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Effects of Adolescent Cannabis Use on Motivation and Depression: a Systematic Review

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Abstract

Purpose of Review This article reviews recent behavioral and neuroimaging studies to elucidate whether adolescent cannabis use is related to reduced motivation and increased risk of depression.

Recent Findings Recent work suggests that heavy adolescent cannabis use predicts poorer educational outcomes, often presumed to reflect reduced academic motivation, as well as increased levels of depressive symptoms. However, evidence of a link between cannabis use and general motivation was lacking. Factors such as concurrent alcohol and tobacco use, trajectories of cannabis use during adolescence, and cannabis-related changes in underlying neurocircuitry may impact associations among cannabis use, motivation, and depression.

Summary Heavy adolescent cannabis use is associated with poorer educational outcomes and increased levels of depressive symptoms. The role of depression in how cannabis may affect motivation, broadly, is not yet clear, as most studies have not examined associations among all three constructs. Future work should explore possible overlap between cannabis effects on motivation and depression and clarify the temporality of these associations.

Keywords Cannabis use · Adolescent · Motivation · Amotivational syndrome · Depression · Academic outcomes

Introduction

Reduced motivation is frequently cited as a consequence of heavy or chronic cannabis use [1•]. McGlothlin and West coined the term "amotivational syndrome" to describe the "introversion, passivity, and lack of achievement orientation" observed among adult heavy cannabis users [2]. Relative to the vast literature examining cannabis-related neurocognitive impairments, a limited number of studies have empirically assessed the impact of cannabis use on motivation. A recent review of the available literature concluded that the evidence for amotivational syndrome among heavy cannabis users is mixed, although there is partial support from longitudinal studies [3]. Neuroimaging studies also suggest a plausible underlying neurobiological mechanism, as cannabis use has been linked to reduced dopamine synthesis capacity and reactivity [4, 5], as well as blunted reward sensitivity in corticostriatal regions [6•]. However, there continues to be significant cross-study variability in the assessment tools employed to capture motivation, as well as in the extent to which studies controlled for relevant confounding variables, such as use of other substances and depression [3].

The inconsistency of prior work in accounting for coexisting depressive symptoms is an important limitation, as reduced motivation is often a hallmark of depression. This makes it particularly difficult to discern whether observed results are due to cannabis effects on depressive symptoms or a result of direct effects on motivation. Although acute cannabis use is often associated with pleasant subjective responses among users [7], a large body of work suggests that heavy and/or chronic cannabis use may result in a greater number of depressive symptoms and a higher likelihood of

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later developing depression [8, 9]. These behavioral changes are often accompanied by abnormalities in the neural response to reward and other stimuli with high emotional valence [10–12]. Similar to the literature on direct cannabis effects on motivation, however, these studies have varied greatly in the measures used to assess depression, as well as in the covariates considered.

Most studies examining cannabis effects on motivation and depression have utilized adult samples, with few focusing on these effects specifically in the context of adolescence. Cannabis use is prevalent among adolescents, with 6.5% of adolescents ages 12 to 17 reporting use in the past year in 2017 [13], although estimates are significantly higher among older adolescents [14]. Furthermore, a majority of adolescents do not perceive great risk of harm from weekly cannabis use [13]. This is concerning, as adolescence is a time of neuromaturational change, which may make the adolescent brain particularly vulnerable to the neurotoxic effects of substance use [15, 16]. It is therefore paramount to understand how cannabis use at this critical neurodevelopmental stage may impact motivation and depression.

The current article reviews findings from two parallel lines of work examining the effects of adolescent cannabis use on motivation and depression with the aim of addressing the following questions: (1) Is adolescent cannabis use associated with reduced motivation? (2) Is adolescent cannabis use associated with increased risk of depression? We first examine each body of work separately, discussing main findings from both behavioral and neuroimaging studies. Finally, we synthesize findings from these studies in order to highlight commonalities across study findings, identify gaps in our knowledge, and suggest future avenues for research that will help tease apart these interrelated constructs while simultaneously moving towards a more integrated understanding of the impact of adolescent cannabis use.

Method

Literature Search Process

We conducted literature searches in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines on PsycInfo and PubMed during March 2019 using the terms (cannabis OR marijuana OR THC) AND (adolescent) AND (emotion OR affect OR mood OR depression OR internalizing OR motivation OR apathy OR amotivation OR "reward sensitivity"). We included peer-reviewed English language studies involving human participants published over the past 5 years (since 2014). Studies were selected if they examined non-acute effects of adolescent cannabis use, defined as cannabis use occurring at age < 18 years, on motivation and/or depression, as measured directly via instruments designed to assess these constructs, or indirectly, via outcomes or brain-based measures thought to underlie these constructs. We excluded non-peer reviewed articles, articles written in foreign languages, non-human studies, studies examining acute effects of cannabis on motivation or depression, and studies focusing exclusively on cannabis use occurring during college or adulthood. We also excluded studies that examined only the effects of motivation or depression on cannabis use, studies focusing on motives for use or motivation to quit, studies focusing on polysubstance use, studies that were unable to isolate the effects of cannabis (versus other drugs) via statistical or sampling methods, and studies focusing on effects on internalizing symptoms, broadly. As depicted in Fig. 1, these search criteria resulted in a total of 28 studies.

Effects of Adolescent Cannabis Use on Motivation

Effects on Motivation

Reduced motivation is often noted as a consequence of cannabis use. As illustrated in Table 1, several studies have examined the impact of cannabis use on motivation specifically among adolescents, a population thought to be particularly at risk for adverse effects of substance use [15, 16]. However, very few studies have employed direct behavioral measures of motivation such as questionnaires, interviews, or performance-based effort tasks in this population. In recent years, only one study examined associations between cannabis use and self-reported motivation among adolescent cannabis users. This cross-sectional study found no support for amotivational syndrome after controlling for demographics, other substance use, and mental health confounds [29]. Thus, more work is needed to determine whether adolescent cannabis use has detrimental effects on general motivation, or willingness to work for a reward, that persist after the effects of acute intoxication have subsided.

More commonly, studies have examined longitudinal associations between adolescent cannabis use and later educational outcomes, which are presumed to reflect academic motivation. Indeed, there is substantial evidence of a link between heavy and/or chronic cannabis use during adolescence and poorer academic outcomes, including lower grade-point average during high school and college, higher rates of high school and college dropout, longer time to graduation, and lower likelihood of pursuing higher education [17, 18•, 19, 20, 21•, 23–25, 27•, 28••, 30•]. Only one study failed to find differences in academic outcomes between early-onset cannabis users, late-onset cannabis users, and abstainers [26]. However, rates of adolescent cannabis use in this sample were relatively low during adolescence (early-onset users reached

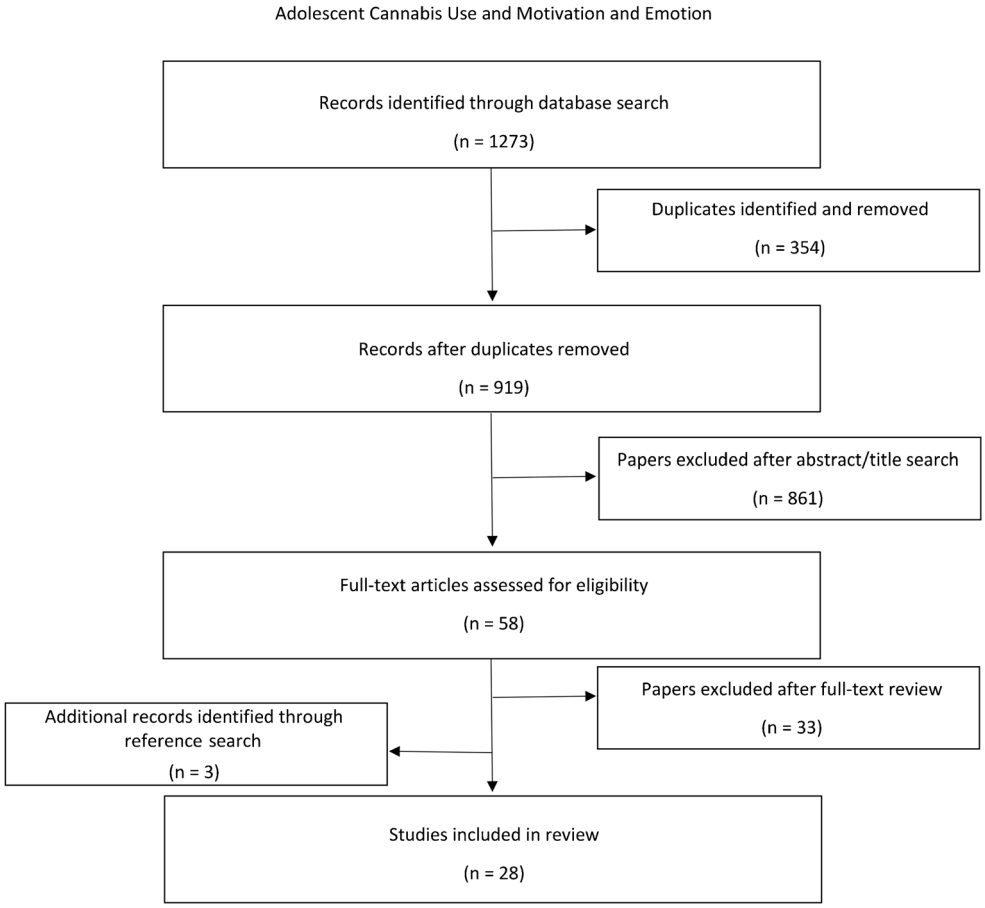

Fig. 1 Our literature search process conducted on PubMed and PsycInfo during March 2019 yielded a total of 28 studies examining nonacute effects of adolescent cannabis use on motivation and/or depression

monthly use by age 19), which may have contributed to these null findings [26].

Several factors have been shown to influence these associations. For instance, some studies suggest that this link may be dose-dependent, such that adolescents with heavy cannabis use, particularly weekly or greater use, had worse academic outcomes than those who used occasionally or those who abstained [19, 20, 24, 27•, 30•]. On the other hand, some suggest that even infrequent cannabis use during adolescence may have detrimental effects on post-secondary academic achievement and educational attainment [17, 30•]. Studies also suggest that the developmental stage during which heavy cannabis use occurred may be important. For instance, earlier age of onset of a cannabis use disorder was associated with lower academic achievement in a sample of abstinent adolescent cannabis users [18]. Additionally, individuals whose use escalated during adolescence but stopped during adulthood showed educational outcomes comparable to chronic users whose use continued to escalate into adulthood, with both of these groups having lower likelihood of graduating high school and college than non-users or individuals who initiated use during adulthood [21]. Concurrent use of other substances may also impact the relationship between cannabis use and lower academic achievement, with some studies finding that these associations can be accounted for by alcohol and/or tobacco use [20, 23, 25], and others suggesting that cannabis use accounted for a greater degree of educational non-progression than use of other substances [24].

Together, these findings provide strong evidence of a causal association between cannabis use and lower academic achievement and educational attainment. The majority of these studies, however, failed to control for concurrent depression. Thus, the extent to which these academic outcomes relate to comorbid depression or to effects on other, non-academic aspects of motivation is not yet clear.

Effects on Underlying Neurocircuitry

Neuroimaging studies have also advanced knowledge on the effects of cannabis use on motivation by examining cannabis-related alterations in corticostriatal regions that comprise the brain's reward/motivation circuitry. Although most of this work has focused on adults, several recent studies have examined the impact of adolescent cannabis use on these brain regions. Evidence from cross-sectional neuroimaging studies is limited, with one study finding no effect of cannabis use on sensitivity to reward among adolescents, suggesting instead

Table 1 Characteristics of reviewed studies examining non-acute effects of adolescent cannabis use on general and academic motivation

Study	Total participants (% male)	Cannabis use assessment	Covariates	Motivation measure used	Key findings
Homel et al. [17]	*N* = 632 (47%)	Cannabis use trajectory from age 15 to 25: abstainers, occasional users, frequent users	Sex, maternal education, high school grades at baseline, conduct problems at baseline, family structure at age 15	Post-secondary enrollment type, timing of enrollment, dropping out	Frequent cannabis users from ages 15 to 25 had lower high school grades and were less likely to enroll in post-secondary education relative to abstainers. Occasional users were more likely than abstainers to delay enrollment and drop out of post-secondary education.
Hooper et al. [18]†	*N* = 113 (63%)	Presence of CUD ages ranging 12–17: abstainers, adolescents with CUD in full remission, adolescents with psychiatric disorders without substance use	ADHD combined type, conduct disorder, sociodemographic variables	Woodcock-Johnson III Tests of Academic Achievement	Earlier age of CUD was associated with lower academic achievement.
Silins et al. [19]	*N* = 2537–3765 - percentage varies by cohort	Maximum frequency of cannabis use prior to age 17: never, less than monthly, monthly or more, weekly or more, daily	Participant and parent cognition, behavioral problems, substance use, mental health, and demographics, deviant peer affiliations	High school completion, degree attainment	Daily cannabis use before age 17 reduced odds of high school completion and degree attainment by age 30.
Stiby et al. [20]	*N* = 4264–4436 - percentage varies by cohort	Cannabis use frequency age 15: never, non-weekly smoker, weekly smoker	Maternal substance use, life course socioeconomic position, child sex, month and year of birth, child educational attainment prior to age 11, child substance use prior to age 15, child conduct disorder	English GCSE results, mathematics GCSE results, not gaining 5+ C+ grade GCSEs, school dropout	Weekly cannabis use and daily tobacco use at age 15 was associated with lower academic achievement at age 16. Following adjustment for substance use, tobacco had stronger effects than cannabis, although both were still significant.
Epstein et al. [21]	*N* = 808 (51%)	Cannabis use trajectory from age 14 to 30: non-users, late-onset users, adolescent-limited users, chronic users	Sex, ethnicity, childhood SES	High school completion or attainment of college degree by age 33	Adolescent-limited cannabis users scored as low as chronic users and worse than non-users and late-onset users on measures of educational attainment at age 33.
Karoly et al. [22]†	*N* = 132 (66%)	Cannabis use frequency ages ranging 14–18: cannabis-only, tobacco only, cannabis + tobacco, alcohol only cannabis + tobacco + alcohol, non-users	None: controlled for other substance use via sampling	Activation during reward anticipation during Monetary Incentive Delay task	Tobacco use, rather than cannabis use, was associated with reduced reward sensitivity.
Meier et al. [23]	*N* = 254 (NA)	Past-year cannabis use frequency grades 9 to 12: never used, Used but never on a monthly basis, monthly use for 1 year of high school, monthly use for	9th grade GPA, delinquency, depression symptoms, and anxiety symptoms; persistent alcohol and tobacco use; sex	12th grade GPA and SAT performance	Persistent cannabis use throughout high school is linked with lower GPA in the 12th grade. This effect became non-significant after controlling for persistent alcohol and tobacco use.

Table 1 (continued)

Study	Total participants (% male)	Cannabis use assessment	Covariates	Motivation measure used	Key findings
		2 years of high school, monthly use for 3–4 years of high school			
Silins et al. [24]	*N* = 2179–3678 - percentage varies by cohort	Maximum frequency of cannabis use prior to age 17: never, less than weekly, weekly or more	Participant and parent cognition, behavioral problems, substance use, mental health, and demographics, deviant peer affiliations	High school non-completion by age 25, university non-enrollment by age 21, degree non-attainment by age 25	Weekly or greater cannabis use before age 17 increased the odds of high school non-completion, university non-enrollment, and degree non-attainment by age 25. Cannabis use accounted for a greater proportion of rates of non-progression than alcohol use.
Mokrysz et al. [25]	*N* = 2235 (47%)	Lifetime cannabis use frequency by age 15: never, fewer than 5 times, 5–19 times, 20–49 times, at least 50 times	Maternal and early-life factors, childhood behavioral factors, childhood mental health, other adolescent drug use at age 15	Educational performance at age 11 and 16	Cumulative cannabis use at age 15 predicted lower academic performance at age 16. This effect became non-significant after controlling for tobacco use.
Scholes-Balog et al. [26]	*N* = 852 (47%)	Cannabis use trajectory from age 12 to 19: abstainers, early-onset users, late-onset occasional users	Sex; parent education; school grades and antisocial behavior at age 12; maximum frequency of alcohol, cigarette, and other illicit drug use between ages 12 and 19	Secondary school completion, post-secondary education completion, and student status in young adulthood (third year post-secondary school)	There were no differences in school completion or educational attainment in young adulthood between adolescent cannabis abstainers, early-onset users, and late-onset occasional users.
Green et al. [27•]	*N* = 330 (65%)	Lifetime cannabis use frequency by age 16: non-heavy adolescent use (used 19 times or less), heavy adolescent use (used 20 times or more)	Sex; female-headed household; poverty status; maternal education, depressed mood, substance use, and school aspirations for child; family punishment; child IQ, first grade reading scores and classroom behavior; self-reports of family behavior	Educational level (assessed in young adulthood and supplemented with midlife interview data): high school dropouts, GED/high school diploma, or college degree or higher	Heavy users were more than 3 times as likely as light or non-users to drop out than to obtain a college degree. This mediated poorer outcomes in midlife.
Lichenstein et al. [28••]	*N* = 158 (100%)	Cannabis use trajectory from ages 14 to 19: stable-high use, escalating use, stable-low use	Lifetime alcohol exposure, daily nicotine use, presence/absence of antisocial personality disorder, SES	Educational attainment at age 22, functional connectivity between nucleus accumbens and mPFC during reward receipt	Escalating cannabis use during adolescence predicted negative functional connectivity between nucleus accumbens and mPFC during monetary reward receipt, which predicted lower educational attainment at age 22.
Pacheco-Colón et al. [29]†	*N* = 79 (53%)	Amount of lifetime and past month cannabis use frequency and amount at ages ranging 14–18: light users (using < 10 times in the past month and never regularly), recent	Sex, IQ, depression, anxiety, ADHD symptoms, lifetime and past 30-day alcohol and nicotine use amount and frequency	Apathy Evaluation Scale, Motivation and Engagement Scale	There were no differences in motivation between light and recent regular users. Lifetime and the past 30-day amount of cannabis use were not associated with reduced motivation.

Table 1 (continued)

Study	Total participants (% male)	Cannabis use assessment	Covariates	Motivation measure used	Key findings
		regular users (using ≥ 10 times in past month)			
Patte et al. [30•]	N = 26,475 (47%)	Past-year cannabis use frequency grades 9–12: never, rare, monthly, weekly, daily	Sex, grade, ethnicity, cigarette use	Academic aspirations, expectations, and performance; school engagement	Changing from abstaining to sporadic or weekly use predicted increased aspirations to pursue higher education, whereas initiating daily cannabis use predicted reduced aspirations to pursue graduate education. Initiating cannabis use, even if rare, predicted reductions in class attendance, homework completion, grades achieved, and perceived value of grades.

CUD cannabis use disorder, *ADHD* attention deficit/hyperactivity disorder, *GCSE* general certificate of secondary education, *SES* socioeconomic status, *GPA* grade point average, *SAT* scholastic aptitude test, *IQ* intelligence quotient, *GED* general education development, *mPFC* medial prefrontal cortex

† Applies to cross-sectional studies

that reductions in reward sensitivity may be caused by concurrent tobacco use [22].

On the other hand, findings from a recent longitudinal study suggest that after controlling for alcohol use, a pattern of escalating cannabis use during adolescence was associated with negative functional connectivity between the nucleus accumbens and the medial prefrontal cortex in response to receiving monetary rewards during young adulthood [28••]. In contrast, adolescents with both stable high and stable low cannabis use patterns demonstrated positive connectivity between these regions [28••]. Further, the pattern of negative connectivity observed in escalating users predicted lower educational attainment, as well as higher levels of anhedonia and depression later in adulthood [28••]. This suggests that increasing cannabis use during adolescence may disrupt the organization of the motivational network, which may ultimately lead to problems enhancing positive affect or focusing on future or current rewards [28••].

Thus, there is some evidence of cannabis-related neurobiological alterations in corticostriatal regions in adolescents which may impact later academic outcomes. However, although these findings are consistent with prior work on adults [6•], more work is needed in this area to replicate these findings on more diverse samples and determine whether alterations in motivational circuitry may predate adolescent cannabis use.

Effects of Adolescent Cannabis Use on Depression

Effects on Depressive Symptoms

A recent meta-analysis of longitudinal studies concluded that heavy cannabis use significantly increases the risk of later developing depression regardless of age of onset of cannabis use [9]. Since then, studies have attempted to elucidate whether cumulative cannabis use during adolescence results in increased risk of depression in adulthood. These recent studies are described in detail in Table 2. Although several found no such links [21, 26, 27•, 33, 37, 40], the majority of the studies here reviewed suggest that heavy adolescent cannabis users are at increased risk of developing depression [19, 31] or report higher levels of depressive symptoms than their non-using counterparts both concurrently [36, 43], and later in life [32•, 34, 38, 39•, 42, 44].

However, these associations may be nuanced and dependent on several other factors. It is possible, for instance that the causality of these relationships is bidirectional, such that adolescents, particularly males, may be self-medicating their depressive symptoms by escalating their cannabis use [38, 40]. Further, pre-existing depressive symptoms may make adolescents slightly more susceptible to cannabis-related increases in

Table 2 Characteristics of reviewed studies examining non-acute effects of adolescent cannabis use on symptoms and risk of depression

Study	Total participants (% male)	Cannabis use assessment	Covariates	Depression measure used	Key findings
Silins et al. [19]	*N* = 2537–3765 - percentage varies by cohort	Maximum frequency of cannabis use prior to age 17: never, less than monthly, monthly or more, weekly or more, daily	Participant and parent cognition, behavioral problems, substance use, mental health, demographics, and deviant peer affiliations	Suicide attempts, moderate or severe depression in the past week to the past month - specific measures vary by cohort	Daily cannabis use before age 17 increased the odds of suicide attempts in 30s.
Epstein et al. [21]	*N* = 808 (51%)	Cannabis use trajectory from ages 14 to 30: non-users, late-onset users, adolescent-limited users, chronic users	Sex, ethnicity, childhood SES	Mental health at age 33 (DSM-IV nine items for depression)	No differences in depression emerged in adulthood between non-users, adolescent-limited users, late-onset users, and chronic users.
Gage et al. [31]	*N* = 1791 (42%)	Lifetime cannabis use frequency at age 16: 0 times (never), < 20 times (experimenter), 21–60 times (weekly), > 60 times (daily)	Family history of depression, maternal education, urban living, sex; IQ at age 8, borderline personality traits, victimization, peer problems, conduct disorders; alcohol and other illicit drug use at age 16; cigarette and cannabis use	Depression at age 18: Clinical Interview Schedule-Revised	Cannabis and tobacco use at age 16 increased the odds of developing depression at age 18. This association, however, was much weaker (although still significant) after controlling for cigarette use.
Heitzeg et al. [32•]	*N* = 40 (65%)	Lifetime cannabis use frequency from age 11 to age of imaging (17–22): minimal users (1–10 times), heavy users (< 100 times)	Prior emotional functioning and resiliency	Emotional functioning at time of initiation in heavy users, before scan, and 1 year after scan: California Q-Sort; activation during emotion-arousal word task (ages 17–22)	Heavy users had less activation than minimal users to negative words across several brain regions as well as higher levels of negative emotionality at age 20. Activation of the caudal DLPFC mediated association between cannabis group and later negative emotionality.
Passaroti et al. [33]	*N* = 1204 (43%)	Cannabis use trajectory ages 14 to 21: never, non-users, low users, medium users, escalating users, high users	None	Center for Epidemiological Studies-Depression	There were no differences in depression between escalators and low and medium non-escalating cannabis users.
Schuler et al. [34]	*N* = 6070 (49%)	Past-month cannabis use frequency ages 12 to 31: any past-month cannabis use, no past-month cannabis use	Race, ethnicity	Center for Epidemiological Studies-Depression	Past-month cannabis use predicted depressive symptoms from ages 12 to 31, with the strongest association during adolescence after controlling for regular cigarette and alcohol use.

Table 2 (continued)

Study	Total participants (% male)	Cannabis use assessment	Covariates	Depression measure used	Key findings
Spechler et al. [35]†	*N* = 140 (65%)	Lifetime frequency of cannabis use at age 14: cannabis-experimenting adolescents (used ≤ 1 time), non-users (never used)	Scanning site	Amygdala activation while viewing angry faces relative to neutral faces	Cannabis users had greater reactivity than controls in the amygdala to angry faces relative to neutral faces, which may put them at risk for later mood disorders.
Womack et al. [36]	*N* = 264 (100%)	Cannabis use frequency age 17: never used, used once or twice, used more often than twice; age 20 and 22: never, no use in last year, less than once a month, once a month, 2–3 times a month, once a week, 2–3 times a week, 4–6 times a week, daily	Primary caregiver depressive symptoms, demographics, youth antisocial behavior, past-year tobacco and alcohol use, youth IQ, adult court records	Beck Depression Inventory at ages 17, 20, 22	Cannabis use predicted increased depressive symptoms but only among people who were mildly depressed already. Depressive symptoms predicted only slight increases in cannabis use.
Cerdá et al. [37]	*N* = 503 (100%)	Past-year cannabis use frequency ages 13 to 19	Family factors, changes in parental supervision, positive parenting, parental stress, parental use of physical punishment, peer variables, age	Ages 7–16: Child Behavior Checklist, Teacher Report Form; Ages 10–19: Youth Self-Report, Young Adult Self-Report	Increases in cannabis use during adolescence did not result in increases in depression.
Scholes-Balog et al. [26]	*N* = 852 (47%)	Cannabis use trajectory from age 12 to 19: abstainers, early-onset users, late-onset occasional users	Sex; parent education; school grades and antisocial behavior at age 12; maximum frequency of alcohol, cigarette, and other illicit drug use between ages 12–19	Depression/anxiety (K-10 Kessler psychological distress scale) in young adulthood (third-year post-secondary school)	There were no differences in depression in young adulthood between abstainers, early-onset, and late-onset occasional users.
Wilkinson et al. [38]	*N* = 11,995 (46%)	Past-month cannabis use frequency ages 12 to 32	Race, ethnicity, educational attainment of both parents and the respondent (as a proxy for SES), age	Center for Epidemiological Studies-Depression	Increases in cannabis use frequency were associated with later increases in depressive symptoms. The reverse was also true, with a greater effect magnitude for females.
Green et al. [27•]	*N* = 330 (65%)	Cannabis use frequency by age 16: non-heavy adolescent use (19 times or less), heavy adolescent	Sex; female-headed household; poverty status; maternal education, depressed mood, substance use, and school aspirations for child; family punishment; child IQ, first grade reading scores and classroom behavior; self-reports of family behavior	Complete International Diagnostic Interview assessment of depression: endorsed two or more suicidality symptoms in midlife	There were no associations between adolescent cannabis use and suicidality in midlife.

Table 2 (continued)

Study	Total participants (% male)	Cannabis use assessment	Covariates	Depression measure used	Key findings
		use (used 20 times or more)			
Jacobus et al. [39]	*N* = 56 (73%)	Lifetime and the past month cannabis use frequency ages ranging 15–18: controls (lifetime use ≤ 7 days, no past month use, past 3-month average use 0–1 days), users (lifetime use ≥ 200 days, past month use 1–28 days, past 3-month average use 7–30 days)	Lifetime and past 28-day alcohol use, lifetime other drug use episodes at day 0	Beck Depression Inventory—Second Edition	Adolescent cannabis users showed reductions in depression over 28 days of monitored abstinence, with late-onset users seeing the greatest change.
Leventhal et al. [40]	*N* = 3394 (46%)	Cannabis use frequency grades 9 to 10: no use in the past 6 months, past 6-month use without use in the last month, 1–2 days in the past month, 3–5 days in the past month, 6–14 days in the past month, ≥ 15 days in the past month	Age, sex, race, ethnicity, highest parental education, depressive symptoms, social phobia levels, ADHD, peer cannabis use, baseline cannabis user status, cannabis use onset before age 14	Snaith–Hamilton Pleasure Scale	Baseline cannabis use was not associated with the rate of change in anhedonia. However, baseline anhedonia was positively associated with the rate of increase in cannabis use frequency from ages 14 to 18.
Lichenstein et al. [28••]	*N* = 158 (100%)	Cannabis use trajectory from ages 14 to 19: stable-high use, escalating use, stable-low use	Lifetime alcohol exposure, daily nicotine use, presence/absence of antisocial personality disorder, SES	Depressive symptoms at age 22: Beck Depression Inventory; anhedonia at age 22: Snaith-Hamilton Pleasure Scale	Escalating cannabis use during adolescence predicted negative functional connectivity between nucleus accumbens and mPFC during monetary reward receipt, which predicted higher levels of anhedonia, and depressive symptoms at age 22.
Aloi et al. [41]†	*N* = 82 (62%)	Level of substance use ages ranging 14–18: non-users, subclinical substance users, adolescents with AUD or CUD	AUDIT and CUDIT scores, age, sex, repeated analyses excluding tobacco users and substance naïve participants	Affective Stroop fMRI task, Mood and Feelings Questionnaire	CUD severity was not associated with amygdala responsiveness to emotional stimuli, whereas AUD severity was.
Assari et al. [42]	*N* = 681 (49%)	Lifetime, the past year, and the past			

Table 2 (continued)

Study	Total participants (% male)	Cannabis use assessment	Covariates	Depression measure used	Key findings
		month cannabis use frequency grades 10, 11, and 1 year after high school: 0 times, 1–2 times, 3–5 times, 6–9 times, 10–19 times, 20–39 times, 40 or more times.	Age, sex, family SES (parental employment status and family structure)	Grades 10–11 and 1 year after high school: Brief Symptom Inventory	Baseline cannabis use at age 16 predicted an increase in depression symptoms over time in males, but not females.
Kaasboll et al. [43]†	*N* = 36,714 (51%)	Lifetime cannabis use frequency ages ranging 13–17: never tried, 1 time, 2–5 times, 6 or more times	None	Three items from the Hopkins Symptom Checklist, three items from the Depressive Mood Inventory, two items developed for survey	Cannabis users reported more depressive symptoms than non-users, with no effect of frequency of use. Although females reported less cannabis use, they reported more depression than males.
Thompson et al. [44]	*N* = 662 (48%)	Cannabis use trajectory ages 12 to 18 and ages 22 to 29: abstainers, occasional users, decreasers, increasers, chronic users	Sex, SES, age at baseline, concurrent levels of all substance use, and mental health symptoms	Brief Child and Family Phone Interview	Chronic cannabis users reported more depressive symptoms in young adulthood. Decreasers reported more depressive symptoms than chronic users during adolescence. Increasing users reported lower depressive symptoms in young adulthood than chronic users.

SES socioeconomic status, *DSM-IV* Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, *IQ* intelligence quotient, *DLPFC* dorsolateral prefrontal cortex, *ADHD* attention deficit/hyperactivity disorder, *mPFC* medial prefrontal cortex, *AUD* alcohol use disorder, *CUD* cannabis use disorder, *AUDIT* Alcohol Use Disorder Identification Test, *CUDIT* Cannabis Use Disorder Identification Test, *fMRI* functional magnetic resonance imaging

† Applies to cross-sectional studies

depression [36]. The use of other substances is also often noted as a potentially confounding factor, with studies varying in the extent to which they control for this. Nonetheless, although some find that links between adolescent cannabis use and depression are attenuated after controlling for use of substances like tobacco [31], others continue to find strong causal links even after accounting for alcohol and tobacco use either statistically [19, 34, 44] or via sampling methods [32•]. Sex is also a plausible moderator, considering well-documented differential effects of cannabis use on males and females [45]. Surprisingly, one study found that adolescent cannabis use predicted increases in depression only for males [42], although it is important to note that males are often overrepresented among heavy cannabis users, which may have contributed to this effect.

Details regarding adolescent cannabis use patterns may also prove influential. For instance, one study found that depressive symptoms decreased with prolonged cannabis abstinence, but they decreased to a lesser degree among users with an earlier age of cannabis use onset [39]. Adolescent cannabis use trajectories may also lead to differential outcomes in adulthood, although the evidence continues to be mixed, with some studies suggesting that chronic use is most harmful [44], others finding worse outcomes among escalating users [28••], and others finding no differences between chronic, escalating, adolescent-limited, late-onset, and low use trajectories [21, 26, 33]. These findings suggest that factors such as earlier age of onset and chronic and/or escalating use patterns may be associated with worse outcomes.

Thus, although the evidence is equivocal, there is sufficient evidence of causal relationships between adolescent cannabis use and later depression to warrant concern. Discrepancies in findings may be at least partially explained by wide variability in the quantification of both cannabis use and depression variables, as well as variable levels of cannabis use captured across samples.

Effects on Underlying Neurocircuitry

Previous work has shown that individuals with depression show a range of neural abnormalities, including mood-congruent activation patterns (e.g., hyper-reactivity in amygdala, and hypoactivation in frontal regions) in response to negative emotional stimuli [11, 12]. Evidence of cannabis effects on this underlying corticostriatal neurocircuitry is more variable, with some studies suggesting that cannabis users show lower activation of amygdala in response to threatening stimuli [46, 47] and others finding no effect [48]. However, it is unclear whether these abnormalities predate the onset of cannabis use.

Although there are few studies examining these effects exclusively in the context of adolescence, recent work continues to yield mixed findings. For instance, one study found that cannabis use during early adolescence was associated with greater amygdala reactivity to angry relative to neutral faces [35], whereas another study found that amygdala reactivity was associated with severity of alcohol rather than cannabis use disorders [41]. These discrepancies may be explained, at least in part, to high variability in population characteristics (e.g., demographics, levels of substance use) included in these cross-sectional studies, the task paradigms employed, and the analytic strategies selected. Additionally, although studies often posit that these abnormalities may place adolescents at risk for mood disorders in young adulthood, they did not empirically assess correlations between their findings and depressive symptoms.

One recent study examined these associations longitudinally among adolescent cannabis users. Despite no differences during early adolescence, heavy cannabis users reported higher levels of negative emotionality during late adolescence and showed less activation to negative words than minimal users in temporal, prefrontal, and occipital cortices, as well as the insula and amygdala [32•]. Furthermore, activation of the caudal dorsomedial prefrontal cortex mediated the association between cannabis group and later negative emotionality. Similarly, another study found that negative connectivity between nucleus accumbens and medial prefrontal cortex in response to rewards predicted later increases in depressive symptoms among escalating adolescent cannabis users [28••].

Overall, although cross-sectional evidence is mixed, findings from longitudinal neuroimaging studies suggest that adolescent cannabis use may lead to alterations in the corticostriatal reward system. These changes predict later increases in depressive symptoms, suggesting that underlying neurobiological processes may mediate the link between adolescent cannabis use and later depression.

Conclusions

Heavy cannabis use during adolescence has been consistently linked to lower academic achievement and educational attainment, which are presumed to reflect lower academic motivation. Although links between cannabis and other aspects of motivation are less clear, adolescent cannabis use has also been shown to predict depressive psychopathology, which includes symptoms that are also related to motivation, such as apathy and anhedonia. Furthermore, recent work suggests that cannabis use at this developmental stage may lead to neurobiological alterations that may underlie these behavioral changes. However, the extent of the overlap across observed outcomes, such as lower educational attainment, reduced motivation, and depression, is still uncertain.

Indeed, 11 out of 12 studies found that heavy cannabis use during adolescence, particularly weekly to daily use, predicts a range of negative academic outcomes, including lower

grade-point average during high school and college, higher rates of high school and college dropout, longer time to graduation, and lower likelihood of pursuing higher education [17, 18•, 19, 20, 21•, 23–25, 27•, 28••, 30•]. However, it is unclear whether this is a true reflection of non-acute effects on motivation or whether it reflects the influence of other factors. For instance, because heavy cannabis users spend more time in a state of acute intoxication than occasional users, these outcomes could be mediated by acute effects of cannabis on motivation, as acute intoxication has been more consistently linked to amotivational states [49••]. Alternatively, this effect could be mediated by amount of time spent studying, as studying is less likely to occur or be effective during acute intoxication due to cannabis effects on neurocognition [50]. It would also be informative to continue to examine correlations between academic aspirations and performance-based metrics to determine whether these outcomes are related to cognitive aspects of motivation or to the planning and execution of goal-directed behavior [30•]. Finally, it is important to note that only five of these studies controlled for comorbid depression, which may simultaneously impact motivation and level of substance use [19, 23–25, 29]. However, depression did not appear to fully explain associations between cannabis use and motivation, as four of these studies reported significant effects after covarying for depression. Specifically, two of these studies found that this association could be explained by use of other substances [23, 25], and two continued to find causal links after controlling for an exhaustive list of covariates including depression [19, 24]. It is important to note that most of these studies used comorbid depression as a nuisance covariate rather than a variable of interest and therefore did not report statistics concerning the effect of depression on relevant motivation outcomes. Thus, these inconsistencies in methodology and reporting make it difficult to ascertain whether cannabis selectively impacts motivation rather than depression symptoms, broadly. To address these gaps in our knowledge, future studies should examine associations among cannabis use and academic aspirations, academic performance, and other measures of motivation, such as effort-based, neuroimaging, and self- or informant-report measures, while controlling for depression.

Eleven of 17 reviewed studies found links between adolescent cannabis use and depression, such that adolescents at the highest levels of use had a higher likelihood of developing depression or higher levels of depressive symptoms [19, 28••, 31, 32•, 34, 36, 38, 39•, 42–44]. Of these, 7 found strong *causal* links [19, 28••, 32•, 34, 38, 39•, 44]. Thus, although not as consistent as links with other forms of psychopathology, such as psychosis, the association between adolescent cannabis use and depression is reported consistently enough to warrant concern. However, due to the high variability across studies in the depression measures employed, it is difficult to determine whether certain symptoms of depression (e.g., anhedonia, apathy) are more adversely impacted by cannabis use. This is an important question, as reduced motivation is a hallmark of depression. Further, previous work has found that patients with depression and a cannabis use disorder display a greater severity of *negative* depressive symptoms, including apathy, than patients without a cannabis use disorder [51]. It is therefore unclear whether higher rates of depression among cannabis users may simply reflect symptoms of "amotivational syndrome," such as apathy or anhedonia, or vice versa. Future work should employ fine-grained measures of depressive symptomatology in order to determine whether the impact of cannabis use varies across different domains of depression (e.g., apathy, suicidality, anhedonia), thereby helping to disentangle cannabis effects on motivation and depression.

Heavy cannabis use has also been found to predict poorer outcomes in adulthood, such as increased likelihood of poverty, lower income, and a higher likelihood of developing internalizing disorders such as anxiety and depression [9, 52, 53]. Importantly, recent work found that these associations may be mediated by poorer academic outcomes (e.g., high school dropout) among heavy cannabis users [27•]. This suggests that low educational attainment, rather than cannabis use directly, may place individuals at increased risk for internalizing psychopathology. In other words, effects of cannabis use on later risk of depression may be socially mediated [8]. On the other hand, neuroimaging work suggests that cannabis use may cause neurobiological alterations, such as changes in neural response to rewards, which impact how individuals process emotionally valenced information, placing them at higher risk for depression [28••, 32•]. The specific mechanisms by which cannabis use leads to greater risk of depression are therefore still unclear.

Although much work is needed to fully understand relationships between these constructs, the reviewed studies have identified several factors that may moderate the impact of cannabis use on motivation and depression. One such factor is the individual's trajectory of cannabis use. Specifically, both escalating and chronically high trajectories of cannabis use during adolescence have been linked to worse outcomes in adulthood [17, 21, 28••, 44]. Additionally, although evidence regarding earlier *age* of onset is mixed, several studies suggest that *adolescent* onset of cannabis use has more deleterious effects on motivation and depression than onset during adulthood [21, 39]. This is expected, as ongoing neuromaturational processes may make the adolescent brain more vulnerable to adverse effects of substance use [16]. Co-occurring use of other substances may also impact and sometimes account for these relationships. Although the majority of studies controlled for other

substance use in some way, findings varied regarding which particular substance had a greater effect on outcomes. For instance, whereas some studies found cannabis-specific effects, others suggested that findings could be better explained by tobacco or alcohol use. Future studies should continue to assess and control for concurrent use of other substances.

Finally, it is important to note that cannabis effects on motivation and depression are usually only present at the highest levels of use, yet few of the reviewed studies examined the impact of cannabis abuse or dependence on these outcomes. This is an important limitation because it makes it difficult to discern whether problems with motivation or depression arise from the use of cannabis, specifically, or whether they can be attributed to addiction, more generally. Indeed, alterations in motivation and its underlying neurocircuitry are central to the process of addiction [54]. Substance use disorders are also highly comorbid with depression [55, 56]. Thus, to be able to attribute observed effects to the use of cannabis, studies should examine whether heavy users in their samples meet criteria for a cannabis use disorder and carefully account for these effects in their analyses.

In conclusion, the reviewed studies provide substantial evidence that adolescent cannabis use leads to poorer academic outcomes, but insufficient evidence to conclude that it results in reduced motivation lasting beyond acute cannabis intoxication. Findings from these studies also provide notable evidence of a causal relationship between adolescent cannabis use and depression. The extent to which observed academic, motivation, and depression outcomes represent the same or separate effects is not yet clear, as most studies examining motivation-related outcomes failed to control for depression. Future longitudinal and interdisciplinary work should examine these intricate relationships and their temporality, as improved understanding of them would result in more targeted prevention and intervention efforts aimed at adolescent substance users.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards and international/national/institutional guidelines).

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- • Of importance
- •• Of major importance

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