Impact of adolescent marijuana use on intelligence: Results from two longitudinal twin studies

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Marijuana is one of the most commonly used drugs in the United States, and use during adolescence—when the brain is still developing—has been proposed as a cause of poorer neurocognitive outcome. Nonetheless, research on this topic is scarce and often shows conflicting results, with some studies showing detrimental effects of marijuana use on cognitive functioning and others showing no significant long-term effects. The purpose of the present study was to examine the associations of marijuana use with changes in intellectual performance in two longitudinal studies of adolescent twins (n = 789 and n = 2,277). We used a quasiexperimental approach to adjust for participants' family background characteristics and genetic propensities, helping us to assess the causal nature of any potential associations. Standardized measures of intelligence were administered at ages 9–12 y, before marijuana involvement, and again at ages 17–20 y. Marijuana use was self-reported at the time of each cognitive assessment as well as during the intervening period. Marijuana users had lower test scores relative to nonusers and showed a significant decline in crystallized intelligence between preadolescence and late adolescence. However, there was no evidence of a dose–response relationship between frequency of use and intelligence quotient (IQ) change. Furthermore, marijuana-using twins failed to show significantly greater IQ decline relative to their abstinent siblings. Evidence from these two samples suggests that observed declines in measured IQ may not be a direct result of marijuana exposure but rather attributable to familial factors that underlie both marijuana initiation and low intellectual attainment.

marijuana use | intelligence | adolescence | longitudinal | twins

Marijuana is one of the most commonly used drugs in the United States, with a lifetime use prevalence of 50% (1, 2). Despite this, research on the long-term effects of marijuana use is scarce compared with that of other illicit substances. Changing cultural attitudes toward marijuana have recently led to social and legal acceptance of recreational use (3, 4), making research on the potential consequences particularly salient.

Previous research has shown that marijuana use can have a high societal cost through increased unemployment, absenteeism, decreased productivity, and increased rates of crime and incarceration (5–8). Given that about 19% of youth and young adults (ages 18–25 y) in the United States have used marijuana in the past month (9), the potential impact is nontrivial. There is evidence to suggest that the adolescent brain may be particularly vulnerable, especially with regard to neurocognitive functioning (10, 11). Marijuana use in adolescence, when the brain is still undergoing major developmental changes, has been associated with decreased intelligence (12, 13), reduced memory (13–15), poorer attention (16–18), and lower verbal ability (19–21). However, these findings come from cross-sectional studies, where the temporal ordering of cause and effect is uncertain. For longitudinal studies examining marijuana use and changes in cognition, the picture is less clear.

Few longitudinal studies have examined change in cognitive ability in relation to marijuana use in adolescence. Fried, Watkinson, and Gray (22) showed significant intelligence quotient (IQ) test declines among current heavy users of marijuana relative to nonusers but no decline in former heavy users of marijuana. Meier et al. (23) focused on marijuana use and cognitive decline, where participants were examined over a three-decade period from childhood to adulthood. In this seminal paper, the authors demonstrated a dramatic drop in intelligence for those with persistent cannabis dependence. Although Meier et al.'s study has been the largest and most complete longitudinal examination of IQ decline and marijuana use, there is disagreement as to whether this decline is a direct consequence of marijuana involvement or perhaps attributable to confounding variables (19, 24).

Although studies have demonstrated that heavy marijuana use may impact IQ test performance even a month after cessation (16, 25), deficits seem to be more related to recent use rather than reflecting a permanent insult to cognition (22, 26, 27). Indeed, some studies find no long-term association of marijuana use and IQ (22, 28) or, if so, only on measures of verbal ability (19). Part of this disagreement in the literature speaks to the complexity of trying to infer causal mechanisms from correlational data. The associations between marijuana use and IQ could simply be a matter of confounding, by which other variables that are causal to both low IQ and marijuana use have not been accounted for. As such, one must consider the totality of evidence that would be suggestive of an underlying causal mechanism and address potential competing explanations.

Significance

Marijuana is the most commonly used recreational drug in the United States. Some studies suggest that marijuana use in adolescence is linked to declines in intellectual functioning. Because of the infeasibility of studying this phenomenon experimentally, it is unclear whether the association can be causally attributed to marijuana use itself or is instead the result of confounding factors. We approach this issue quasiexperimentally using longitudinal samples of adolescent twins. Among twin pairs discordant for marijuana use, we assessed intelligence quotient (IQ) score changes while adjusting for the effects of genetic influences and other factors shared by members of the same twin pair. Results suggest that familial confounds underlie the association between adolescent marijuana use and declining IQ scores.

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If marijuana use is a direct cause of neurocognitive decline, then one would expect that (*i*) marijuana use would precede poor cognitive functioning; (*ii*) a dose–response relationship would exist between marijuana use and IQ decline; and (*iii*) the association would persist after adjusting for genetic influences and family upbringing. The present study will address each of these criteria in the largest longitudinal examination undertaken on this topic to date. We use a quasiexperimental methodology by using genetically informative datasets from two longitudinal cohorts of twin youth: The Risk Factors for Antisocial Behavior (RFAB) study from Southern California and the Minnesota Twin Family Study (MTFS).

The present study focuses on two community samples with markedly different ethnic compositions, allowing us to explore the generalizability and replicability of any emerging associations between marijuana use and IQ change. Moreover, we exploit the cotwin control design to determine whether the putative marijuana use–IQ association is attributable to the confounding influences of genetic propensity and family environment. If the neurotoxicity hypothesis is tenable (23), then marijuana-exposed twins should show greater IQ decline relative to their marijuana-abstinent sibling. Alternatively, many youth could presumably be predisposed to IQ declines attributable to family-wide environmental factors and/or genetic liabilities that discourage intellectual attainment and promote marijuana use during adolescence.

Methods

Participants and Procedure.

RFAB twin study at the University of Southern California. RFAB is a longitudinal study of 614 families of twins and triplets (n = 1,241) recruited from the greater Los Angeles area school districts. The twins were 9–10 y old at the time of enrollment, in 2001, and have to date been assessed on five occasions over the course of 10 y of development at ages 9–10, 11–13, 14–15, 16–18, and 19–20 y. The sample is 52% female, 46% monozygotic (MZ), 29% dizygotic (DZ) same-sex, and 24% opposite-sex twins. Participating families were socioeconomically and ethnically diverse and representative of the greater Los Angeles urban population (29) at the time of enrollment, including Hispanic (37%), Caucasian (27%), mixed ethnicity (17%), African American (14%), and Asian (5%) participants. For more details on study protocol and procedures, including zygosity determination, see Baker et al. (30).

MTFS. Participants were drawn from two population-based samples of twins from the state of Minnesota. The first sample (n = 1,527) comprised the younger cohort of the original MTFS (31). The participants' initial assessment occurred between 1990 and 1996. The more recent second sample (n = 1,000) participated in the Enrichment Study (ES) component of the MTFS (32), starting in the years 1999 to 2006. The two samples were separated in time by approximately a decade but shared highly similar testing protocols. In both cases, the twins were recruited at age 11 y and followed up at ∼3-y intervals. Across both samples, twin pairs consisted of like-sex siblings that overall were 51% female, 63% MZ, and 93% Caucasian.

The ES sample was "enriched" for externalizing problems during recruitment; that is, half of the twins were selected for disruptive behavior problems and academic disengagement. These participants were screened for these signs via a phone interview with a parent. The remaining ES participants were randomly selected from an unscreened sample of twins born between 1988 and 1994. Participants from the original (non-ES) component of the MTFS, by contrast, were never selected on the basis of manifesting behavioral problems. Nonetheless, we combined the two samples when conducting analyses, because both were tested in the same laboratory under similar conditions.

The institutional review boards of the University of Minnesota and the University of Southern California approved these studies at each wave. After the study protocol was explained, caregivers provided permission for their minor children to participate. Written assent was also given by the children. Informed consent was obtained from the participants if they were older than 17 y. During the consent process, issues about confidentiality and the voluntary nature of participation were highlighted.

Measures.

Assessment of intelligence. In the RFAB, the four subtests of the Wechsler Abbreviated Scale of Intelligence (WASI) (33)—Vocabulary, Similarities, Block Design, and Matrix Reasoning—were administered at the initial visit (ages 9–10 y). These same tests from the WASI were administered again at the most recent visit (ages 19–20 y). The Vocabulary subtest is a measure of learning and comprehension of verbal knowledge, where participants are asked to define words. The Similarities subtest is a test of abstract verbal reasoning, where participants must determine how a set of two words are similar (e.g., "In what way are a pen and pencil alike"). The Block Design subtest is a timed test that measures abstract visuospatial processing and problem solving by requiring participants to arrange blocks with different color patterns to match a prespecified design. The Matrix Reasoning subtest is a measure of abstract problem solving and spatial reasoning that involves selecting the best option to fill an incomplete matrix of abstract patterns.

In the MTFS, four subtests of the Wechsler Intelligence Scale for Children-Revised (WISC-R) (34) were administered at the initial visit (ages 11–12 y): Vocabulary, Information, Block Design, and Picture Arrangement. These same tests were then administered as part of the Wechsler Adult Intelligence Scale–R (WAIS-R) (35) to the non-ES sample at the second follow-up visit (ages 17–19 y). The Information subtest is a measure of general knowledge that is culturally valued, such as geographic information and historical events. Picture Arrangement is a timed measure of perception of visual detail, where the participant is asked to sequence a series of pictures to create a sensible story. For the ES sample, however, a shorter form of the WAIS-R was administered at the second follow-up, incorporating only Vocabulary and Block Design. These particular subtests were selected because they concisely assess the verbal and nonverbal domains and are highly correlated with full-scale IQ (36).

In both the RFAB and MTFS, raw scores were converted to scaled score equivalents, which were age-standardized. Although the subtests from the WISC-R and WAIS-R are comparably named and conceptually analogous, they contain different item pools, prohibiting an examination of absolute (raw) change in performance between childhood and late adolescence. In the MTFS, test scores were scaled to have a mean of 10 and SD of 3. In both the MTFS and RFAB, each score was ultimately converted into a common IQ metric with a mean of 100 and SD of 15.

Block Design, Matrix Reasoning, and Picture Arrangement are considered measures of fluid intelligence (Gf), because they measure nonverbal logic and problem solving independent of acquired knowledge. Vocabulary and Information are considered measures of crystallized intelligence (Gc), measuring knowledge acquired through experience or learning. Similarities is a measure of both Gf and Gc, relying upon the knowledge of words and their meanings as well as the ability to abstract common patterns (37).

Assessment of marijuana use. In the RFAB, self-reported marijuana use was assessed using a substance use survey which asked "Have you ever tried marijuana?" at each wave of assessment. In the most recent (fifth) wave, participants were also asked "Have you ever smoked marijuana every day for at least 6 months?" and "Have you smoked marijuana at least 30 times in your entire life?". These questions were completed in-laboratory or at the participant's home (via mailed or online questionnaires). In the MTFS, participants were assessed using a semistructured interview format [Diagnostic Interview for Children and Adolescents or Substance Abuse Module of the Composite International Diagnostic Interview (38, 39)] as well as a self-report computerized substance use (CSU) survey. Our comprehensive, multimethod approach to ascertaining marijuana use is described in more detail in *Measurement of Marijuana Use in the Minnesota Twin Family Study*. Participants were classified as having ever used marijuana if they endorsed use on any occasion. Frequent marijuana use was assessed as a binary measure representing whether or not participants used marijuana 30 or more times. Additionally, we determined whether participants had ever used marijuana daily over a period of 6–12 mo by the fifth wave of assessment in the RFAB (ages 19–20 y) and by the second follow-up in the MTFS (ages 17–19 y).

Other substance involvement. Drug use was treated as a dichotomous variable. In the MTFS, interviewers asked participants whether they had ever used any drugs within the following 10 categories: amphetamines, barbiturates, tranquilizers, cocaine, heroin, opiates, PCP, psychedelics, inhalants, and steroids. The participant was queried about each drug class using the Diagnostic Interview for Children and Adolescents (administered at ages 11 and 14 y) and the Composite International Diagnostic Interview-Substance Abuse Module (CIDI-SAM) at age 17 y. At all five waves in the RFAB study, interviewers probed participants for the abovementioned drug categories in addition to nitrous oxide.

Binge drinking was assessed in the MTFS by combining information from a CSU survey and the CIDI-SAM. At all three assessment waves (ages 11, 14, and 17 y), the CSU asked participants whether they ever drank alcohol without parental permission. In the event of a positive response, they were further asked, 'What is the largest number of drinks you had at one time? (a drink is a glass of wine, a bottle or can of beer, a shot glass of liquor, or a mixed

Table 1. Demographics in the RFAB and MTFS studies

	RFAB			MTFS		
Characteristic	Nonusers (n = 314)	Users (n = 475)	Significant, P	Nonusers (n = 1,455)	Users (n = 822)	Significant, P
Age at baseline, y	9.6 ± 0.5	9.6 ± 0.6		11.8 ± 0.4	11.8 ± 0.4	
Age at follow-up, y	19.5 ± 1.1	20.0 ± 1.2	<0.05	18.0 ± 0.6	18.2 ± 0.7	<0.05
Marijuana use >30 times, %		49.3			37.0	
Daily marijuana use, %		20.8			22.6	
Maximal binge drinking*	2.7 ± 2.5	7.3 ± 2.1	<0.05	2.6 ± 2.8	11.3 ± 2.2	<0.05
Other drug use, %	1.6	38.3	<0.05	6.6	39.4	<0.05
SES, percentile	59.4 ± 30.2	56.2 ± 30.5		52.1 ± 21.1	48.6 ± 21.7	<0.05
Male, %	43.9	46.7		44.6	55.0	<0.05
MZ, %	51.1	40.7	<0.05	63.2	61.0	
Race, %						
Caucasian	26.8	32.6	<0.05	95.3	88.9	<0.05
African American	12.4	11.4				
Hispanic	34.7	37.5				
Asian	7.6	1.5				
Multiracial	18.5	17.1				

*RFAB, n = 270 and 421. Maximal binge drinking was measured as the largest number of drinks consumed in a 24-h period.

drink)." Answers were based on an 11-point rating scale, ranging from "less than 1" to "10 or more." In the CIDI-SAM, interviewers asked participants for a numerical count (or estimate) of the largest amount consumed in 24 h. The highest value across the CSU and CIDI-SAM was used to operationalize binge drinking. (In the event that participants endorsed "10 or more drinks" on the CSU but provided a number smaller than 10 on the CIDI-SAM, the participants' count value was set to 10.) In the RFAB, the highest response to the relevant item ("What is the most number of drinks you ever had in one day?") was taken across all five waves. In both studies, the count variable was log-transformed (after adding a constant of 1) and winsorized at the 99th percentile to reduce positive skew. Individuals were assigned a value of 0 if they never consumed a whole drink of alcohol.

Sociodemographic. Age, sex, race, zygosity, and socioeconomic status (SES) were used as covariates in adjusted models. In supplementary analyses, we also controlled for other drug and alcohol use. In the RFAB, family socioeconomic status was determined at the baseline assessment by the Hollingshead Index,* an index comprising parental education and occupation. This score was then converted to a percentile rank.

For the MTFS, SES was determined by aggregating across four variables: household income (US dollars), maternal educational attainment (years), paternal educational attainment (years), and highest parental occupational status (seven-category Hollingshead Index). Each score was converted into a percentile rank, and then averaged across the four ranks to form an SES composite.

Statistical Analysis. Mixed-effects linear regression models were used to test for differences in within-subject IQ change between marijuana user groups in the RFAB and MTFS studies separately. Models were fit using maximum likelihood estimation with a random intercept for twin family, a random intercept for the twin nested within family, and a random slope for dichotomous time (baseline vs. follow-up). A significant time-by-group interaction would indicate that change in IQ was different between marijuana user groups. All analyses were conducted in Stata version 13.1 (Stata Corp).

Comparison of effect size between RFAB and MTFS. To determine whether the differences in IQ change between marijuana user groups were the same in both studies, 1,000 bootstrap estimates of the interaction coefficients from each study were compared using a bias-corrected percentile bootstrap method. To facilitate comparison of the effect sizes, time was treated as continuous (i.e., age at measurement) in a mixed-effects model to account for differences in the length of follow-up between the studies.

Cotwin control. To control for the potentially confounding effects of genetic and family environmental influences on marijuana use and IQ change, a cotwin control design (40) was adopted whereby twin pairs discordant for having ever used marijuana were compared on IQ change. These analyses were conducted separately within MZ and DZ twins using a mixed-effects model with dichotomous time and discordance (user vs. nonuser) as fixed effects and random slopes nested within the family random intercept. A significant time-by-user status interaction would indicate differences in IQ change between twins discordant for marijuana use. A significant difference in IQ change among twins discordant for marijuana use would support the plausibility of the neurotoxicity hypothesis (i.e., marijuana exposure causes a change in IQ). The last born sibling from 14 sets of triplets (RFAB, n = 9; MTFS, n = 5) were excluded from these analyses.

Results

Description of Analytic Sample. Demographic information is presented in Table 1 for the two samples. The final analytic N values for the RFAB were 436 families (789 twins). For the MTFS, 1,171 families (2,277 twins) received a baseline IQ assessment and had valid marijuana use data. The reasons for exclusion from the analysis are presented in Table S1. Marijuana users in the RFAB were more likely to be DZ and less likely to be Asian. In the MTFS, marijuana users were more likely to be male, non-Caucasian, and of lower SES. In both studies, marijuana users were significantly older at follow-up and had greater involvement with other drugs and alcohol.

Participants who were missing marijuana use information had significantly lower SES and baseline IQ scores than participants who returned for follow-up. In the RFAB, these participants were also more likely to be MZ, male, and nonwhite (Table S2). Of participants who provided marijuana use information, there was attrition in the RFAB, such that 323 twins did not complete the follow-up IQ measurement (n = 466 at follow-up). The baseline assessments for these twins were still included in the analyses using a model fitting approach (i.e., maximum likelihood) that has been shown to produce unbiased estimates in the presence of data that are presumed missing at random (41). Although the amount of attrition in the MTFS was lower (10–20%), the Picture Arrangement and Information subtests were not administered to the ES sample at follow-up, resulting in substantially fewer observations for these subtests. The aforementioned analytic approach was used to allow for maximal inclusion of information from these tests. More details about sample sizes at baseline and follow-up for both studies can be found in Table S3.

Marijuana use was prevalent in the RFAB, where 60% of the participants reported having previously used marijuana. By contrast, only 36% of MTFS participants had used marijuana, but they were nearly 2 y younger than RFAB participants. Among the users in

*Hollingshead, AA (1975) Four-factor index of social status. Unpublished manuscript (Yale University, New Haven, CT).

Table 2. Mean IQ in marijuana user groups

	RFAB, IQ				MTFS, IQ			
	Baseline (age 9–10 y)		Follow-up (age 19–20 y)		Baseline (age 11–12 y)		Follow-up (age 17–19 y)	
IQ subtest	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Vocabulary								
Nonusers	100.2	15.0	102.0	14.8	100.7	15.3	102.0	15.1
Users	99.9	15.0	98.1	15.0	98.8	14.3	96.3	14.1
Information								
Nonusers					101.2	15.0	102.3	15.0
Users					97.9	14.7	96.4	14.2
Similarities								
Nonusers	100.8	14.9	100.6	14.9				
Users	99.5	15.0	99.4	15.1				
Block Design								
Nonusers	100.7	14.9	100.7	14.8	100.7	15.0	100.9	15.3
Users	99.5	15.1	99.3	15.2	98.7	14.9	98.3	14.3
Matrix Reasoning								
Nonusers	101.2	15.1	100.2	15.2				
Users	99.2	14.9	99.9	14.9				
Picture Arrangement								
Nonusers					100.3	15.2	100.2	15.3
Users					99.5	14.6	99.8	14.6

N values are presented in Table S3.

the RFAB, 50% had used marijuana >30 times and 21% had been daily users for >6 mo. In the MTFS, these numbers were 37% and 23%, respectively (Table 1).

Baseline Differences in IQ. The mean IQ subtest scores are presented for each of the marijuana user groups in Table 2. A mixed effects model was used to test for between-group differences in IQ. For the Vocabulary subtest, there were no differences at baseline in the RFAB between user groups, whereas in the MTFS, the baseline Vocabulary score was lower for those who later used marijuana (mean difference, −1.9; $P < 0.01$), Table 2. Similarly, the baseline Information score was lower on average in the MTFS users (−2.7; $P < 0.001$). For Block Design, there were no baseline differences in the RFAB, whereas in the MTFS, the mean score was significantly lower at baseline in marijuana users (−2.0; $P < 0.01$). For Similarities, Matrix Reasoning, and Picture Arrangement, there were no mean differences between marijuana user groups at baseline.

IQ Change Between Marijuana User Groups. Change in Vocabulary score from baseline to follow-up was found to be significantly different between groups in both the RFAB and MTFS. Participants who had used marijuana showed greater decreases in Vocabulary score relative to nonusers (Fig. 1). These differences were significant even after adjustment for cohort effects (MTFS) and sociodemographic variables (i.e., age, sex, race, zygosity, and SES; Table 3), indicating that the average change in IQ was 4.0 points lower for those who had used marijuana in the RFAB and 3.4 points lower for users in the MTFS. A similar finding was found for the Information subtest, wherein the mean amount of change was 2.0 points lower in marijuana users relative to nonusers (Table 3). After adjustment for other substance use, these declines were substantially attenuated and no longer statistically significant in the MTFS (Table S4).

Change in Block Design performance was not related to marijuana use in either study. Moreover, there were no significant differences in the extent of change between marijuana user groups for Similarities and Matrix Reasoning in the RFAB or for Picture Arrangement in the MTFS (Table 3).

A subgroup analysis was run within participants who had used marijuana to determine whether frequency or heaviness of use was related to IQ change. Marijuana use greater than 30 times and daily marijuana use were not associated with significant IQ declines among the users (Table 4) even after adjustment for other substance use (Table S5). In fact, those who used marijuana daily for 6 mo or longer did not show greater IQ change relative to those who had tried marijuana fewer than 30 times. Although there was no evidence of a dose–response relationship between marijuana use and IQ change, the substance use data collected does not allow for a full examination of dose-dependent effects.

Comparison of Effect Size Between RFAB and MTFS. The effect size of the time-by-marijuana group interaction on Vocabulary score was compared between studies through a bias-corrected percentile bootstrap method. Differences in follow-up time between the studies necessitated using the age at IQ assessment in the interaction rather than a dichotomous follow-up vs. baseline.

In the RFAB ($n = 785$), nonusers showed no significant changes in Vocabulary score per year of age ($b = 0.01$; $P = 0.90$), whereas users showed significant declines ($b = -0.39$; $P < 0.001$) in IQ per year. The average difference between these rates was 0.397 ($P < 0.001$), which, over the 10 y follow-up of RFAB, would equate to the growth of a 3.97 point gap between the two groups.

In the MTFS ($n = 2{,}271$), nonusers showed increases ($b = 0.12$; $P = 0.028$) in Vocabulary score per year of age, whereas marijuana users showed significant declines ($b = -0.45$; $P < 0.001$). The average difference between these rates was 0.57 ($P < 0.001$), which, over the 7-y follow-up of MTFS, would equate to a 4.00 point difference in IQ change between the two groups.

The differences between the marijuana user groups within each study were not significantly different between the RFAB and MTFS samples ($\Delta 0.176$; $P = 0.35$).

Cotwin Control Analyses. Lastly, a cotwin control analysis was conducted to compare siblings discordant for marijuana use on the IQ measures. The cotwin control design allows for comparison between marijuana users and nonusers within the same twin pair, thereby holding constant the potentially confounding influences of genetics and shared environment. There were no significant differences in IQ change between MZ or DZ siblings for Vocabulary, Similarities, Information, Block Design, or Picture Arrangement (Table 5). These regression coefficients remained nonsignificant when we increased statistical power by

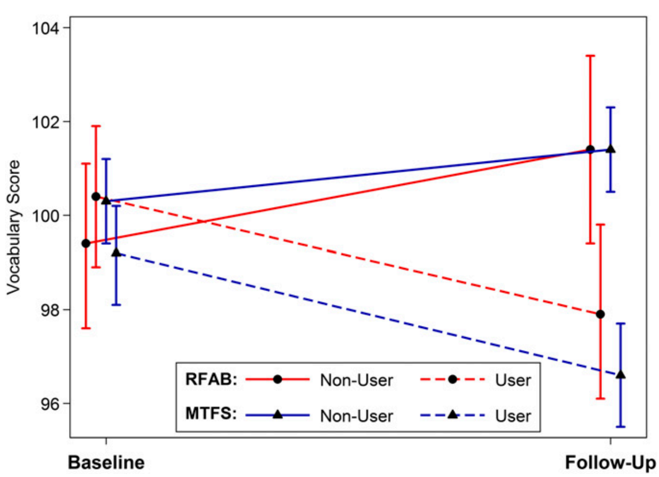

Fig. 1. Vocabulary score decline in marijuana users.

Table 3. Estimated mean differences in IQ change between marijuana user groups

	RFAB		MTFS	
IQ subtest	β (95% CI)	*P*	β (95% CI)	*P*
Vocabulary	−4.0 (−6.3 to −1.7)	0.001	−3.4 (−4.5 to −2.3)	<0.001
Information			−2.0 (−3.3 to −0.7)	0.002
Similarities	−0.1 (−2.8 to 2.5)	0.932		
Block Design	0.2 (−2.0 to 2.5)	0.833	−0.6 (−1.8 to 0.6)	0.293
Matrix Reasoning	1.9 (−0.7 to 4.4)	0.162		
Picture Arrangement			0.4 (−1.6 to 2.4)	0.721

The coefficients denote the time-by-marijuana use interaction. Models are adjusted for age, sex, race, zygosity, SES, and MTFS cohort. *N* values are presented in Table S3. CI, confidence interval.

collapsing across MZ and DZ groups. In the RFAB, the rate of change for Matrix Reasoning was different between the discordant siblings such that the marijuana-using twin showed relatively greater increases in performance (Δ6.6; $P = 0.036$).

We also examined a subset of discordant twin pairs in which one sibling had never used marijuana before and the cotwin had frequently used marijuana (i.e., greater than 30 lifetime uses and/or a period of daily use). This provides the strongest test of the neurotoxicity hypothesis. Because of sample size concerns, this was only conducted in the MTFS using 47 applicable twin pairs. There were no significant differences in IQ trajectory between these discordant twins on any of the subtests (Table S6). Moreover, the effects from these analyses were modest in magnitude and ran in opposing directions. For example, heavy marijuana users showed a decrease of 1.5 points in Vocabulary and an increase of 0.2 points in Information relative to their abstinent siblings.

Discussion

In two prospective longitudinal samples of youth, those who subsequently used marijuana experienced greater cognitive decline by late adolescence in measures of verbal ability (Vocabulary) and general knowledge (Information) relative to nonusers. Baseline IQ performance was assessed at ages 11–12 y in a largely white sample from Minnesota (MTFS) and at ages 9–10 y in a predominantly Hispanic sample from Southern California (RFAB). At the baseline assessment—before marijuana involvement—future users already had significantly lower scores on these subtests than nonusers in the MTFS. The decline in Vocabulary score in marijuana users was statistically equivalent across the two samples, translating into a change of nearly four IQ points.

There are many potential variables related to adolescent marijuana use that could be confounding its relationship with IQ. Although some of the more salient factors (e.g., socioeconomic background and ethnicity) were explicitly measured in the present study, it would be impossible to identify and/or operationalize all relevant factors. The cotwin control design is advantageous because it allows researchers to account for any unmeasured influences experienced in common by members of the same twin pair. By controlling for genetic propensity and shared environment, we can determine the feasibility of a direct (i.e., nonshared environmental) mechanism underlying the IQ-marijuana use association (42). A nonshared environmental etiology would be compatible with the hypothesis that marijuana exposure causes IQ decline.

When comparing IQ change between twins discordant for marijuana use, effects did not consistently emerge in the expected direction. That is, the marijuana-using twin did not exhibit consistently greater deficits relative to his/her marijuana-abstinent cotwin. This fails to support the implication by Meier et al. (23) that marijuana exposure in adolescence causes neurocognitive decline.

Does Marijuana Use Precede IQ Decline? In the RFAB, baseline IQ performance (at ages 9–10 y) was not significantly different between

Table 4. Interactions of marijuana use frequency (>30 times and daily use) with change in IQ among marijuana users

	RFAB			MTFS		
IQ subtest	*N*	β (95% CI)	*P*	*N*	β (95% CI)	*P*
Vocabulary						
Use >30 times	372	−0.8 (−4.2 to 2.6)	0.657	813	−0.6 (−2.4 to 1.2)	0.530
Daily use	375	−0.4 (−4.5 to 3.7)	0.841	783	−0.7 (−2.7 to 1.4)	0.537
Information						
Use >30 times				815	0.7 (−1.4 to 2.8)	0.523
Daily use				785	−1.5 (−4.0 to 1.0)	0.241
Similarities						
Use >30 times	372	1.7 (−2.1 to 5.5)	0.383			
Daily use	375	0.5 (−4.1 to 5.1)	0.833			
Block Design						
Use >30 times	372	0.4 (−2.9 to 3.8)	0.794	815	−0.8 (−3.0 to 1.4)	0.465
Daily use	375	1.5 (−2.5 to 5.5)	0.468	785	0.2 (−2.3 to 2.7)	0.846
Matrix Reasoning						
Use >30 times	372	−1.6 (−5.2 to 2.1)	0.399			
Daily use	375	1.9 (−2.5 to 6.3)	0.393			
Picture Arrangement						
Use >30 times				815	−0.1 (−3.5 to 3.3)	0.959
Daily use				785	0.3 (−3.7 to 4.2)	0.894

Models were adjusted for age, sex, race, zygosity, SES, and MTFS cohort. CI, confidence interval.

Table 5. Cotwin control analysis of discordant use on change in IQ

	RFAB			MTFS		
IQ subtest	*N*	β (95% CI)	*P*	*N*	β (95% CI)	*P*
Vocabulary						
MZ	25	−5.4 (−11.2 to 0.5)	0.098	112	−0.7 (−3.9 to 2.4)	0.639
DZ	54	−2.8 (−7.7 to 2.2)	0.281	99	0.2 (−2.8 to 3.3)	0.883
Information						
MZ				112	2.2 (−0.7 to 5.2)	0.136
DZ				99	−2.5 (−6.9 to 1.9)	0.545
Similarities						
MZ	25	−5.8 (−13.9 to 2.2)	0.161			
DZ	54	1.8 (−4.5 to 8.1)	0.572			
Block Design						
MZ	25	−3.9 (−11.1 to 3.4)	0.295	112	−0.6 (−4.7 to 3.5)	0.776
DZ	54	−2.8 (−8.4 to 2.9)	0.338	99	0.5 (−3.3 to 4.2)	0.811
Matrix Reasoning						
MZ	25	5.7 (−1.5 to 13.0)	0.305			
DZ	54	6.6 (0.6 to 12.7)	0.036			
Picture Arrangement						
MZ				112	−3.1 (−8.3 to 2.1)	0.244
DZ				99	3.8 (−2.7 to 10.4)	0.255

N represents the no. of discordant twin pairs in MZ and DZ groups. Models in DZ twin pairs were adjusted for sex. CI, confidence interval.

future users and nonusers. However, baseline differences in IQ were already present at ages 11–12 y in the MTFS, demonstrating that marijuana use does not necessarily precede lower IQ. Notwithstanding the cross-sectional nature of the data at ages 9–12 y, this finding suggests that part of the marijuana use-IQ association is attributable to common risk factors that unfold in early adolescence during middle school. Indeed, among future marijuana users in the MTFS, low baseline IQ scores were more evident in individuals tested at age 12 y than those tested at age 11 y. It may be interpreted that children who are predisposed to intellectual stagnation in middle school are on a trajectory for future marijuana use.

The presence of baseline differences in the MTFS was not surprising, as previous evidence suggests that there are common antecedents for substance abuse and low cognitive ability (43). Tarter et al. (44) found that behavioral disinhibition was predictive of substance use disorder diagnosis and lower IQ. Similarly, conduct disorder and general delinquency are associated with lower IQ and increased substance use (45). It is perhaps these innate or acquired differences before initiation that are the drivers of further IQ decline and marijuana use rather than reflecting a causal mechanism. It has been posited that individuals with diminished intellectual ability may be more vulnerable to substance use and that drug involvement may serve as a coping mechanism (46). Alternately, individuals exhibiting greater delinquency are less likely to perform well in school and are also more likely to use drugs as a consequence of their delinquency (47).

Are Developmentally Emerging IQ Deficits Found in Those Who Use Marijuana Widespread or Specific? Differences in IQ decline were specific to measures of Gc, specifically Vocabulary and Information test scores. Both the Vocabulary and Information subtests measure acquired knowledge and concur with many other studies showing decreased verbal performance in marijuana users (19–21). Our findings also concur with those of Meier et al. (23) showing deficits in Vocabulary and Information subtests and no significant differences in visuospatial tests such as Block Design and Picture Arrangement. Our results are in contrast to Meier et al. in that we did not find differences in Similarities nor were we able to assess for differences in the Digit Symbol Coding and Arithmetic subtests. Taken together, the overlap in findings from the RFAB, MTFS, and the study by Meier el al. indicate that marijuana use is related to a vulnerability in measures of Gc.

Although Rogeberg (24) claimed that the findings from Meier et al. (23) could be explained by socioeconomic status, we did not find attenuation in the effects after adjustment for a comprehensive measure of socioeconomic status. However, we postulate that it may not be the material disadvantages resultant from low parental income and occupational status that explain IQ decline but rather the consequences of other familial–cultural deficits (e.g., less parental monitoring, poor parent-to-child affect, less emphasis on scholarship, etc.) that may be present across the SES spectrum. The specificity of IQ deficits to measures of acquired knowledge suggests that a third variable, likely sociocultural, is confounding the observed relationship. Crystallized intelligence, relative to fluid intelligence, is preferentially related to characteristics such as schooling quality and access to enrichment opportunities (37).

It is relevant to note that a longitudinal study examining tobacco use and IQ decline found greater decline among tobacco users, relative to nonusers, on Vocabulary and Information subtests (48). Similarly, delinquent/antisocial youth show their worst performance on these two particular subtests (45). Although one might argue for a causal association, we believe what is being captured is a common delinquency-related propensity for substance involvement and low scholastic growth. Although there is little prior literature examining the source of overlap between changes in intelligence and substance use, there are studies that show a set of common genetic liabilities underlying low verbal ability and alcohol use problems (49) as well as low IQ and criminal offending (50).

Is There a Dose–Response Relationship Between Extent of Marijuana Use and IQ Decline? If marijuana use has a long-term neurotoxic effect, then one would expect that heavier use would correspond to greater decreases in intellectual performance. However, heavy marijuana use was not significantly associated with greater IQ decline in either the RFAB or MTFS. Rather, the operative variable was whether participants had ever initiated use. This is in contrast to other cross-sectional studies showing increased amount or frequency of marijuana use is associated with lower intelligence (13, 15, 25). Part of this discrepancy is likely attributable to the fact that these cross-sectional studies were measuring current use, whereas we were considering any previous

use. Additionally, our measures did not account for recent use nor allow for a dose–response continuum, which may have masked true effects in our study. Although our findings concur with other studies showing that previous heavy use does not appear to have long-term impact (22, 26, 27, 51, 52), continuous dose–response measures are needed that can account for recency, frequency, and duration to comprehensively address this question. Meier et al. (23) found greater IQ decline with increased occasions of a marijuana use disorder diagnosis, but this type of categorization captures more than simply the hypothesized neurotoxic effects. For example, those with greater occasions of being diagnosed with an illicit drug use disorder are also likely to be deviant in other domains (e.g., antisocial behavior) that are known to be associated with both substance use involvement and IQ (45, 53).

Are the Deficits in Crystallized Intelligence Specific to Marijuana Use? Adolescent marijuana use is typically not an isolated activity but rather occurs within a broader delinquent context in which alcohol and other drugs are used. Although our primary analyses did not adjust for other substance involvement to maximize the potential to detect a marijuana–IQ association, it would be imprudent to attribute any putative neurotoxic effects to marijuana use without accounting for cooccurring substance use. After including binge drinking and other drug use as covariates, the effect of marijuana use on Vocabulary decline was completely eliminated in the MTFS. Although the attenuation in the RFAB was more modest, it is important to note that RFAB participants were of college age at the last assessment (ages 19–20 y), whereas MTFS participants were generally still in high school (ages 17–18 y). Indeed, we would expect students attending 4-y universities to engage in more binge-drinking behavior relative to their non-college-attending peers (54). Thus, there is reason to believe that alcohol misuse is less predictive of IQ decline in college-aged individuals compared with 17-y-olds.

Given our results from the MTFS, IQ decline does not appear to be specific to marijuana use but is rather a correlate of general substance involvement. This contrasts with the interpretation of Meier et al. (23), who found that persistent marijuana users continued to show greater IQ decline after excluding individuals with persistent diagnoses of alcohol, tobacco, and hard drug dependence. However, the latter diagnoses represent severe, mature forms of substance use problems. Unlike Meier et al., we operationalized our substance use covariates using variables that are appropriate for adolescent populations. Binge drinking, in particular, is thought to exert negative consequences on adolescent brain development (55). Indeed, our continuous measure of binge drinking provides much greater sensitivity to individual differences in alcohol misuse than any categorical diagnosis could do.

Can Within-Pair Differences in IQ Be Attributed to a Possible Causal Effect of Marijuana Use? If marijuana use was to have a unique effect on IQ that is not related to an individual's genetic liability or family environment, then we would expect there to be differences in IQ change between twins discordant for marijuana use. We found little evidence for this in either sample, especially in the larger MTFS where over 200 discordant twin pairs were identified. The lack of such a finding implicates either genetic or family-wide environmental factors—not marijuana use—as the potential driver of differences in cognitive ability between marijuana user groups. If genetics were the primary driver, then one would expect greater effect sizes to emerge in discordant DZ twins, who vary in their genetic makeup unlike identical twins. Because greater effect sizes were not the case, we postulate that aspects of the family-wide environment are the primary source of observed differences in IQ change between the marijuana user groups.

Although use of genetically informative designs to examine marijuana use and IQ decline have been scarce, our findings concur with a study by Lyons et al. (28), who found few differences in test performance between adult twins discordant for regular marijuana use. Only a significant difference in Block Design emerged, which the authors attributed to type 1 error. Although the number of discordant twin pairs was modest or moderate in the RFAB and MTFS, the lack of consistency in the magnitude and direction of effects—with some tests showing an advantage in the marijuana-using twin—challenges the hypothesis that marijuana use has a deleterious effect on general cognitive ability. Although one could argue that we are underpowered to detect what is potentially a small effect, when examining the estimates from the much larger MTFS, we find no change in conclusions despite a threefold increase in sample size. The agreement in conclusions across two samples warrants suspicion against the claim of a direct effect of marijuana use on intelligence.

Limitations. This study is not without its limitations. Of primary concern is the inability to delineate precise mechanisms responsible for the association between marijuana use and IQ change. Many explanatory mechanisms may exist whereby marijuana use has an indirect effect on IQ. Marijuana is also associated with amotivational behavior, increased truancy, and lower educational attainment (47, 56), which are reflected in some IQ measures. Additionally, as Pope et al. (19) argued, marijuana users may be culturally divergent from the rest of society and consequently do not acquire the same skillsets that are measured on tests standardized to mainstream culture. The absence of evidence for a direct effect of marijuana use on IQ in the present study demonstrates the need for future research to focus on these alternate mechanisms.

Furthermore, the examination in this study was limited in scope in that we examined a small number of IQ subtests and did not examine measures of executive function or working memory. Differences between marijuana user groups have appeared in these other cognitive domains (18, 23, 57, 58). Nevertheless, there is no reason to expect such a difference would emerge in the present study. A subset of participants from the MTFS (n = 1,452), in fact, completed the WAIS-III (59) Digit Span subtest—a measure of working memory—during their follow-up assessment at ages 17–18 y. Those who used marijuana in adolescence performed slightly better on this test (mean, 9.4; SD, 2.4) relative to their abstinent peers (mean, 9.2; SD, 2.4). Despite these null findings, our results have no bearing on whether marijuana contributes causally to declines in other measures of cognition or other important outcomes such as psychosocial adjustment and mental and physical health.

Attrition is also a concern for this study, because there were a number of participants who were excluded for failing to have marijuana use information. It is likely that individuals with greater severity of marijuana use are less likely to participate in the later waves, potentially skewing our analyses toward null findings by examining only the least severe users. Despite this possibility, we note that ~21% of our marijuana users were daily users for greater than 6 mo. Additionally, we found that those missing marijuana use information were significantly more likely to have lower IQ at baseline. There is some evidence to suggest that low IQ may pose a risk factor for marijuana use (46), which, if so, may further complicate the situation.

Our marijuana users were a heterogeneous group that included individuals with normal adolescent drug experimentation as well as more regular users. Although we examined dose–response relationships to isolate the effects of heavy use, we cannot rule out a neurotoxic effect of long-term marijuana use, particularly given that our measures were discretely measured and did not account for how recently the participants had used marijuana. Although our study evaluated a subset of subjects who had been daily users over the course of 6 mo to a year, all participants were still young adults at their last assessment. Perhaps regular use over a more prolonged period would result in greater differentiation across groups. This is a possible explanation for the discrepancy of our findings from those of Meier et al. (23), whose subjects were aged 38 y at their last assessment. We additionally were not able

to differentiate current heavy users from former heavy users, and thus our results cannot disentangle the acute from nonacute effects of marijuana use on intellectual functioning.

Lastly, our measures of marijuana use relied upon participant recall, which may underestimate their substance use. This recall bias may be exacerbated in our frequency measures, particularly given the multiyear period between assessments. Our measure of binge drinking may be especially prone to memory errors, because it would be difficult for participants to recall the maximum number of drinks ever consumed in a day, particularly if they were intoxicated. Although our drinking measure should, in many cases, be viewed as an approximation rather than a precise count, we believe it adequately discriminates between abstinent/modest drinkers and heavy drinkers.

Conclusion

In the largest longitudinal examination of marijuana use and IQ change, using two samples to replicate results and a genetically informative design, we find little evidence to suggest that adolescent marijuana use has a direct effect on intellectual decline. Although marijuana users showed greater decline than nonusers in areas of Gc, the presence of baseline differences before marijuana involvement, the lack of a dose–response relationship, and an absence of meaningful differences between discordant siblings lead us to conclude that the deficits observed in marijuana users are attributable to confounding factors that influence both substance initiation and IQ rather than a neurotoxic effect of marijuana.

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