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Associations between adolescent cannabis use and neuropsychological decline: a longitudinal co-twin control study

Madeline H. Meier[1], Avshalom Caspi[2,3,4], Andrea Danese[4,5,6], Helen L. Fisher[4], Renate Houts[2,3], Louise Arseneault[4] & Terrie E. Moffitt[2,3,4]

Department of Psychology, Arizona State University, Tempe, AZ, USA,[1] Department of Psychology and Neuroscience, Duke University, Durham, NC, USA,[2] Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, USA,[3] Medical Research Council Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology, and Neuroscience, King's College London, UK,[4] Department of Child and Adolescent Psychiatry, Institute of Psychiatry, Psychology, and Neuroscience, King's College London, UK[5] and National and Specialist Service Foundation Trust, London, UK[6]

ABSTRACT

Aims This study tested whether adolescents who used cannabis or met criteria for cannabis dependence showed neuropsychological impairment prior to cannabis initiation and neuropsychological decline from before to after cannabis initiation. **Design** A longitudinal co-twin control study. **Setting and Participants** Participants were 1989 twins from the Environmental Risk (E-Risk) Longitudinal Twin Study, a nationally representative birth cohort of twins born in England and Wales from 1994 to 1995. **Measurements** Frequency of cannabis use and cannabis dependence were assessed at age 18. Intelligence quotient (IQ) was obtained at ages 5, 12 and 18. Executive functions were assessed at age 18. **Findings** Compared with adolescents who did not use cannabis, adolescents who used cannabis had lower IQ in childhood prior to cannabis initiation and lower IQ at age 18, but there was little evidence that cannabis use was associated with IQ decline from ages 12–18. For example, adolescents with cannabis dependence had age 12 and age 18 IQ scores that were 5.61 ($t = -3.11$, $P = 0.002$) and 7.34 IQ points ($t = -5.27$, $P < 0.001$) lower than adolescents without cannabis dependence, but adolescents with cannabis dependence did not show greater IQ decline from age 12–18 ($t = -1.27$, $P = 0.20$). Moreover, adolescents who used cannabis had poorer executive functions at age 18 than adolescents who did not use cannabis, but these associations were generally not apparent within twin pairs. For example, twins who used cannabis more frequently than their co-twin performed similarly to their co-twin on five of six executive function tests ($Ps > 0.10$). The one exception was that twins who used cannabis more frequently than their co-twin performed worse on one working memory test (Spatial Span reversed; $\beta = -0.07$, $P = 0.036$). **Conclusions** Short-term cannabis use in adolescence does not appear to cause IQ decline or impair executive functions, even when cannabis use reaches the level of dependence. Family background factors explain why adolescent cannabis users perform worse on IQ and executive function tests.

Keywords Cannabis, executive functions, IQ, longitudinal, marijuana, neuropsychological impairment.

Correspondence to: Madeline H. Meier, Department of Psychology, Arizona State University, PO Box 871104, Tempe, AZ 85287-1104, USA.
E-mail: madeline.meier@asu.edu
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INTRODUCTION

Debate concerning cannabis legalization has led to increased urgency to understand the effects of cannabis use on health and behavior [1]. The effect of cannabis use on neuropsychological functions has received considerable research attention, and the general consensus is that heavy cannabis use is associated with neuropsychological impairment [2–7]. However, there is uncertainty regarding the extent to which neuropsychological impairment is apparent prior to cannabis use initiation, the age at which cannabis-related neuropsychological impairment first emerges and the level and duration of cannabis exposure that is sufficient to produce impairment. One hypothesis is that neuropsychological impairment is apparent in childhood, prior to cannabis use initiation. A second hypothesis is that cannabis-induced neuropsychological impairment first emerges in adolescence shortly after cannabis use

initiation. Yet a third hypothesis is that cannabis-induced neuropsychological impairment emerges only after years of heavy use. Determining which hypothesis has more support will have critical implications for prevention and remediation.

To address these questions, prospective longitudinal studies are needed. There are only nine cohort studies of the association between cannabis use and neuropsychological impairment that could inform these questions [8–17]. These studies included adolescents or young adults in the sample and administered neuropsychological tests at two or more time-points (Supporting information, Table S1 [8–18]). Six of these studies assessed neuropsychological functions in childhood, prior to cannabis use initiation, and therefore had 'before and after' assessments of neuropsychological functions [8,11,12,14–17]. These six studies found inconsistent evidence for the hypothesis that neuropsychological impairment predates cannabis initiation [8,11,12,14–17].

Across all nine studies, there was mixed evidence that cannabis use was associated with neuropsychological decline (or neuropsychological impairment after accounting for baseline neuropsychological functioning). However, studies varied in terms of length of follow-up and the cohorts' level of cannabis exposure. In general, studies with the longest follow-up [8,9] and greatest cannabis exposure [8,9,11] tended to show the strongest evidence of cannabis-related neuropsychological decline, and studies with the shortest follow-up period and least cannabis exposure [14–17] (i.e. studies of adolescent cannabis use) tended to show the weakest evidence. This pattern is consistent with the hypothesis that cannabis-induced neuropsychological impairment emerges only after years of heavy cannabis use. Nonetheless, firm conclusions cannot be drawn for several reasons. First, there are relatively few cohort studies, particularly studies that assessed neuropsychological functions prior to cannabis initiation. Second, existing cohort studies of adolescents examined low-level cannabis use [14–17], leaving open the possibility that neuropsychological impairment might emerge only for adolescents with more problematic use. Third, there are many potential confounders of cannabis–neuropsychological impairment associations, limiting causal inference.

The purpose of the present study was to test associations between adolescent cannabis use and neuropsychological decline in a cohort of British children followed prospectively from ages 5 to 18. Like the few existing cohort studies of adolescent cannabis use [11,14–17], we assessed intelligence (IQ) in childhood, prior to cannabis use initiation. We also assessed IQ and executive functions at age 18, after some cohort members had begun using cannabis. Unlike other cohort studies of adolescent cannabis use [11,14–17], we examined cannabis dependence as our cannabis exposure, in addition to frequency of cannabis use, as cannabis dependence is an indicator of more problematic use. Further, because the cohort comprises twin pairs, it enabled a comparison of neuropsychological decline for twins in the same family who differed in their cannabis use. This within-pair comparison is important because it controls for family background factors that might lead to a spurious association between cannabis use and neuropsychological decline.

METHODS

Participants

Participants were members of the Environmental Risk (E-Risk) Longitudinal Twin Study, which tracks the development of a birth cohort of 2232 British children. The sample was drawn from a larger birth register of twins born in England and Wales in 1994–95 [19]. Full details about the sample are reported elsewhere [20]. Briefly, the E-Risk sample was constructed in 1999–2000, when 1116 families (93% of those eligible) with same-sex 5-year-old twins participated in home-visit assessments. This sample comprised 56% monozygotic (MZ) and 44% dizygotic (DZ) twin pairs; sex was distributed evenly within zygosity (49% male). Families were recruited to represent the UK population of families with newborns in the 1990s, on the basis of residential location throughout England and Wales and mother's age. Teenaged women with twins were overselected to replace high-risk families lost to the register through non-response. Older women having twins via assisted reproduction were underselected to avoid an excess of well-educated older women. These strategies ensured that the study sample represents the full range of socio-economic conditions in Great Britain, as reflected in the families' distribution on a neighborhood-level socio-economic index [ACORN (A Classification of Residential Neighborhoods), developed by CACI Inc. for commercial use] [21,22]: 25.6% of E-Risk families live in 'wealthy achiever' neighborhoods compared with 25.3% nation-wide; 5.3% versus 11.6% live in 'urban prosperity' neighborhoods; 29.6% versus 26.9% live in 'comfortably off' neighborhoods; 13.4% versus 13.9% live in 'moderate means' neighborhoods; and 26.1% versus 20.7% live in 'hard-pressed' neighborhoods. E-Risk under-represents 'urban prosperity' because such households are significantly more likely to be childless.

Follow-up home visits were conducted when the children were aged 7 (98% participation), 10 (96% participation), 12 (96% participation) and 18 years (93% participation). Home visits at ages 5, 7, 10 and 12 included assessments with participants and their mothers; we conducted interviews only with participants at age 18 (n = 2066). There were no differences between those who did and did not take part in the study at age 18 in terms of key measures when the cohort was initially defined at age 5: socio-economic status (SES) (χ^2 = 0.86, P = 0.65),

IQ (t = 0.98, P = 0.33) or internalizing or externalizing problems (t = 0.40, P =0.69 and t = 0.41, P = 0.68, respectively). Here we report on 1989 individuals with IQ data at ages 5, 12 and 18, which comprised 96% of all participants seen at age 18. Sample characteristics are shown in Table 1.

The Joint South London and Maudsley and the Institute of Psychiatry Research Ethics Committee approved each phase of the study. Parents gave written informed consent and twins gave assent between ages 5 and 12 and written informed consent at age 18.

MEASURES

Cannabis use

Participants were evaluated for past-year cannabis dependence at age 18 according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria [23]. Four per cent (n = 84) of participants were diagnosed with cannabis dependence. Of the 977 complete twin pairs, most were concordant for not having cannabis dependence (n = 908 pairs). Twelve pairs were concordant for dependence and 57 pairs were discordant for cannabis dependence.

Participants reported on how often they used cannabis in the past year at age 18. Responses were: 0 = never (63%), 1 = less than monthly (28%), 2 = monthly (3%), 3 = weekly (3%), 4 = daily (2%) and 5 = many times a day (1%). The correlation between twins within a pair on frequency of use was r = 0.55 ($P < 0.001$).

Intelligence quotient (IQ)

Intelligence was assessed at ages 5 and 12, before cannabis initiation, and again at age 18. (Only 19 participants had tried cannabis at age 12). At age 5, we used a short form of the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) [24]. Using two subtests (vocabulary and block design), we pro-rated children's age-5 IQ following procedures described by Sattler [25]. At age 12, we used the Wechsler Intelligence Scale for Children–Revised (WISC-R) [26]. At age 18, we used the Wechsler Adult Intelligence Scale–IV (WAIS-IV) [27]. At ages 12 and 18, two of the same subtests were administered—information and matrix reasoning. These two subtests were used to obtain pro-rated full-scale IQ at ages 12 and 18. Pro-rated full-scale IQ scores were standardized on the full sample at each age to mean = 100, standard deviation (SD) = 15, and subtest scores were standardized to mean = 10, SD = 3.

Executive functions

At age 18, executive functions tapping attention/vigilance and working memory were assessed with tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) [28]. The CANTAB is a computerized test battery of neuropsychological functioning that uses touchscreen technology. Tests are described in Supporting information, Table S2. Scores on each executive function test were standardized to mean = 0, SD = 1.

Statistical analyses

We used linear regression to test whether age-18 cannabis use was associated with (a) lower IQ at ages 5, 12 and 18, (b) IQ decline from ages 12 to 18 (with IQ decline represented as a change score: age-18 IQ minus age-12 IQ) and (c) poorer executive functioning at age 18. We focused on IQ decline from ages 12 to 18 (and not ages 5 to 18) because the age-12 and age-18 IQ scores were based on the same two subtests (information and matrix reasoning),

Table 1 Sample characteristics.

Characteristic	*Full sample (n = 1989)* *Mean (SD)*	*Girls (n = 1049)* *Mean (SD)*	*Boys (n = 940)* *Mean (SD)*	*Test of sex difference*	
				β/OR	*P*
Sex (% male)	47.26	–	–	–	–
Zygosity (% dizygotic)	43.99	42.70	45.42	OR = 1.12[a]	0.39
SES	2.00 (0.82)	2.01 (0.82)	1.99 (0.81)	−0.01	0.79
Age 5 IQ	100.19 (15.00)	100.21 (14.37)	100.17 (15.69)	0.00	0.97
Age 12 IQ	100.33 (14.75)	99.31 (13.64)	101.47 (15.83)	0.07	0.012
Age 18 IQ	100.17 (14.88)	98.27 (13.95)	102.30 (15.59)	0.14	< 0.001
Cannabis use (% used in past year)	37.56	30.03	45.96	OR = 1.98[a]	< 0.001
Cannabis dependence (%)	4.22	2.57	6.06	OR = 2.44[a]	< 0.001

SES = socio-economic status. SES was assessed on a three-point scale with 1 = low SES and 3 = high SES; SD = standard deviation; OR = odds ratio. [a]These analyses used logistic regression to test whether boys had greater odds of being a dizygotic (versus monozygotic) twin than girls; greater odds of past-year cannabis use; and greater odds of cannabis dependence than girls. All other analyses used linear regression (i.e. to test whether boys had higher SES and higher IQ than girls), and standardized beta coefficients are reported.

whereas the age-5 IQ scores were based on different subtests. However, age-5 IQ was included as a covariate in analyses of IQ decline. For tests of associations between cannabis use and executive functioning at age 18, we included age-12 IQ as a covariate. Sex was included as a covariate in all analyses as, relative to girls, boys had higher rates of cannabis use and dependence, had slightly higher IQ at ages 12 and 18 and showed a greater increase in IQ from ages 12 to 18 (Table 1). However, there was little evidence that associations between cannabis use and neuropsychological functioning differed for boys and girls.

We conducted analyses in the full sample of twins, which approximates the general population, and adjusted for the non-independence of observations (twins nested within twin pairs) by using the SURVEYREG procedure in SAS. The SURVEYREG procedure uses Taylor linearization to estimate sampling errors of estimators. We also conducted co-twin control analyses comparing twins within the same family who differed in their level of cannabis use. Co-twin control analyses allow us to come closer to causal inference because they inherently control for a variety of unmeasured family background factors. The logic is as follows. In the full sample of twins, differences between cannabis-dependent and non-dependent adolescents, for example in terms of SES, neighborhood or educational opportunities, could lead to a spurious association between cannabis dependence and lower IQ. In contrast, twins from the same family share family backgrounds, and therefore these family factors cannot explain IQ differences between twins discordant for dependence.

Co-twin control analyses differed slightly depending on the cannabis exposure. For cannabis dependence, analyses were conducted as described above for the full sample, but the sample was limited to the 57 twin pairs discordant for dependence. For frequency of cannabis use, we used all complete twin pairs (n = 977) and computed twin difference scores for frequency of use (e.g. twin-1 frequency minus twin-2 frequency) and outcomes (IQ at ages 5, 12 and 18; IQ decline from 12 to 18; and age-18 executive functions). Then, we regressed twin differences in outcomes on twin differences in frequency of use. Findings from co-twin control analyses are reported for the combined sample of DZ and MZ twins to avoid loss of power resulting from reporting on them separately. There was little evidence that associations differed by zygosity.

RESULTS

Associations between cannabis dependence and IQ

Table 2 shows mean pro-rated IQ scores for cannabis-dependent and non-dependent adolescents in the full sample and in the subsample of discordant twin pairs. First, we review findings for the full sample. Adolescents with cannabis dependence at age 18 had lower IQ at ages 5, 12 and 18 (95.18, 94.95 and 93.14, respectively) compared with non-dependent adolescents (100.48, 100.56 and 100.48, respectively), but there was only weak evidence that adolescents with cannabis dependence showed greater IQ decline from ages 12 to 18 (−1.81 IQ points) than non-dependent adolescents (−0.08 IQ points) (t = −1.27, P = 0.20) (Table 2). Findings were similar after controlling for age-5 IQ.

Results for discordant twin pairs differed from results for the full sample, in that twins with cannabis dependence performed similarly to their co-twins without cannabis dependence on the IQ tests at each age (Table 2). For example, cannabis-dependent twins had an age-5 IQ of 94.26, and their non-dependent co-twins had an age-5 IQ of 93.50 (Table 2). Thus, the average age-5 IQ difference between discordant twins was only 0.76 IQ points. (This same result is obtained by subtracting twin-1 IQ from twin-2 IQ within a discordant pair and averaging that difference across twins.) Therefore, unlike in the full sample, there was no evidence from discordant pairs that cannabis-dependent adolescents had lower IQ at any age, suggesting that family background factors explain why, in the full sample, cannabis-dependent adolescents had lower IQ. That family factors confounded the cannabis–IQ association is also apparent in the means for discordant twin pairs, which show that both the cannabis-dependent and non-dependent twins from discordant pairs had lower IQ relative to the full sample. That is, non-dependent adolescents from families in which a sibling had dependence had lower IQ relative to norms (mean IQ = 100).

Findings for the full sample and the subsample of discordant twins were similar after excluding 19 participants who had used cannabis at age 12 (Supporting information, Table S3). Results for the information and matrix reasoning subtests were similar to results for full-scale IQ (Supporting information, Tables S4 and S5).

Associations between frequency of cannabis use and IQ

Because only 4% of twins were cannabis-dependent but 37% of them had used cannabis, we repeated all analyses based on frequency of cannabis use. This allowed for greater variation and power to detect differences. In the full sample, more frequent cannabis use at age 18 was associated with lower IQ at ages 12 and 18 (but not age 5) and greater IQ decline from ages 12 to 18, but the effect was small (Table 3). For every standard deviation increase in frequency of cannabis use, IQ declined by an additional 0.05 standard deviations. Associations were similar after controlling for age-5 IQ. Among twin pairs, we found that the more frequently cannabis-using twin did not show lower IQ at any age or greater IQ decline than their co-twin (Table 3).

Table 2 Mean pro-rated IQ scores at ages 5, 12 and 18 and average within-person IQ change from ages 12 to 18 as a function of cannabis dependence at age 18.

Full sample	*Non-dependent adolescents (n = 1905)*	*Cannabis dependent adolescents (n = 84)*	*Difference between non-dependent and cannabis-dependent adolescents*[a]	*t*	*P*	*Difference between non-dependent and cannabis-dependent adolescents after controlling for age 5 IQ*[a]	*t*	*P*
Age 5 IQ	100.41	95.18	**−5.23**	**−2.94**	**0.003**	–	–	–
Age 12 IQ	100.56	94.95	**−5.61**	**−3.11**	**0.002**	−2.80	−1.78	0.08
Age 18 IQ	100.48	93.14	**−7.34**	**−5.27**	**< 0.001**	**−4.82**	**−3.88**	**< 0.001**
IQ change from age 12 to 18[b]	−0.08	−1.81	−1.73	−1.27	.20	−2.02	−1.49	0.14
Discordant twins	*Non-dependent twins (n = 57)*	*Cannabis-dependent co-twin (n = 57)*	*Difference between discordant twin pairs*[a]	*t*	*P*	*Difference between discordant twin pairs after controlling for age 5 IQ*[a]	*t*	*P*
Age 5 IQ	93.50	94.26	0.76	0.39	0.70	–	–	–
Age 12 IQ	95.47	93.97	−1.50	−0.80	0.43	−1.81	−0.94	0.35
Age 18 IQ	94.31	92.86	−1.45	−0.81	0.42	−1.77	−0.97	0.33
IQ Change from age 12 to 18[b]	−1.16	−1.11	0.05	0.02	0.98	0.04	0.02	0.99

Means and statistical tests are adjusted for sex. [a]Negative scores indicate that adolescents with cannabis dependence showed lower IQ/greater IQ decline than non-dependent adolescents. For example, results for the full sample show that IQ decline for adolescents with cannabis dependence was 1.73 points greater than IQ decline for adolescents without cannabis dependence. [b]IQ change was represented as a change score (age-18 IQ–age-12 IQ). We focused on IQ decline from ages 12 to 18 because the age-12 and age-18 pro-rated IQ scores were based on the same two subtests (information and matrix reasoning), whereas the age-5 pro-rated IQ scores were based on different subtests (vocabulary and block design). Results are shown with and without adjustment for age-5 IQ. Statistically significant differences are shown in bold type.

Table 3 Associations between frequency of cannabis use at age 18 and (a) pro-rated IQ at ages 5, 12 and 18 and (b) IQ decline from ages 12 to 18.

	Before controlling for age 5 IQ		*After controlling for age 5 IQ*	
Full sample (n = 1989)	β[a]	*P*	β[a]	*P*
Age 5 IQ	−0.05	0.07	–	–
Age 12 IQ	**−0.11**	**< 0.001**	**−0.08**	**< 0.001**
Age 18 IQ	**−0.15**	**< 0.001**	**−0.12**	**< 0.001**
IQ change from ages 12 to 18[c]	**−0.05**	**0.035**	**−0.05**	**0.023**
Twin pairs (n = *977 twin pairs)*	β[b]	*P*	β[b]	*P*
Age 5 IQ	0.02	0.56	–	–
Age 12 IQ	0.03	0.32	0.03	0.37
Age 18 IQ	0.00	0.94	0.00	0.97
IQ change from age 12 to 18[c]	−0.02	0.46	−0.02	0.47

Estimates are standardized regression coefficients. All associations are adjusted for sex. [a]Negative estimates indicate that more frequent cannabis use at age 18 was associated lower IQ/greater IQ decline from ages 12 to 18. [b]Positive estimates indicate that the twin who used cannabis more frequently at age 18 showed higher IQ/less IQ decline than their co-twin. [c]IQ change was represented as a change score (age-18 IQ–age-12 IQ). We focused on IQ decline from ages 12 to 18 because the age-12 and age-18 pro-rated IQ scores were based on the same two subtests (information and matrix reasoning), whereas the age-5 pro-rated IQ scores were based on different subtests (vocabulary and block design). Results are shown with and without adjustment for age-5 IQ. Statistically significant differences are shown in bold type.

We conducted sensitivity analyses comparing IQ for adolescents who did not use cannabis at age 18 with adolescents who used cannabis at least weekly, under the hypothesis that relatively trivial differences between adolescents in frequency of use obscure effects at the extremes of use. However, there was little evidence that

weekly cannabis users showed greater IQ decline than non-users (Supporting information, Table S6).

Associations between cannabis dependence and executive functions

Table 4 shows mean executive function scores at age 18 for cannabis-dependent and non-dependent adolescents in the full sample and in the subsample of discordant twins. In the full sample, cannabis-dependent adolescents performed worse on four of six tests (RVP A Prime, SWM strategy, Spatial Span forward and Spatial Span reversed). After controlling for age-12 IQ, cannabis-dependent adolescents performed worse on only two of six tests (Spatial Span forward and reversed). However, no differences were apparent among discordant twins.

Associations between frequency of cannabis use and executive functions

In the full sample, more frequent cannabis use at age 18 was associated with worse performance on all executive function tests except one, even after controlling for age-12 IQ (Table 5). However, most of these associations were not apparent within twin pairs—i.e. when we compared each twin to their co-twin (Table 5). Twins used who cannabis more frequently than their co-twin performed similarly to their co-twin on 5 of 6 executive function tests. The only exception was that twins who used cannabis more frequently than their co-twin performed worse on the Spatial Span reversed task, but the effect was small ($\beta = -0.07$, $P = 0.022$).

We conducted sensitivity analyses comparing adolescents who had not used cannabis in the past year with adolescents who had used cannabis at least weekly in the past year (Supporting information, Table S7). Findings were similar.

DISCUSSION

In a cohort of British youth followed from ages 5 to 18, we found that youth who used cannabis at age 18 had lower IQ in childhood, prior to cannabis initiation, and had lower IQ at age 18, but there was little evidence that cannabis use was associated with IQ decline from ages 12 to 18. Moreover, although cannabis use was associated with lower IQ and poorer executive functions at age 18, these associations were generally not apparent within pairs of twins from the same family, suggesting that family background factors explain why adolescents who use cannabis perform worse on IQ and executive function tests. Results were similar regardless of how we defined cannabis exposure—i.e. in terms of frequency of use or the more problematic outcome of dependence. Findings suggest that cannabis use does not cause IQ decline or impair executive

Table 4 Mean executive function scores at age 18 as a function of cannabis dependence at age 18.

	Full sample						*Discordant twins*					
	Before controlling for age 12 IQ				*After controlling for age 12 IQ*			*Before controlling for age 12 IQ*			*After controlling for age 12 IQ*	
Executive function test	*Not dep (n = 1902)*	*Dep (n = 84)*	*t*	*P*	*Not dep (n = 1902)*	*Dep (n = 84)*	*t*	*P*	*Not dep (n = 57)*	*Dep (n = 57)*	*t*	*P*	*Not dep (n = 57)*	*Dep (n = 57)*	*t*	*P*
RVP A Prime	**0.02**	**−0.22**	**−2.26**	**0.024**	0.01	−0.07	−0.85	0.39	−0.12	−0.21	−0.65	0.52	−0.13	−0.20	−0.49	0.62
RVP total false alarms[a]	0.00	0.02	0.21	0.83	0.00	−0.06	−0.57	0.57	0.30	0.07	−1.11	0.27	0.32	0.06	−1.23	0.22
SWM total errors[a]	−0.01	0.18	1.80	0.07	−0.01	0.04	0.54	0.59	0.25	0.15	−0.69	0.49	0.27	0.13	−0.97	0.34
SWM strategy[a]	**−0.01**	**0.21**	**2.40**	**0.017**	0.00	0.08	1.00	0.32	0.24	0.19	−0.36	0.72	0.26	0.17	−0.62	0.54
Spatial span forward	**0.02**	**−0.48**	**−4.57**	**< 0.001**	**0.01**	**−0.35**	**−3.60**	**< 0.001**	−0.18	−0.38	−1.30	0.20	−0.19	−0.37	−1.15	0.26
Spatial span reversed	**0.01**	**−0.33**	**−3.37**	**< 0.001**	**0.01**	**−0.20**	**−2.17**	**0.030**	−0.16	−0.26	−0.75	0.46	−0.17	−0.25	−0.59	0.56

Means and statistical tests are adjusted for sex. [a]Higher scores are worse. Not dep = not cannabis-dependent; Dep = cannabis-dependent; RVP = rapid visual processing; SWM = spatial working memory. For the full sample, *ns* ranged from 1895 to 1902 for the non-dependent group and 83–84 for the dependent group, as a few people from each group did not complete all executive function tests. For discordant twins, *ns* ranged from 56 to 57 twin pairs. Statistically significant differences are shown in bold type.

Table 5 Associations between frequency of cannabis use at age 18 and performance on executive function tests at age 18.

	Full sample (n = 1985)				*Twin pairs (n = 974 pairs)*			
	Before controlling for age 12 IQ		*After controlling for age 12 IQ*		*Before controlling for age 12 IQ*		*After controlling for age 12 IQ*	
Executive function test	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*
RVP A prime	**−0.10**	< 0.001	**−0.05**	**0.020**	0.00	0.96	−0.01	0.76
RVP total false alarms[a]	0.04	0.08	0.01	0.56	−0.01	0.77	−0.01	0.84
SWM total errors[a]	**0.10**	**< 0.001**	**0.06**	**0.005**	0.03	0.40	0.03	0.29
SWM strategy[a]	**0.10**	**< 0.001**	**0.06**	**< 0.001**	0.01	0.87	0.01	0.75
Spatial Span forward	**−0.13**	**< 0.001**	**−0.09**	**< 0.001**	−0.04	0.22	−0.05	0.14
Spatial Span reversed	**−0.13**	**< 0.001**	**−0.09**	**< 0.001**	**−0.07**	**0.036**	**−0.07**	**0.022**

Ns for the full sample ranged from 1978–1985; *n*s for twin pairs ranged from 967–974 twin pairs.; *n*s varied slightly, as not all adolescents completed each executive function test. Estimates are standardized beta coefficients, adjusted for sex. RVP = rapid visual processing; SWM = spatial working memory. [a]Higher scores are worse, so on these tests positive coefficients for the full sample indicate that more frequent cannabis use was associated with worse performance on executive functions tests, and positive coefficients for twin pairs indicate that the twin who used cannabis more frequently performed worse on the executive function test than their co-twin. For all other tests, lower scores are worse, so negative coefficients indicate that more frequent cannabis use was associated with worse test performance. Statistically significant associations are shown in bold type.

functions in adolescence after relatively short-term use, even when use reaches the level of dependence.

Our finding that lower IQ predates cannabis use contributes to already mixed findings in this area. Of the six cohort studies that obtained neuropsychological data prior to cannabis use initiation, four found no evidence that lower IQ predated cannabis use [8,12,15,17], and two found at least some evidence that lower IQ or poorer executive functions predated cannabis use [14,16] (Supporting information, Table S1). The reasons for this discrepancy are unclear. One potential explanation is that birth-cohort differences in structural factors (e.g. cannabis price, ease of access to cannabis) explain between-study differences in adolescent characteristics (e.g. SES, IQ) associated with cannabis use.

We found that adolescents with cannabis dependence showed similar changes in IQ from age 12 to 18 to adolescents without cannabis dependence. This lack of an association between cannabis dependence and IQ decline was apparent in the full sample of twins, a sample that approximates the general population, and in the subsample of twins discordant for cannabis dependence. Results were generally similar when we considered frequency of cannabis use as our exposure, with one exception. There was some evidence that more frequent cannabis use (considered on a continuum from no use to many uses per day) was associated with IQ decline in the full sample, but the effect size was small. Further, this association was not apparent within twin pairs in an analysis that inherently controlled for family background factors. Overall, there was limited evidence that cannabis use was associated with IQ decline during adolescence.

Our finding that adolescent cannabis use was not associated with IQ decline is broadly consistent with findings from several recent cohort studies [14–17], one of which used a co-twin control design [14], similar to the current study. Our study builds upon these previous studies by showing no effect of a more problematic level of cannabis use—cannabis dependence. Notably, accumulating findings of no association between cannabis use and IQ decline in adolescence do not conflict with our previous report from the Dunedin Study that persistent cannabis use is associated with IQ decline. In that study, adolescents who met criteria for cannabis dependence persistently through adulthood showed an eight-point IQ decline from ages 18–38, whereas adolescents who met criteria for cannabis dependence only at age 18 (and not thereafter) did not show IQ decline [8], similar to what we report here.

In the current study, adolescent cannabis use was associated with impaired executive functions, including impaired attention/vigilance and spatial working memory, in the full sample but not in the subsample of twin pairs. For example, twins with cannabis dependence performed no worse on executive function tests than their co-twins without cannabis dependence, suggesting that family background factors contribute to a spurious association between cannabis dependence and impaired executive functions in the general population. However, when we used frequency of cannabis use as our exposure, we found that more frequently cannabis using twins performed slightly worse on the Spatial Span Reversed test than their co-twins who used cannabis less frequently, suggesting a possible causal association between cannabis use and impairment on this one test. However, this finding might have been a false positive, particularly given previous inconsistent findings of an association between cannabis use and working memory [5].

This study has limitations. First, cannabis use was based on self-reports. Although this is typical for cohort studies, biological tests could have helped to detect under-

reporting. Second, although we tested associations between cannabis use and multiple executive function tests, we lacked tests of other neuropsychological functions, such as memory, which has been shown to be impaired in adolescent cannabis users [7,29]. Third, due to small sample sizes, discordant twin analyses may have been underpowered to detect effects. We note, however, that effect sizes were close to zero in many analyses. Fourth, although we were able to examine cannabis dependence, a level of problem use that has not been studied in previous cohorts of adolescents, it is possible that cannabis-related neuropsychological impairment becomes apparent only after more intense cannabis use (e.g. multiple uses per day), which was rare in our cohort at 1% prevalence. Very large cohort studies, such as the Adolescent Brain Cognitive Development study of 10 000 9–10 years followed for 10 years [30], are needed to obtain a sufficient number of adolescents from the general population who use cannabis intensely.

This study has a number of implications. First, to accurately interpret associations between cannabis use and neuropsychological impairment, it is important to test neuropsychological functions before cannabis initiation. Second, relatively short-term cannabis use in adolescence does not appear to cause IQ decline or impair executive functions, even when cannabis use reaches the level of dependence. Third, more research is needed to test the possibility that cannabis-related neuropsychological impairment develops gradually over time, such that obvious impairment is apparent only in older, longer-term persistent users.

Declaration of interests

None.

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Supporting Information

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

Table S1 Cohort studies of associations between cannabis use and neuropsychological functioning. Studies are organized by length of follow-up and date.

Table S2 Description of executive function measures from the Cambridge Neuropsychological Test Automated Battery (CANTAB).

Table S3 Mean pro-rated intelligence quotient (IQ) scores at ages 5, 12 and 18 and average within-person IQ change from ages 12 to 18 as a function of cannabis dependence at age 18. These analyses exclude the 19 participants who had used cannabis at age 12.

Table S4 Mean information subtest scores at ages 12 and 18 and average within-person subtest score change from ages 12 to 18 as a function of cannabis dependence at age 18.

Table S5 Mean matrix reasoning subtest scores at ages 12 and 18 and average within-person subtest score change from ages 12 to 18 as a function of cannabis dependence at age 18.

Table S6 Mean pro-rated intelligence quotient (IQ) scores at ages 5, 12 and 18 and IQ subtest scores at ages 12 and 18. Means are shown for adolescents who did not use cannabis in the past year at age 18 and adolescents who used cannabis on a weekly or greater basis at age 18. Means for IQ change represent average within-individual IQ change.

Table S7 Mean executive function scores for adolescents who did not use cannabis in the past year at age 18 and adolescents who used cannabis weekly or more in the past year at age 18.