

Concurrent and Sustained Cumulative Effects of Adolescent Marijuana Use on Subclinical Psychotic Symptoms

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Objective: Adolescents who regularly use marijuana may be at heightened risk of developing subclinical and clinical psychotic symptoms. However, this association could be explained by reverse causation or other factors. To address these limitations, the current study examined whether adolescents who engage in regular marijuana use exhibit a systematic increase in subclinical psychotic symptoms that persists during periods of sustained abstinence.

Method: The sample comprised 1,009 boys who were recruited in 1st and 7th grades. Self-reported frequency of marijuana use, subclinical psychotic symptoms, and several time-varying confounds (e.g., other substance use, internalizing/externalizing problems) were recorded annually from age 13 to 18. Fixed-effects (within-individual change) models examined whether adolescents exhibited an increase in their subclinical psychotic symptoms as a function of their recent and/or cumulative history of regular marijuana use and whether these effects were sustained following abstinence. Models controlled

for all time-stable factors (default) and several time-varying covariates as potential confounds.

Results: For each year adolescent boys engaged in regular marijuana use, their expected level of subsequent subclinical psychotic symptoms rose by 21% and their expected odds of experiencing subsequent subclinical paranoia or hallucinations rose by 133% and 92%, respectively. The effect of prior regular marijuana use on subsequent subclinical psychotic symptoms persisted even when adolescents stopped using marijuana for a year. These effects were after controlling for all time-stable and several time-varying confounds. No support was found for reverse causation.

Conclusions: These results suggest that regular marijuana use may significantly increase the risk that an adolescent will experience persistent subclinical psychotic symptoms.

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As a growing number of states are legalizing medicinal and recreational marijuana use, it is increasingly important to understand the consequences that regular use may have on physical and mental health. One area of particular concern is the effect that adolescent marijuana use may have on the development of psychotic symptoms (e.g., hallucinations, paranoia). Multiple longitudinal and cross-sectional studies have reported that marijuana use, particularly during adolescence, is related to acute psychotic episodes and future psychotic disorders (1–4). More recent research suggests that regular marijuana use might increase adolescents' risk for developing a psychotic illness by causing them to experience persistent subclinical psychotic symptoms, which are typically transitory and fairly common during adolescence (5). However, we are not aware of any published longitudinal studies that have examined whether adolescents who regularly use marijuana (i.e., weekly or more often) over several years exhibit a systematic increase in their subclinical psychotic symptoms that persists during periods of sustained abstinence.

One critical issue is to determine whether a prior history of regular marijuana use, independent of current use, increases an adolescent's risk for experiencing persistent psychotic symptoms. Experimental administration of the primary psychoactive chemical in marijuana, tetrahydrocannabinol (THC), can cause acute feelings of paranoia and other features of psychosis in healthy volunteers (6–9), but these symptoms largely subside when acute intoxication wanes (10). Many negative effects of adolescent marijuana use on cognitive functioning also tend to dissipate following a few months of abstinence (11). Nearly all prior longitudinal studies examining the association between marijuana use and future psychotic symptoms have not controlled for recent patterns of use (12–17), have not repeatedly assessed marijuana use across adolescence, or have combined prior and recent use (18). Therefore, it is impossible to delineate the enduring effect that regular use has on emergent psychotic symptoms and whether this effect is sustained when individuals remain abstinent for several months.

A second issue is whether the association between adolescent marijuana use and later psychotic symptoms is causal or a function of confounding factors (19–23). Together, prior studies have collectively controlled for approximately 60 confounding factors (e.g., other substance use, mental health problems), with estimates suggesting that these factors account for nearly half of the association between marijuana use and psychosis (3). Although no single study can accurately, comprehensively, and directly quantify the myriad preexisting individual differences that may explain the linkage between marijuana use and psychosis, it is possible to eliminate these factors as potential confounds by using within-individual change models. By examining the association between changes in marijuana use and psychotic symptoms within individuals over time, all preexisting time-stable differences between individuals (whether measured or not) are eliminated as potential confounds (24). Moreover, only within-individual change models can address two key questions regarding the association between adolescent marijuana use and psychotic symptoms: 1) During periods of regular marijuana use, do adolescents experience an increase in their psychotic symptoms (concurrent effect)? and 2) Do adolescents who engage in regular marijuana use across multiple years exhibit an incremental and sustained increase in their psychotic symptoms that remains even during periods of abstinence (cumulative/sustained effect)?

Findings from, to our knowledge, the only published longitudinal study that has examined the association between within-individual changes in marijuana use and subclinical psychotic symptoms indicated that adolescents experienced a significant increase in their psychotic symptoms during years when they increased their marijuana use; however, whether this increase was short-lived or persisted across multiple years was not examined (25).

The direction of any causal association between marijuana use and psychotic symptoms is also debated. For example, the self-medication hypothesis suggests that adolescents may begin engaging in regular marijuana use as a way to cope with prodromal psychotic symptoms. Studies directly examining the self-medication hypothesis have produced mixed findings. Fergusson and colleagues (25) found that within-individual increases in subclinical psychotic symptoms were unrelated to concurrent changes in adolescent marijuana use after controlling for several time-varying confounds. In contrast, another longitudinal study found evidence of a bidirectional association between psychosis vulnerability and marijuana use in adolescence (26).

The present study was designed to address several key issues regarding the association between adolescent marijuana use and subclinical psychotic symptoms. Using within-individual change modeling, analyses examined whether adolescents experienced a systematic increase in their subclinical psychotic symptoms during periods when they used marijuana regularly (concurrent effect) and whether this increase persisted over time, even during periods of sustained abstinence (cumulative/sustained effect). These effects were

further examined for different features of psychosis (e.g., paranoia, hallucinations, bizarre behavior). Analyses controlled for all time-stable factors and several potential time-varying confounds (e.g., other substance use, externalizing and internalizing problems). The possibility of reverse causation was also tested by examining whether increases in subclinical psychotic symptoms predicted current and/or sustained increases in regular marijuana use.

METHOD

Participants and Procedures

The participants were 1,009 boys (55.1% black, 41.1% white, 3.8% other) who were recruited from a list of students enrolled in the 1st and 7th grades (referred to as the youngest and oldest cohorts, respectively) in Pittsburgh public schools in 1987–1988. Students enrolled in classes for severe intellectual and physical disabilities were not eligible for the study. A random sample of boys enrolled in each grade was selected for a multi-informant (parents, teachers, self-report) screening to assess conduct problems (e.g., fighting, stealing). Parental consent rates for the screening were 84.6% (N=849) and 83.9% (N=855) for the youngest and oldest cohorts, respectively. Boys who scored in the upper 30th percentile on the screener within each grade were selected for longitudinal follow-up (youngest cohort: N=256; oldest cohort: N=257), along with an approximately equal number of boys who were randomly selected from those scoring below the 70th percentile (youngest: N=247; oldest: N=249). At screening, boys in the youngest cohort (age: mean=6.96 years, SD=0.55) and oldest cohort (age: mean=13.38 years, SD=0.79) were predominantly living with their biological mother (95% and 92%, respectively), and approximately half had a biological father living in the home (42% and 44%, respectively). In both the youngest and oldest cohorts, approximately one-fifth of the mothers (20.6% and 22.8%, respectively) and fathers (16.9% and 23.3%, respectively) living in the home had not graduated from high school. The proportion of families with no employed parental figure in the oldest and youngest cohorts was 14.5% and 12.0%, respectively. Boys in the follow-up sample were not significantly different from the screening sample in terms of race, family composition, and parental education and employment (27).

Following screening, the boys in the youngest cohort were interviewed every 6 months for 4 years, followed by nine annual assessments and follow-ups when participants were, on average, ages 26 and 29. Following screening, the boys in the oldest cohort were assessed every 6 months for 30 months, then annually for 10 years, and again when they were, on average, age 36. For this analysis, data from the two cohorts were combined by aligning assessments by participant age at the time of the interview, resulting in overlapping annual assessments from age 13 to 18. We focused on this age range because 1) the last annual assessment for participants in the 1st-grade cohort was conducted when they were approximately 18 years old and 2) prior studies have suggested that

TABLE 1. Descriptive Statistics for Substance Use and Subclinical Psychotic Symptoms in Adolescent Boys^a

Substance Use or Symptom Variable	Age 13		Age 14		Age 15		Age 16		Age 17		Age 18	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Substance use frequency												
Days using marijuana	3.8	27.9	10.8	47.9	16.9	62.1	27.0	81.1	33.5	89.0	51.8	110.8
Days using alcohol	4.6	24.7	10.5	38.3	13.8	41.9	20.7	56.8	31.4	70.0	49.6	91.6
Days using tobacco	24.3	83.7	50.3	118.5	73.3	137.8	89.6	149.8	107.3	159.6	135.5	170.2
Days using other illicit drugs	0.2	2.5	0.3	3.2	0.5	8.6	0.7	9.4	1.3	14.4	0.7	5.7
	N	%	N	%	N	%	N	%	N	%	N	%
Weekly marijuana use	15	1.7	47	5.0	71	7.8	93	10.6	112	12.9	177	20.3
Weekly alcohol use	17	1.9	47	5.0	67	7.4	93	10.6	148	17.1	213	24.4
Daily tobacco use	44	5.0	106	11.3	150	16.5	189	21.5	224	25.9	296	33.9
Other illicit drug use	18	2.0	32	3.4	34	3.7	43	4.9	48	5.5	53	6.1
Subclinical psychotic symptoms												
Paranoia	164	18.5	162	17.3	130	14.3	110	12.5	111	12.8	117	13.4
Hallucinations	79	8.9	88	9.4	72	7.9	55	6.2	41	4.7	37	4.2
Bizarre thinking	309	34.8	286	30.5	221	24.3	172	19.5	141	16.3	148	17.0
Any symptom	404	45.5	384	41.0	309	34.0	250	28.4	223	25.8	236	27.0
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Total symptoms	0.73	0.96	0.66	0.98	0.53	0.89	0.44	0.84	0.39	0.79	0.41	0.79

^a Original sample included 1,009 boys. Sample size for each age: N=888 (age 13), N=937 (age 14), N=908 (age 15), N=881 (age 16), N=866 (age 17), N=873 (age 18).

TABLE 2. Changes in Current and Cumulative Years of Weekly Marijuana Use Influencing Fluctuations in Subclinical Psychotic Symptoms From Age 13 to 18^a

Marijuana Use	Total Subclinical Psychotic Symptoms			
	Without Covariates		With Covariates	
	Incidence Rate Ratio	95% CI	Incidence Rate Ratio	95% CI
Current weekly use	1.37***	1.16, 1.62	1.12	0.93, 1.35
Years of prior weekly use				
0 years	—		—	
1 year	1.20	0.97, 1.48	1.15	0.91, 1.46
≥2 years	1.45*	1.09, 1.93	1.51*	1.08, 2.11
Test of linear trend	1.20**	1.05, 1.38	1.21*	1.03, 1.42

^a Sample size is 657 because participants who experienced no within-person change in subclinical symptoms were dropped from the analysis by default. Total number of observations=3,545. Age and age² are included as predictors in all models. Covariates were psychotic symptoms at T-1, current internalizing and externalizing problems, current and cumulative years of weekly alcohol use, daily tobacco use, and any other illicit drug use. Contrasts for prior weekly use represent the predicted change in adolescents' subclinical psychotic symptoms following 1 year and ≥2 years of weekly use relative to years preceding the initiation of weekly use, after other model covariates were controlled for. For linear trend analysis, the number of years of prior use was treated as a continuous predictor.

*p<0.05; **p<0.01; ***p<0.001.

regular marijuana use during adolescence is most strongly associated with psychotic symptoms and other forms of cognitive impairment (1, 3, 12, 28). Further details about the sample and study methods are available elsewhere (27).

Measures

Regular marijuana use. Marijuana use was assessed with the youth-reported Substance Use Questionnaire (29). At each annual assessment, the participants reported the number of days they used marijuana in the past year. Adjacent 6-month assessments for the oldest cohort were summed to index past year use. A binary variable, created at each age to index at least

weekly marijuana use (i.e., ≥52 times), was used given evidence suggesting that weekly use before age 18 might be associated with longer-term impairments in cognitive functioning (28). A cumulative history of marijuana use was indexed at each age by counting the number of prior years participants reported weekly use. Cumulative years of weekly use was truncated at 2 years because only 3.7% of participants had 3 or more years of prior weekly use by age 18.

Subclinical psychotic symptoms. Five items from the Youth Self Report (30) were used to index subclinical psychotic symptoms in the past year at each age. As in prior studies, a symptom was considered present if a youth rated it as "sometimes true" or "very true" (31). The items indexed feelings of paranoia ("You feel that others are out to get you"), hallucinations ("You see things that nobody else seems able to see," "You hear things that nobody else seems able to hear"), and bizarre thinking ("You have thoughts that other people would think are strange," "You do things that other people think are strange"). A count of past-year subclinical psychotic symptoms was calculated for each age, as well as three binary variables indexing whether participants experienced each symptom subtype (i.e., paranoia, hallucinations, bizarre thinking). Longitudinal evidence indicates that adolescents who endorse experiencing these subclinical symptoms are at increased risk for developing a psychotic disorder later in life (32).

TABLE 3. Changes in Current and Cumulative Years of Weekly Marijuana Use Influencing Fluctuations in Psychotic Symptom Subtypes From Age 13 to 18^a

Symptom and Marijuana Use	Without Covariates		With Covariates	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Paranoia (N=343)^b				
Current weekly use	2.46***	1.69, 3.58	2.04**	1.29, 3.23
Years of prior weekly use				
0 years	—	—	—	—
1 year	1.93**	1.20, 3.08	2.75**	1.53, 4.94
≥2 years	2.23*	1.19, 4.20	4.96***	2.14, 11.50
Test of linear trend	1.57**	1.16, 2.12	2.33***	1.55, 3.49
Hallucinations (N=218)^b				
Current weekly use	1.49	0.85, 2.62	0.94	0.49, 1.82
Years of prior weekly use				
0 years	—	—	—	—
1 year	1.88†	0.92, 3.84	1.94	0.87, 4.35
≥2 years	2.60†	0.99, 6.77	3.64*	1.07, 12.38
Test of linear trend	1.67*	1.06, 2.62	1.92*	1.09, 3.38
Bizarre thinking (N=511)^b				
Current weekly use	1.34	0.93, 1.93	0.90	0.59, 1.39
Years of prior weekly use				
0 years	—	—	—	—
1 year	0.98	0.61, 1.59	0.88	0.50, 1.53
≥2 years	1.34	0.70, 2.60	1.41	0.63, 3.16
Test of linear trend	1.11	0.82, 1.52	1.10	0.75, 1.62

^a Total number of observations=1,908 (paranoia), 1,175 (hallucinations), 2,796 (bizarre behavior). Age and age² are included as predictors in all models. Covariates were psychotic symptoms at T-1, current internalizing and externalizing problems, current and cumulative years of weekly alcohol use, daily tobacco use, and other illicit drug use. Contrasts for prior weekly use represent the predicted change in adolescents' subclinical psychotic symptoms following 1 year and ≥2 years of weekly use relative to years preceding the initiation of weekly use, after other model covariates were controlled for. For linear trend analysis, the number of years of prior use was treated as a continuous predictor.

^b Sample sizes vary because participants who experienced no within-person change in the dependent variable were dropped from the analysis by default.

†p<0.09; *p<0.05; **p<0.01; ***p<0.001.

Time-Varying Covariates

Prior subclinical psychotic symptoms (T-1). Psychotic symptoms at the prior assessment wave (T-1) were included as covariates. For total psychotic symptoms, the number of symptoms at T-1 was truncated at 2 (i.e., upper 9%–20% at each age). For analyses involving symptom subtypes, binary items indexing the presence/absence of the symptom at T-1 were used.

Other substance use. The Substance Use Questionnaire was used to assess the number of days participants used alcohol, tobacco, and other illicit drugs (tranquilizers, barbiturates, or codeine without prescription; other prescription drugs without prescription; amphetamines; hallucinogens; cocaine; crack; heroin; PCP) in the past year. As with marijuana use, alcohol use was dichotomized to index at least weekly use (≥52 days). Tobacco use was dichotomized to index near daily or daily use (≥312 days). Other illicit drug use was dichotomized to index use or nonuse due to the low prevalence at each age (i.e., 2%–6%). Variables indexing a prior history of use were created for each age by summing the

number of prior years of weekly alcohol use (truncated at 2; 3.7% used weekly for 3 or more years by age 18), daily tobacco use (truncated at 3; 5.7% used daily for 4 or more years by age 18), and other illicit drug use (truncated at 1; 4.0% used for 2 or more years by age 18).

Internalizing and externalizing problems. The extensively validated internalizing and externalizing problems scales from the Youth Self Report were used to control for fluctuations in other forms of psychopathology (33). Participants rated items using a 3-point scale (0=not true to 2=very true/often true), and items were summed to generate scores for internalizing problems (34 items) and externalizing problems (34 items). The item “You feel that others are out to get you” was excluded from the internalizing scale because it was used as an index of paranoia.

Data Analysis Plan

Fixed-effects regressions in Stata 13.1 (34) were used to examine the within-individual association between changes in weekly marijuana use and psychotic symptoms between ages 13 and 18. Because these models focus exclusively on modeling within-individual change, all time-stable factors that may vary between individuals are ruled out as potential confounds (24). Poisson fixed-effects regression models (for total subclinical symptoms) and logistic fixed-effects regression models (for binary symptom subtypes) were used.

Incidence rate ratios are reported for total symptoms, and odds ratios are reported for symptom subtypes. A series of three models were run for each outcome (for the formulas, see Table S1 in the data supplement accompanying the online version of this article). The base model examined the effects of current weekly marijuana use and prior years of weekly marijuana use on subclinical psychotic symptoms, after controlling for age-related changes in subclinical psychotic symptoms. Next, all time-varying covariates were added to the model to control for potential confounds (i.e., psychotic symptoms at T-1, current internalizing and externalizing problems, current and prior use of tobacco, alcohol, and illicit drugs). In the final model, the number of years of prior marijuana use was subdivided into two orthogonal variables to delineate the impact of prior use on subsequent subclinical psychotic symptoms during years when adolescents reported no marijuana use versus years when they reported some use. This model tested whether the cumulative effect of prior marijuana use dissipated or remained significant during subsequent periods of year-long abstinence.

TABLE 4. Linear Association Between the Number of Years of Prior Weekly Marijuana Use and Subclinical Psychotic Symptoms During Subsequent Years of Abstinence Versus Continued Marijuana Use^a

Symptom Type	Effect of Years of Prior Weekly Marijuana Use			
	No Marijuana Use in Past Year		Some Marijuana Use in Past Year	
	Incidence Rate Ratio or Odds Ratio ^b	95% CI	Incidence Rate Ratio or Odds Ratio ^b	95% CI
Total subclinical psychotic symptoms (N=657) ^c	1.29*	1.00, 1.66	1.19*	1.00, 1.41
Paranoia (N=343) ^c	2.12*	1.16, 3.89	2.41**	1.55, 3.74
Hallucinations (N=218) ^c	2.58*	1.07, 6.20	1.73†	0.93, 3.22
Bizarre thinking (N=511) ^c	1.16	0.64, 2.09	1.08	0.71, 1.64

^a Total number of observations=3,545 (total symptoms), 1,908 (paranoia), 1,175 (hallucinations), 2,796 (bizarre behavior). Effects represent the linear association between the number of years of prior weekly marijuana use and changes in psychotic symptoms for subsequent years when adolescents reported no marijuana use versus years when they used at least once. Effects are after controlling for age, age², psychotic symptoms at T-1, current internalizing and externalizing problems, and current and cumulative years of weekly alcohol use, daily tobacco use, and other illicit drug use.

^b Incidence rate ratio is reported for total symptoms (fixed-effects Poisson regression), and odds ratios are reported for symptom subtypes (fixed-effects binary logistic regressions).

^c Sample sizes vary because participants who experienced no within-person change in the dependent variable were dropped from the analysis by default.

†p<0.09; *p<0.05; **p<0.001.

To examine the possibility of reverse causation, logistic fixed-effects regressions examined whether changes in current and prior subclinical psychotic symptoms predicted changes in weekly marijuana use. A variable indexing a cumulative history of subclinical psychotic symptoms was created by counting the number of prior years with 2 or more subclinical symptoms (truncated at 2; 7.9% had 3 or more years with 2 or more symptoms). The same covariates were included in these models, except that reports of prior use of tobacco, alcohol, and hard drugs were not included as covariates, and marijuana use at the preceding assessment (T-1) was included.

Missing Data

The models were run by using conditional maximum likelihood estimation, which uses all available information in a time series to generate model parameters rather than resorting to complete case analysis. The parameters are unbiased when data in a time series are missing at random (35), meaning the probability that the dependent variable Y is missing is not associated with the value of Y after controlling for all observed covariates (24).

Sample retention at the measurement occasions used in the present study ranged from 83% to 99%. Of the original 1,009 participants, 69.6% (N=702) had no missing data, 14.4% (N=145) were missing 1 year of data, 5.0% were missing 2 years (N=50), 4.8% were missing 3 years (N=48), 2.8% were missing 4 years (N=28), 1.6% were missing 5 years (N=16), and 2.0% were missing all 6 years (N=20). Compared with participants with complete data, individuals with missing data were more likely to be black and to have higher levels of subclinical psychotic symptoms, internalizing problems, and externalizing problems. However, these variables were only weakly associated with missingness (r values from 0.07 to 0.19), suggesting that any deviation from the missing-at-random assumption was likely minor.

RESULTS

Descriptive Statistics

Table 1 contains descriptive statistics for substance use and subclinical psychotic symptoms by age. Between ages 13 and 18, the prevalence of psychotic symptoms gradually declined. By the last assessment, 695 participants had reported at least one subclinical psychotic symptom, 391 had reported paranoia, 231 had reported hallucinations, and 574 had reported bizarre thinking.

As expected, substance use increased from age 13 to 18. By the last assessment, 270 participants had used marijuana weekly, 325 had used alcohol weekly, 377 had used tobacco daily, and 134 had used other illicit drugs at least once. The average age at onset was 16.1 years (SD=1.6) for weekly marijuana use, 16.3 (SD=1.6) for weekly alcohol use, 15.6 (SD=1.7) for daily tobacco use, and 15.7 (SD=1.7) for any other illicit drug use.

Predicting Changes in Subclinical Psychotic Symptoms

The primary results for total subclinical psychotic symptoms and symptom subtypes are presented in Table 2 and Table 3, respectively. Sample sizes for these analyses vary because participants with no variation in the dependent variable (i.e., no within-individual change) are excluded by default from Poisson and logistic fixed-effects models (24). Findings related to significant model covariates are included in Table S2 in the online data supplement.

Changes in current weekly marijuana use and the number of prior years of weekly use were both significantly associated with increases in total number of subclinical psychotic symptoms before covariate adjustment (Table 2). However, only the cumulative effect of prior weekly marijuana use remained significant after controlling for all time-varying covariates. In the model with covariates, linear trend analysis indicated that for each additional year adolescents engaged in weekly marijuana use, their expected number of subsequent psychotic symptoms rose by 21%.

Models examining specific symptom subtypes indicated that current weekly use and the number of prior years of weekly marijuana use were both significantly associated with paranoia, before and after controlling for time-varying covariates (Table 3). Linear trend analysis in the model with covariates indicated that for each additional year adolescents engaged in weekly marijuana use, their predicted odds of experiencing subsequent paranoia rose by 133%. Similarly, the number of prior years adolescents engaged in weekly

marijuana use was significantly associated with subclinical hallucinations, although the effect of current weekly marijuana use was not significant (Table 3). Linear trend analysis in the model with covariates indicated that for each additional year adolescents engaged in weekly marijuana use, their expected odds of experiencing future hallucinations rose by 92%. Current and prior marijuana use were not associated with changes in bizarre thinking (Table 3).

Cumulative Effect of Weekly Marijuana Use Following Abstinence

The results indicate that the linear effect of the number of prior years of weekly marijuana use on total subclinical psychotic symptoms, paranoia, and hallucinations persisted even when adolescents stopped using marijuana for a year (Table 4, Figure 1). The results from the model with covariates indicate that for each additional year adolescents engaged in weekly marijuana use, their expected number of total subclinical psychotic symptoms rose by 29% during subsequent periods of year-long abstinence, and their expected odds of experiencing paranoia and hallucinations rose by 112% and 158%, respectively.

Potential Reverse Causation

Models examining whether changes in current and prior psychotic symptoms predicted changes in weekly marijuana use are presented in Table S3 in the online data supplement. After controlling for time-varying covariates, changes in prior and current psychotic symptoms did not predict increases in weekly marijuana use. Instead, there was some indication that prior psychotic symptoms were associated with a reduced likelihood of engaging in weekly marijuana use.

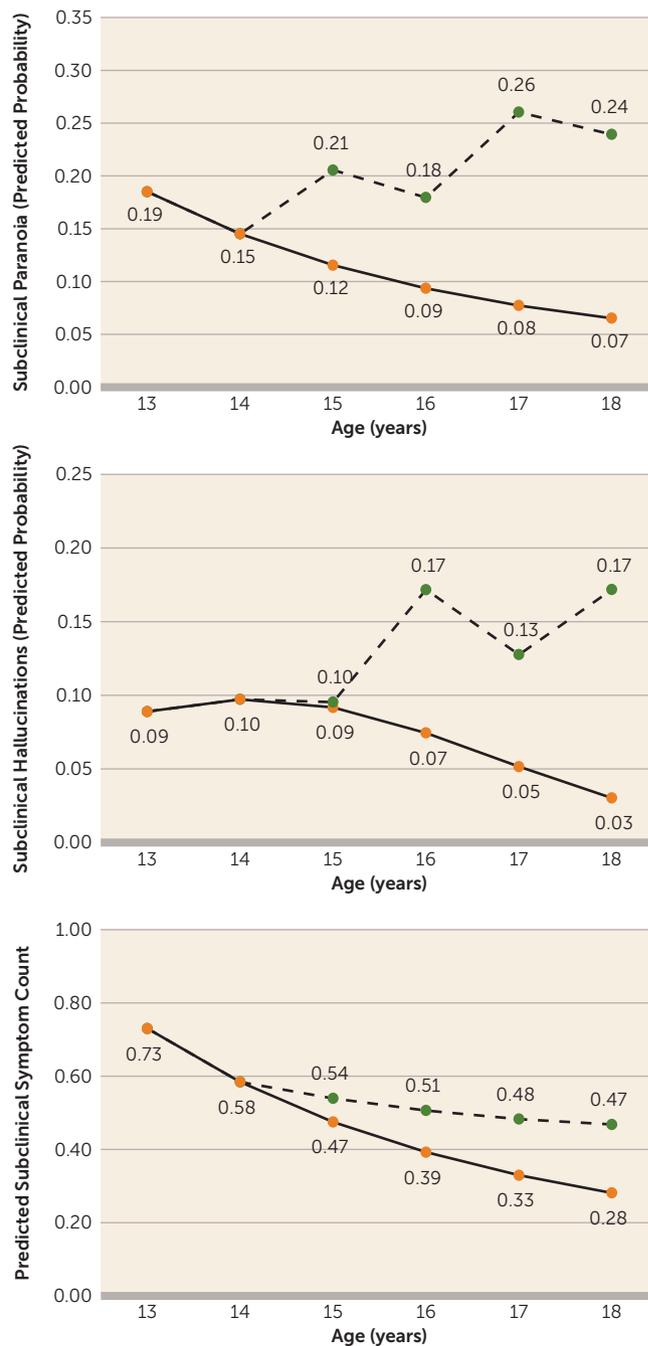
DISCUSSION

This study found evidence suggesting that regular marijuana use may increase an adolescent’s risk of experiencing persistent subclinical psychotic symptoms. This association remained significant after the models controlled for all stable between-individual factors and within-individual changes in current marijuana use, current and prior use of tobacco, alcohol, and other illicit drugs, and internalizing and externalizing problems. Importantly, the effect of prior weekly marijuana use on subclinical psychotic symptoms did not dissipate when adolescents remained abstinent for a year. Moreover, no support was found for the self-medication hypothesis; adolescents were not more likely to engage in regular marijuana use following an increase in their psychotic symptoms. The cumulative effect of regular marijuana use was most pronounced for subclinical symptoms of paranoia and hallucinations.

Transient Versus Sustained Effect of Regular Marijuana Use

Consistent with findings in prior studies, the prevalence of subclinical psychotic symptoms tended to decrease from

FIGURE 1. Model-Predicted Association Between Regular Marijuana Use by Adolescent Boys and Changes in Subclinical Psychotic Symptoms^a



^a The solid lines represent the predicted levels of the outcomes if an adolescent boy never engaged in weekly marijuana use, and the dashed lines indicate the predicted outcomes for the same adolescent if he used marijuana weekly at ages 15 and 17 but abstained from marijuana use during the past year at ages 16 and 18. The sample mean for total number of subclinical psychotic symptoms (0.73) and the sample prevalences of paranoia (18.5%) and hallucinations (8.9%) at age 13 were used as baselines for illustration purposes. The predicted values assume all other model covariates remained unchanged over time. The age-related patterns for the outcomes show some differences in relation to the timing of weekly marijuana use and abstinence; however, each graph illustrates that adolescent boys are more likely to exhibit a chronic pattern of elevated subclinical psychotic symptoms when they engage in weekly marijuana use and that this higher level of symptoms persists despite year-long periods of abstinence.

TABLE 5. Years of Weekly Marijuana Use and Subclinical Psychotic Symptoms at Ages 13–18 Predicting the Emergence of a Psychotic Disorder by Young Adulthood (N=908)^a

Use or Symptom Measure	Odds Ratio	95 CI	Lifetime Psychotic Disorder			
			Yes (N=21)		No (N=887)	
			N	%	N	%
Years of weekly marijuana use						
0 years	—	—	14	2.1	649	97.9
1–2 years	0.85	0.26, 2.78	3	1.6	183	98.4
≥3 years	3.63*	1.22, 10.83	4	6.8	55	93.2
Test of linear trend	1.61	0.89, 2.93				
Years with paranoia						
0 years	—	—	6	1.1	546	98.9
1–2 years	3.63*	1.35, 9.75	10	4.0	243	96.1
≥3 years	4.69**	1.48, 14.91	5	4.9	98	95.2
Test of linear trend	2.21***	1.30, 3.76				
Years with hallucinations						
0 years	—	—	12	1.7	677	98.3
1–2 years	1.67	0.60, 4.61	5	2.7	178	97.3
≥3 years	7.50***	2.42, 23.31	4	11.1	32	88.9
Test of linear trend	2.43***	1.34, 4.39				
Years with bizarre thinking						
0 years	—	—	5	1.3	380	98.7
1–2 years	2.21	0.78, 6.27	10	3.0	328	97.0
≥3 years	2.51	0.79, 7.91	6	3.2	179	96.8
Test of linear trend	1.57	0.91, 2.71				
Years with any subclinical psychotic symptom						
0 years	—	—	2	0.7	270	99.3
1–2 years	3.20	0.79, 13.00	9	2.7	321	97.3
3–4 years	2.74	0.61, 12.33	5	2.3	217	97.8
>4 years	7.49**	1.64, 34.08	5	6.0	79	94.1
Test of linear trend	1.69*	1.09, 2.62				

^a Significance tests were calculated by using Firth's penalized likelihood estimation method for examining rare events. The contrast group comprised participants who had 0 years on each predictor. Lifetime prevalence of a psychotic disorder (i.e., schizophrenia, schizophreniform disorder, schizoaffective disorder, mood disorder with psychotic features, delusional disorder) was assessed by using the Diagnostic Interview Schedule (DIS), which was administered on three occasions in the youngest cohort (mean ages=20, 26, and 29) and twice in the oldest cohort (mean ages=26 and 36). Participants in both cohorts were also asked whether they were currently seeking treatment for schizophrenia at the last assessment. Participants were classified as having a lifetime psychotic disorder if they met diagnostic criteria on the DIS interview or reported receiving treatment for schizophrenia. Unlike a prior study conducted using only data from the age 36 assessment in the oldest cohort (40), this study did not consider individuals who met criteria for a psychotic disorder not otherwise specified on the DIS to have a lifetime psychotic disorder because they may have experienced only subclinical symptoms. Participants were included in the analysis if they completed at least one assessment from age 13 to 18 and at least one diagnostic interview in adulthood. Reanalysis limited to the 571 participants who completed all assessments produced comparable results and is available on request.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.005$.

early to late adolescence (36–39). Despite this normative developmental decline, our findings indicate that regular marijuana use increases the likelihood that teens will experience persistent subclinical psychotic symptoms across adolescence, particularly paranoia. These findings build on experimental work showing that acute administration of THC can cause paranoia among healthy adult volunteers in laboratory settings (10). Although feelings of paranoia typically subside within 24 hours in experimental studies, our findings suggest that as adolescents regularly use marijuana over multiple years, their odds of experiencing chronic paranoia increase. More concerning, evidence suggests that this effect persists even when adolescents abstain from using marijuana for 1 year. A cumulative history of regular

marijuana use also increased adolescents' risk of experiencing subclinical hallucinations, which also persisted during periods of year-long abstinence. This effect is particularly concerning as evidence suggests that adolescents who report chronic subclinical hallucinations are at heightened risk for developing psychotic disorders by young adulthood (31).

Current and cumulative marijuana use were not associated with an increase in strange thoughts or behaviors. The prevalence of these symptoms was fairly high in the current sample, with approximately one-third of participants reporting some odd thinking or behavior at age 13. This finding might reflect the fact that participants were asked to indicate whether "others" viewed their thoughts or behaviors as strange. During adolescence, many youths may feel misunderstood by parents and other authority figures as they begin establishing their autonomy. As a result, endorsement of these items may be more indicative of a normative individuation process than emergent psychopathology.

Accounting for Potential Confounds

An area of contentious debate is whether the well-established link between adolescent marijuana use and features of psychosis is due to pre-existing individual differences (19–23). By focusing on the association between changes in marijuana use and changes in subclinical psychotic symptoms within individuals, the current study eliminated all preexisting time-stable individual differences as potential confounds. In these models, for example, a genetic predisposition toward schizophrenia cannot directly explain why an adolescent's psychotic symptoms fluctuate from year to year (within-individual change), although it may explain why some people are more likely than others to develop psychotic symptoms when exposed to environmental risk factors (between-individual differences). Furthermore, by including a series

of time-varying confounding variables in the analysis, the findings indicate that this association was not accounted for by recent and cumulative changes in other substance use. In fact, during periods when adolescents used other substances, they did not experience an increase in subclinical psychotic symptoms. The unique linkage between regular marijuana use and increases in adolescents' subclinical psychotic symptoms was further exemplified by the fact that the significant associations remained after the models controlled for changes in other forms of psychopathology.

Accounting for Potential Reverse Causation

Consistent with prior work, the present study also found no evidence supporting a possible reverse causal pathway model (14, 25). After controlling for several time-varying covariates, the results indicated that adolescents were not more likely to engage in weekly marijuana use during years when their subclinical psychotic symptoms increased. Furthermore, no consistent evidence supported a systematic association between a cumulative history of psychotic symptoms and an increased risk for engaging in weekly marijuana use.

Limitations and Future Directions

The findings presented here must be considered in the context of several limitations. First, the findings were based on a longitudinal sample of urban boys followed between ages 13 and 18 in one geographical area. Future research should investigate whether these findings hold for girls and adults living in geographically diverse locales and whether the effect of regular adolescent marijuana use on subclinical psychotic symptoms persists into adulthood.

It is also important to note that this study investigated subclinical symptoms by using a self-report rating scale. Although evidence suggests that adolescents who report experiencing subclinical symptoms are at a heightened risk for developing psychotic disorders later in life (31, 32, 36), these symptoms are transient for many youths and may reflect accurate appraisals of reality rather than cognitive distortions. Consistent with this notion, data collected on participants at follow-up assessments in adulthood indicated that only 2.3% of participants in the current study had developed a psychotic disorder by their late 20s or early 30s (Table 5). Although adolescents who engaged in heavy marijuana use across multiple years and those who experienced chronic paranoia and hallucinations were at significantly greater risk for developing a psychotic disorder, this adverse outcome occurred for only a small proportion of these participants and other between-individual difference factors may account for these associations (Table 5). It will be important for future studies with much larger samples to examine why only a subset of adolescents who engage in regular marijuana use develop chronic subclinical psychotic symptoms, why an even smaller portion develop psychotic disorders, and whether these linkages remain significant after controlling for potential confounding factors.

Another limitation is that only self-reported frequency of marijuana use was assessed in the present study. Other factors, such as THC potency and mode of administration, may affect the association between marijuana use and psychotic symptoms. Given that the data presented here were collected in the mid-1990s and early 2000s and that the THC concentration in marijuana has increased in recent years (41), our analysis might underestimate the risks associated with regular use. Future research should investigate how potent marijuana concentrates that can be vaporized, inhaled, or eaten may affect current and future psychotic symptoms. Future experimental research should also investigate whether reducing the proportion of THC (and increasing the proportion of cannabidiol) in medical and recreational marijuana may reduce the risk of experiencing subclinical psychotic symptoms.

Conclusions

This study demonstrates that adolescents are more likely to experience subclinical psychotic symptoms (particularly paranoia) during and after years of regular marijuana use. Perhaps the most concerning finding is that the effect of prior weekly marijuana use persists even after adolescents have stopped using for 1 year. For every additional year adolescents engage in regular marijuana use, their risk of exhibiting subclinical paranoia and hallucinations in future years increases in a linear manner, and the effect of cumulative use remains significant even during periods of abstinence lasting a year. Given the recent proliferation of marijuana legalization across the country, it will be important to enact preventive policies and programs to keep adolescents from engaging in regular marijuana use, as chronic use seems to increase their risk of developing persistent subclinical psychotic symptoms.

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