3%)</td>
</tr>
<tr>
<td>1–2 days in the last 30 days</td>
<td>230 (7.0%)</td>
<td>368 (11.4%)</td>
<td>410 (12.7%)</td>
<td>415 (13.1%)</td>
</tr>
<tr>
<td>3–5 days in the last 30 days</td>
<td>82 (2.5%)</td>
<td>120 (3.7%)</td>
<td>135 (4.2%)</td>
<td>144 (4.5%)</td>
</tr>
<tr>
<td>6–14 days in the last 30 days</td>
<td>49 (1.5%)</td>
<td>83 (2.6%)</td>
<td>92 (2.9%)</td>
<td>92 (2.9%)</td>
</tr>
<tr>
<td>≥15 days in the last 30 days</td>
<td>29 (0.9%)</td>
<td>37 (1.1%)</td>
<td>40 (1.2%)</td>
<td>32 (1.0%)</td>
</tr>
<tr>
<td>Available data, n&lt;sup&gt;b&lt;/sup&gt;</td>
<td>n = 3279</td>
<td>n = 3229</td>
<td>n = 3228</td>
<td>n = 3180</td>
</tr>
<tr>
<td>Cigarette use, n (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No use in the past 6 months</td>
<td>3194 (95.9%)</td>
<td>2986 (92.0%)</td>
<td>2993 (92.5%)</td>
<td>2946 (92.2%)</td>
</tr>
<tr>
<td>Past 6-month use without use in last 30 days</td>
<td>55 (1.7%)</td>
<td>132 (4.1%)</td>
<td>110 (3.4%)</td>
<td>93 (2.9%)</td>
</tr>
<tr>
<td>1–2 days in the last 30 days</td>
<td>46 (1.4%)</td>
<td>71 (2.2%)</td>
<td>72 (2.2%)</td>
<td>80 (2.5%)</td>
</tr>
<tr>
<td>3–5 days in the last 30 days</td>
<td>17 (0.5%)</td>
<td>13 (0.4%)</td>
<td>20 (0.6%)</td>
<td>28 (0.9%)</td>
</tr>
<tr>
<td>6–14 days in the last 30 days</td>
<td>10 (0.3%)</td>
<td>25 (0.8%)</td>
<td>23 (0.7%)</td>
<td>19 (0.6%)</td>
</tr>
<tr>
<td>≥15 days in the last 30 days</td>
<td>10 (0.3%)</td>
<td>18 (0.6%)</td>
<td>18 (0.6%)</td>
<td>30 (0.9%)</td>
</tr>
<tr>
<td>Available data, n&lt;sup&gt;b&lt;/sup&gt;</td>
<td>n = 3312</td>
<td>n = 3245</td>
<td>n = 3236</td>
<td>n = 3196</td>
</tr>
<tr>
<td>Anhedonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score, mean (SD)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>23.66 (6.94)</td>
<td>24.17 (8.19)</td>
<td>24.19 (8.48)</td>
<td>24.55 (8.79)</td>
</tr>
<tr>
<td>Meet clinical cut-off, n (%)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>858 (25.7%)</td>
<td>893 (27.4%)</td>
<td>861 (26.5%)</td>
<td>725 (22.9%)</td>
</tr>
<tr>
<td>Available data, n&lt;sup&gt;b&lt;/sup&gt;</td>
<td>n = 3335</td>
<td>n = 3255</td>
<td>n = 3247</td>
<td>n = 3161</td>
</tr>
</tbody>
</table>

<sup>a</sup>Available (non-missing) data for respective variable and denominator for within-column/within-time-point percentages. <sup>b</sup>Based on Snaith-Hamilton Pleasure Score (SHAPS) (sum of responses to 14 statements of pleasure response rated on 0–3 scale). <sup>c</sup>Based on those who surpass the recommended SHAPS cut-off for clinically significant anhedonia [34]. SD = standard deviation.

constituted the analytical sample (see Tables 1 and 2 for ns of available data). Participants who did not complete wave 4 (n = 131, 3.9%) were compared with those who completed all waves (n = 3252, 96.1%) to examine attrition effects. Those without wave 4 data reported higher baseline anhedonia (mean = 0.310, P < 0.001) and marijuana use frequency (d = 0.45, P < 0.001). Ps < 0.001. There were no significant differences in demographics and depressive symptoms by attrition status.

As depicted in Table 1, the sample was balanced on gender, and was socio-demographically diverse. Overall, 15% of youth reported having ever used marijuana at baseline. The distribution of marijuana, alcohol and cigarette use frequency was characteristic of general population adolescent samples (see Table 2). Across waves, 23–27% of students reported clinically significant anhedonia based on SHAPS scores. Correlations among study variables at baseline are presented in in Table 3.

Latent growth curve models

Univariate models

Univariate latent growth curve models including linear slopes for anhedonia and marijuana use exhibited a better fit of the data than quadratic models (Supporting information, Table S2). In the linear univariate models, the mean slope was significantly larger than zero for anhedonia (mean = 0.568, P < 0.001) and marijuana (mean = 0.568, P < 0.001) indicating that, averaged across all participants, anhedonia and marijuana use increased across time-points. Significant variability in marijuana use initial levels (variance of intercepts = 15.077, P < 0.001) and rates of change over time (variance of slopes = 2.169, P < 0.001) were also observed. With sufficient interindividual
variability in both marijuana use and anhedonia, we proceeded to model associations between anhedonia and marijuana use growth factors.

Two-process models of associations between anhedonia and marijuana use

The two-process latent growth model with covariates exhibited adequate fit (Fig. 1). Longitudinal directional path estimates indicate that baseline level of anhedonia was associated positively with the rate of change in marijuana use across time \( [\beta, 95\% \text{ confidence interval (CI)} = 0.115 \text{ (0.022, 0.252)}, P = 0.03] \). Baseline marijuana use level was not related significantly to the rate of change in anhedonia \( \beta, 95\% \text{ CI} = -0.015 \text{ (−0.350, 0.321)}, P = 0.93 \). Non-directional correlational paths indicated a significant positive association between the baseline levels of anhedonia and marijuana use and no association between the rate of change in anhedonia and rate of change in marijuana use. Detailed presentation of parameter estimates, including covariate paths are reported in the Supporting information, Table S3. Of interest, depressive symptoms, social phobia and ADHD symptoms were not associated significantly with changes in marijuana use over time (see Supporting information, Table S3).

Moderators of the association of baseline anhedonia with changes in marijuana use over follow-up

Given the significant directional association from initial anhedonia level to increased marijuana use over time, we examined whether the strength of this relationship differed across subgroups. Friends’ marijuana use moderated the association of initial anhedonia levels with rates of change in marijuana use over time (interaction test result \( \Delta \chi^2(1) = 4.19, P = 0.04 \)). The association of baseline anhedonia with the rate of change in marijuana use was amplified among adolescents with friends who used marijuana at baseline \( [n = 1178; \beta, 95\% \text{ CI} = 0.179 \text{ (0.043, 0.334)}, P = 0.02] \) in comparison to those without friends who had used marijuana at baseline \( [n = 2127; \beta, 95\% \text{ CI} = 0.064 \text{ (−0.071, 0.187)}, P = 0.32] \). The path from baseline anhedonia level to changes in marijuana use over time was not moderated significantly by gender \( (\Delta \chi^2(1) = 1.12, P = 0.29) \) or baseline ever marijuana use \( (\Delta \chi^2(1) = 0.81, P = 0.37) \).

Sensitivity analyses

Sensitivity analyses showed that the association between baseline anhedonia level with the rate of change in marijuana use across the follow-up: (a) was consistent regardless of concomitant use of alternative marijuana products (e.g. edible or vaporized marijuana); (b) did not differ after removing students whose reports were of questionable validity (e.g. use of a fictitious drug) or who completed a follow-up survey by an alternate mode of survey administration (i.e. telephone, internet or mail); (c) persisted among the subsample of participants who completed all waves of data collection \( (n = 3252, 96.1\%) \); (d) generalized to an alternative measure of marijuana use quantity and (e) was also found in an ordinal logistic regression model in which anhedonia clinical cut-off status (above versus below) was used to predict the five-level marijuana use frequency at wave 4 [odds ratio (OR), 95\% CI = 1.316 (1.055, 1.640)]. Additional analyses testing whether early onset marijuana used amplified paths of...
baseline anhedonia to marijuana use trend and marijuana use trend to anhedonia and found no evidence of effect modification by age of marijuana use onset. See sensitivity analyses in the online Supporting information for a detailed description of these results.

**DISCUSSION**

Youth with higher (versus lower) levels of anhedonia at baseline were at increased risk of marijuana use escalation during early adolescence in this study. In addition, levels of anhedonia and marijuana use reported at the beginning of high school were associated cross-sectionally with each other. To the best of our knowledge, the only prior study on this topic found higher levels of anhedonia in 32 treatment-seeking marijuana users than 30 healthy controls in a cross-sectional analysis of French 14–20-year-olds who did not adjust for confounders [24]. The current data provide new evidence elucidating the nature and direction of this association in a large community-based sample, which advances a literature that has addressed the role of anhedonia predominately in adult samples [7].

The association of baseline anhedonia with marijuana use escalation was observed after adjustment of numerous possible confounders, including demographic variables, symptom levels of three psychiatric syndromes linked previously with anhedonia (i.e., depression, social phobia, and ADHD) [16,46,47] and alcohol and tobacco use. Consequently, it is unlikely that anhedonia is merely a marker of these other psychopathological sources of marijuana use risk or a non-specific proclivity to any type of substance use. The temporal ordering of anhedonia relative to marijuana was addressed by the overarching bidirectional modeling strategy, which showed evidence of one direction of association (anhedonia → marijuana use) and not the other direction (marijuana use → anhedonia). Ordering was confirmed further in moderator tests showing that the association of anhedonia with subsequent marijuana use did not differ by baseline history of marijuana use. Thus, differences in risk of marijuana use between adolescents with higher (versus lower) anhedonia may be observed in cases when anhedonia precedes the onset of marijuana use.

Why might anhedonia be associated uniquely with subsequent risk of marijuana use escalation in early adolescence? Anhedonic individuals require a higher threshold of reward stimulation to generate an affective response and therefore may be particularly motivated to seek out pharmacological rewards to satisfy the basic drive to experience pleasure, as evidenced by prior work linking anhedonia to subsequent tobacco smoking escalation [37]. The risk pathway from anhedonia to marijuana use may be incremental to risk of other drug use. Among the three most commonly used drugs of abuse in youth (i.e., nicotine, alcohol and marijuana), marijuana may possess the most robust mood-altering psychoactive effects in young adolescents [48]. Consequently, marijuana may have unique appeal for anhedonic youth driven to experience pleasure that they may otherwise be unable to derive easily via typical non-drug rewards.

The study results may open new opportunities for marijuana use prevention. Brief measures of anhedonia that have been validated in youth, such as the SHAPS scale used here, may be useful for identifying teens at risk who may benefit from interventions. If anhedonia is ultimately deemed a causal risk factor, targeting anhedonia may prove useful in marijuana use prevention. Interventions promoting youth engagement in healthy alternative rewarding behaviors without resorting to drug use have shown promise in prevention [49], and could be useful for offsetting anhedonia-related risk of marijuana use update.

Moderator results raise several potential scientific and practical implications. The association was stronger among adolescents with (versus without) friends who used marijuana, suggesting that expression of a proclivity to marijuana use may be amplified among teens in environments in which marijuana is easily accessible and socially normative. The association of anhedonia with marijuana use escalation did not differ by gender or baseline history of marijuana use. Thus, preventive interventions that address anhedonia may: (1) benefit both boys and girls (2), aid in disrupting risk of onset as well as progression of marijuana use following initiation and (3) be particularly valuable for teens in high-risk social environments.

While anhedonia increased linearly over the first 2 years of high school on average, the rate of change in anhedonia was not associated with baseline marijuana use or changes in marijuana use across time. Given that anhedonia is a manifestation of deficient reward activity [11], this finding is discordant with pre-clinical evidence of THC-induced dampening of brain reward activity and prior adult observational data, showing that heavy or problematic marijuana use is associated with subsequent anhedonia [6] and diminished brain reward region activity during reward anticipation [27]. Perhaps the typical level and chronicity of exposure to marijuana use in this general sample of high school students was insufficient for detecting cannabinoid-induced manifestations of reward deficiency. Longer periods of follow-up may be needed to determine the extent of marijuana exposure at which cannabinoid-induced reward functioning impairment and resultant psychopathological sequelae may arise.

Strengths of this study include the large and demographically diverse sample, repeated-measures follow-up over a key developmental period, modeling of multi-directional associations, rigorous adjustment of potential.
CONCLUSIONS

Anhedonia is associated with increased risk of marijuana use escalation during the first 2 years of high school. Anhedonia warrants consideration in efforts to understand and prevent adolescent marijuana use uptake. If anhedonia is a consequence of marijuana use, this effect may not have ubiquitous generalizability.

Declaration of interests

None.

Acknowledgements

This research was supported by National Institutes of Health grant R01-DA033296. The funding agency had no role in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; and decision to submit the manuscript for publication. A.M.L. and J.C. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

References


23. Leventhal A. M., Chasson G. S., Tapia E., Miller E. K., Pettit J. W. Measuring hedonic capacity in depression: a psychometric
24. Dorard G., Berthoz S., Phan O., Corcos M., Bungener C. Affect
25. Bosson M. G., van Berckel B. N., Boellaard R., Zuurman L.,
Schuit R. C., Windhorst A. D. et al. Delta 9-
tetrahydrocannabinol induces dopamine release in the
26. Rubin T., Vigan D., Realini N., Guidali C., Braida D., Capurro
V. et al. Chronic delta 9-tetrahydrocannabinol during adoles-
cence provokes sex-dependent changes in the emotional
profile in adult rats: behavioral and biochemical correlates.
27. Martz M. E., Trucchi E. M., Cope L. M., Hardee J. E., Jester J. M.,
Zucker R. A. et al. Association of marijuana use with blunted
nucleus accumbens response to reward anticipation. JAMA
Psychiatry 2016; 73: 838–44.
Overview: Key findings on adolescent drug use. Monitoring
Abuse at The National Institutes of Health; 2014. Available
at: http://www.monitoringthefuture.org/pubs/monographs/
29. Squeglia L. M., Jacobus J., Tapert S. F. The influence of subst-
ance use on adolescent brain development. Clini EEG
30. Chen P., Jacobson K. C. Developmental trajectories of subst-
cance use from early adolescence to young adulthood: gender and racial/ethnic differences. J Adolesc Health
differences in the relationship between affect and adolescent
Transitions from first substance use to substance use disor-
ders in adolescence: is early onset associated with a rapid
33. Glaser B., Shelton K. H., van den Breer M. B. The moderating
role of close friends in the relationship between conduct prob-
lems and adolescent substance use. J Adolesc Health
2010; 47: 35–42.
34. Snaith R. P., Hamilton M., Morley S., Humayan A.,
Hargreaves D., Trigwell P. A scale for the assessment of hedonic
tone the Snaith-Hamilton pleasure scale. Br J Psychiatry
35. Johnston L. D., O’Malley P. M., Miech R. A., Bachman J. G.,
Schulenberg J. E. Monitoring the Future national survey results
on drug use: 1975–2014: Overview, key findings on adolescent
drug use. Ann Arbor: Institute for Social Research, The
University of Michigan; 2015.
36. Bidwell L. C., Knopik V. S., Audrain-McGovern J., Glynn T. R.,
Spillane N. S., Ray L. A. et al. Novelty seeking as a phenotypic
marker of adolescent substance use. Subst Abuse Res Treat
37. Audrain-McGovern J., Rodriguez D., Leventhal A. M., Cuevas
J., Rodgers K., Sass J. Where is the pleasure in that? Low he-
donic capacity predicts smoking onset and escalation. Nicotine
38. Radloff L. S. The CES-D scale a self-report depression scale for
research in the general population. Appl Psychol Measur
39. Chorpita B. E., Yim L., Moffitt C., Umemoto L. A., Francis S. E.
Assessment of symptoms of DSM-IV anxiety and depression in
children: a revised child anxiety and depression scale. Behav
40. Chorpita B. E., Moffitt C. E., Gray J. Psychometric properties of
the revised child anxiety and depression scale in a clinical
41. Barkley R. A., Murphy K. R. Attention-deficit/hyperactivity
42. Wickrama K. A., Conger R. D., Lorenz F. O., Jung T.
Family antecedents and consequences of trajectories of de-
pressive symptoms from adolescence to young adulthood: a
43. Muthén B., Asparouhov T. Latent variable analysis with cate-
gorical outcomes: multiple-group and growth modeling in
46. Brown L. H., Silvia P. J., Myin-Germeys I., Lewandowski K. E.,
Kwapil T. R. The relationship of social anxiety and social an-
hedonia to psychometrically identified schizotypy. J Soc Clin
47. Pizzagalli D. A. Depression, stress, and anhedonia: toward a
synthesis and integrated model. Annu Rev Clin Psychol
48. Zeiger J. S., Haberstick B. C., Corley R. P., Ehringer M. A.,
Crowley E. J., Hewitt J. K. et al. Subjective effects for alcohol,
tobacco, and marijuana association with cross-drug
49. Murphy J. G., Correia C. J., Barnett N. P. Behavioral economic
approaches to reduce college student drinking. Addict Behav

Supporting Information
Additional Supporting Information may be found online in
the supporting information tab for this article.

Table S1 Characteristics of participating schools in refer-
ence to Los Angeles county schools.
Table S2 Linear and quadratic latent growth curve models
for anhedonia and marijuana use.
Table S3 Standardized parameter estimates for all paths
from two-process latent growth curve model of associa-
tions between anhedonia and marijuana use.