

Supplemental Table 1. Cohort studies of associations between cannabis use and neuropsychological functioning. Studies are organized by length of follow-up and date.

Study	Sample Size	Length of Follow-Up	Baseline Age or Age Range	Follow-Up Age or Age Range	Level of Cannabis Exposure	Same Tests Across Time?	Neuropsychological Domains	Findings: Neuropsychological Differences Before Cannabis Initiation	Findings: Cannabis-Related Change in Neuropsychological Function
Meier et al. 2012 (8)	874	25 y	7-13	38	28% never used cannabis; 58% used cannabis but never regularly (at least 4 days per week); 5% used regularly at one point in their lives; 9% were persistent regular users (used regularly at two or more points in their lives). Of those who had used cannabis, 55% never diagnosed with cannabis dependence; 9% diagnosed at one point in their lives; and 8% diagnosed	Partially	IQ, executive functions, memory, processing speed, perceptual reasoning, verbal comprehension	There was no evidence that neuropsychological impairment was apparent prior to cannabis use initiation.	Persistent cannabis use from age 18-38 was associated with IQ decline from age 7-13 to age 38, even after accounting for a variety of covariates. Persistent cannabis use from age 18-38 was also associated with poorer executive functions, memory, processing speed, perceptual reasoning, and verbal comprehension at age 38, even after accounting for age 7-13 IQ.

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					with cannabis dependence persistently.				
Auer et al. 2016 (9)	3,385	25 y	18-30	43-55	16% never used cannabis; 44% had used cannabis daily for <0.5 years; 24% had used cannabis daily for 0.5-2 years; 7% had used cannabis daily for 2-5 years; 9% had used cannabis daily for >5 years.	No	Verbal memory, processing speed, executive functions	This study could not test whether neuropsychological impairment was apparent prior to cannabis use, as participants had already initiated cannabis use at the time of the first neuropsychological assessment.	Cumulative lifetime cannabis use was associated with worse verbal memory, processing speed, and executive function in adulthood. After accounting for earlier cognitive functioning and a variety of covariates, cumulative cannabis use was associated with worse verbal memory in adulthood.
Lyketzos et al. 1999 (10)	1,318	12 y	18-64	30-76	61% had never used cannabis (non-users); 28% had used cannabis but never used it daily or more often for over 2 weeks (light	Yes	Mini-Mental Status Exam	This study could not test whether neuropsychological impairment was apparent prior to cannabis use, as participants had already initiated cannabis use at the time of the first neuropsychological	Light and heavy cannabis users did not show greater decline on the mini-mental status exam than non-users.

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					users); 11% had used cannabis daily or more often for over 2 weeks (heavy users).			assessment.	
Fried et al. 2005 (11)	113	~8 y	9-12	17-21	52% of the sample had never used cannabis; 17% of the sample were current light users (<5 joints per week) and had consumed a total of M=122 joints; 17% of the sample were current heavy users (>5 joints per week) and had consumed a total of M=1884	Partially	IQ, processing speed, vocabulary, immediate and delayed memory, working memory, sustained attention, abstract reasoning	This study did not report on whether neuropsychological impairment was apparent prior to cannabis use initiation, although a prior report based on this cohort found no evidence that cannabis users had lower IQ prior to cannabis use initiation (12).	Current heavy cannabis users performed worse than non-users on IQ, processing speed, and immediate and delayed memory in young adulthood, even after accounting for pre-drug performance on the relevant cognitive test and a variety of covariates. Current light users and former cannabis users did not perform worse than non-users on any test.

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					joints; and 14% were former users (no regular use for 3+ months and <3 joints in the past 2 months at the age 17-21 assessment) and had consumed a total of M=2203 joints.				
Tait et al. 2011 (13)	1,499	8 y	20-24	28-32	28% of the sample had never used; 44% were classified as always former users (had used cannabis prior to baseline but not thereafter); 15% were classified as	Yes	Immediate and delayed recall, short-term memory, verbal ability, processing speed	This study could not test whether neuropsychological impairment was apparent prior to cannabis use, as participants had already initiated cannabis use at the time of the first neuropsychological assessment.	Analyses compared change in neuropsychological functions for the following groups: former heavy cannabis users vs. remain heavy cannabis users; former light users vs. remain light users; never users vs. former heavy users; never users vs. former light users; and never users versus always former users. After adjustment for covariates, the only statistically significant findings were as

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					former light (monthly or less) users (light use prior to the last wave of data collection and no use at the last wave); 4% were classified as former heavy (at least weekly) users; 5% were classified as remain light users; and 4% were classified as remain heavy users.				follows: Former heavy cannabis users showed improvement in immediate recall relative to heavy users.
Jackson et al. 2016 (14)	Sample 1: 789; Sample 2: 2,277	10 y; ~7 y	Sample 1: 9-10; Sample 2: 11-12	Sample 1: 19-20; Sample 2: 17-19	Sample 1: 60% of the sample had used cannabis; 30% had used cannabis 30+ times; 12.5% had used cannabis daily	Yes	IQ	There was mixed evidence that cannabis users had lower IQ prior to cannabis use initiation.	Cannabis use (defined as ever use) was associated with decline in Vocabulary and Information subtests, even after accounting for a variety of sociodemographic covariates. Associations were no longer apparent in sample 2 after accounting for other substance

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					for 6-12 months; Sample 2: 36% of the sample had used cannabis; 13% had used cannabis 30+ times; 8% had used cannabis daily for 6-12 months.				use. There was no evidence that cannabis use was associated with decline in Similarities, Block Design, Matrix Reasoning, and Picture Arrangement subtests. Use of cannabis 30+ times and daily cannabis use for 6-12 months were also not associated with IQ decline among users. Moreover, among twins discordant for cannabis use, cannabis use was not associated with IQ decline on any subtest.
Mokrysz et al. 2016 (15)	2,235	7 y	8	15	77% had never used cannabis; 11% had used cannabis <5 times; 6% had used cannabis 5-19 times; 3% has used cannabis 20-49 times; 3% had used cannabis 50+ times.	No	IQ	There was no evidence that cannabis users had lower IQ prior to cannabis use initiation.	Cumulative cannabis use by age 15 was associated with lower IQ at age 15, after controlling for age 8 IQ. This association was no longer apparent after controlling for covariates.

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Castellanos-Ryan et al. 2016 (16)	294	7 y	13	20	Average cannabis use ranged from no use in the past year at age 14 to between 3-5 and 6-9 uses in the past year at age 17.	Partially	Verbal IQ, short-term memory, executive functions	Higher verbal IQ at age 13 was associated with an earlier age of onset of cannabis use and greater increases in frequency of cannabis use from ages 14-17. Poorer short-term memory and working memory at age 14 were associated with an earlier age of onset of cannabis use.	Greater frequency of cannabis use at age 14 was associated with decline in one of several tests of executive functions, even after controlling for a variety of covariates. Greater increases in cannabis use from age 14-17 were associated with decline in verbal IQ and one of several tests of executive functions, with the association with verbal IQ becoming non-significant after controlling for covariates.
Boccio & Beaver, 2017 (17)	Varied from 373 to 6,584	6 y	12-21 (Wave I)	18-26 (Wave III)	No participants had used cannabis at Wave I. 12% had used cannabis in the past year at Wave II and 70% had used cannabis in the past year at Wave III. Among cannabis	Yes	Verbal IQ	There was no evidence that cannabis users had lower IQ prior to initiation.	Dichotomous measures of cannabis use (e.g. past-year cannabis use vs. no use) at Waves II and III were each associated with verbal IQ decline from Waves I-III. However, number of cannabis use days in the past month at Waves II and III were not associated with verbal IQ decline from Waves I-III. There was also inconsistent evidence of cannabis-related verbal IQ decline based on cannabis use data combined across Waves II

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					users, the average number of days of cannabis use in the past-month at Waves II and III was 3 and 7 days, respectively.				

Note. This table includes only those cohort studies with (a) adolescents or young-adults in the sample, (b) neuropsychological testing at two or more time points, and (c) follow-up of at least 1 year. There was one longitudinal case-control study of adolescents with and without a diagnosis of substance use disorder, and it found that cumulative cannabis use from ~ age 16 to 24 was associated with poorer attention in young adulthood, even after controlling for baseline attention and other covariates. However, cannabis use was not associated with poorer neuropsychological function in other domains (language, visuospatial abilities, verbal learning and memory, and executive functions) (18).

Supplemental Table 2. Description of executive function measures from the Cambridge Neuropsychological Test Automated Battery (CANTAB).

Test	Description
Rapid Visual Information Processing (RVP)	This is a test of sustained attention and vigilance. A white box appears in the center of the computer screen, inside which digits from 2 to 9 appear in a pseudo-random order at the rate of 100 digits per minute. Subjects are requested to detect target sequences of digits (for example, 2-4-6, 3-5-7, 4-6-8) and to register responses using the press pad. At the most difficult level, the participant scans simultaneously for two target sequences.
RVP A-prime	This is a signal detection measure of sensitivity to the target, regardless of response tendency (range 0.00 to 1.00; bad to good) and is a measure of how good the subject is at detecting target sequences using "Probability of Hit" and "Probability of False Alarm." Higher scores are better.
RVP Total False Alarms	This measure records impulsive jumping to respond too soon before the correct target digit sequence is complete. Because relatively few participants made numerous false alarms, this measure is categorical, coded 0=none, 1=1 false alarm, 2=2 or more false alarms. Higher scores are worse.
Spatial Working Memory Test	The test begins with a number of colored squares (boxes) being shown on the screen. The aim of this test is that, by touching the boxes and using a process of elimination, the participant should find one blue 'token' in each of a number of boxes and use them to fill up an empty column on the right hand side of the screen. The number of boxes is gradually increased, until it is necessary to search a total of eight boxes. The color and position of the boxes used are changed from trial to trial to discourage the use of stereotyped search strategies.
Spatial Working Memory Total Errors	This measures assesses capacity to hold information about spatial location in active memory while searching for information. At the most difficult level, participants memorize 10 locations in one problem. Higher scores are worse.

Spatial Working Memory Strategy	This measure records trials on which the participant applied a problem-solving strategy by opening boxes in a systematic sequence. Higher scores are worse (more non-strategic trials).
Spatial Span	This measure is the visual non-verbal equivalent of the oral-auditory Digit Span test and measures working memory. At the most difficult level, participants memorize a sequence of 9 colored stimuli.
Spatial Span Forward	This measure is the visual non-verbal equivalent of the oral-auditory Digit Span forward test. Higher scores are better.
Spatial Span Reversed	This measure is the visual non-verbal equivalent of the oral-auditory Digit Span backward test. Higher scores are better.

Supplemental Table 3. Mean pro-rated IQ scores at ages 5, 12, and 18 and average within-person IQ change from age 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.

	Non-Dependent Adolescents (N=1889)	Cannabis Dependent Adolescents (N=81)	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
Full sample								
Age 5 IQ	100.40	95.25	-5.15	-2.80	.005	-	-	-
Age 12 IQ	100.61	95.20	-5.41	-2.94	.003	-2.66	-1.66	.10
Age 18 IQ	100.53	93.57	-6.96	-4.95	<.001	-4.86	-3.58	<.001
IQ Change From Age 12-18 ^b	-0.08	-1.63	-1.55	-1.11	.27	-1.83	-1.31	.19
	Non-Dependent Twins (N=54)	Cannabis Dependent Co-Twin (N=54)	Difference Between Discordant Twin Pairs ^a	t	p	Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a	t	p
Discordant Twins								
Age 5 IQ	93.76	94.28	0.52	0.25	.80	-	-	-
Age 12 IQ	95.26	94.24	-1.02	-0.55	.58	-1.23	-0.64	.52
Age 18 IQ	94.58	93.39	-1.19	-0.64	.52	-1.40	-0.79	.45
IQ Change From Age 12-18 ^b	-0.68	-0.85	-0.17	-0.08	.94	-0.18	-0.08	.94

Note. 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 1.55 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 age 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.

Supplemental Table 4. Mean Information subtest scores at ages 12 and 18 and average within-person subtest score change from age 12 to 18 as a function of cannabis dependence at age 18.

	Non-Dependent Adolescents (N=1905)	Cannabis Dependent Adolescents (N=84)	Difference Between Non- Dependent and Cannabis Dependent Adolescents ^a			Difference Between Non-Dependent and Cannabis Dependent Adolescents After Controlling for Age 5 IQ ^a		
				t	p		t	p
Full sample								
Age 12 Information Subtest	10.10	9.01	-1.09	-2.91	.004	-0.54	-1.70	.09
Age 18 Information Subtest	10.10	8.55	-1.55	-5.58	<.001	-1.04	-4.11	<.001
Change in Subtest Score ^b	0.00	-0.46	-0.46	-1.49	.14	-0.49	-1.64	.10
	Non-Dependent Twins (N=57)	Cannabis Dependent Co-Twin (N=57)	Difference Between Discordant Twin Pairs ^a			Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a		
Discordant Twins				t	p		t	p
Age 12 Information Subtest	8.99	8.94	-0.05	-0.14	.89	-0.11	-0.31	.76
Age 18 Information Subtest	9.12	8.77	-0.35	-1.21	.23	-0.40	-1.35	.18
Change in Subtest Score ^b	0.13	-0.17	-0.30	-0.88	.38	-0.29	-0.82	.41

Note. 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. b. Change in the Information subtest score was represented as a change score (age 18 Information – age 12 Information). We focused on subtest decline from age 12 to 18 because the age 12 and age 18 IQ tests were based on the same two subtests (Information and Matrix Reasoning) whereas the age 5 IQ test was 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.

Supplemental Table 5. Mean Matrix Reasoning subtest scores at ages 12 and 18 and average within-person subtest score change from age 12 to 18 as a function of cannabis dependence at age 18.

	Non-Dependent Adolescents (N=1905)	Cannabis Dependent Adolescents (N=84)	Difference Between Non-Dependent and Cannabis Dependent Adolescents ^a			Difference Between Non-Dependent and Cannabis Dependent Adolescents After Controlling for Age 5 IQ ^a		
			t	p		t	p	
Full sample								
Age 12 Matrix Reasoning Subtest	10.10	9.29	-0.81	-2.44	.015	-0.39	-1.25	.21
Age 18 Matrix Reasoning Subtest	10.07	9.25	-0.82	-2.48	.014	-0.51	-1.60	.11
Change in Subtest Score ^b	-0.03	-0.04	-0.01	-0.04	.97	-0.11	-0.34	.73
Discordant Twins	Non-Dependent Twins (N=57)	Cannabis Dependent Co-Twin (N=57)	Difference Between Discordant Twin Pairs ^a			Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a		
			t	p		t	p	
Age 12 Matrix Reasoning Subtest	9.45	9.02	-0.43	-0.96	.34	-0.47	-1.04	.30
Age 18 Matrix Reasoning Subtest	9.00	8.90	-0.10	-0.20	.84	-0.16	-0.31	.76
Change in Subtest Score ^b	-0.45	-0.12	0.33	0.58	.56	0.32	0.55	.58

Note. 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. b. Change in the Matrix Reasoning subtest score was represented as a change score (age 18 Information – age 12 Information). We focused on subtest decline from age 12 to 18 because the age 12 and age 18 IQ tests were based on the same two subtests (Information and Matrix Reasoning) whereas the age 5 IQ test was 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.

			for Age 5 IQ ^a					
Age 12 IQ	10.16	8.76	-1.40	-5.49	<.001	-0.96	-4.34	<.001
Age 18 IQ	10.24	8.44	-1.80	-7.79	<.001	-1.40	-6.72	<.001
IQ Change From Age 12-18 ^b	0.08	-0.32	-0.40	-1.95	.05	-0.44	-2.09	.037
			Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a					
Discordant Twins	Non-User (N=23)	Weekly+ User (N=23)	Difference Between Discordant Twin Pairs ^a	t	p		t	p
Age 12 IQ	8.76	10.10	1.34	1.91	.06	1.31	1.90	.06
Age 18 IQ	9.15	10.24	1.09	1.48	.15	1.05	1.47	.15
IQ Change From Age 12-18 ^b	0.39	0.14	-0.25	-0.38	.70	-0.25	-0.38	.70

Matrix Reasoning Subtest

			Difference Between Non-Users and Weekly+ Users After Controlling for Age 5 IQ ^a					
			Difference Between Non-Users and Weekly+ Users After Controlling for Age 5 IQ ^a					
Full Sample	Non-User (N=1242)	Weekly+ User (N=132)	Difference Between Non-Users and Weekly+ Users ^a	t	p		t	p
Age 12 IQ	10.15	9.33	-0.82	-3.32	<.001	-0.50	-2.23	.026
Age 18 IQ	10.12	9.33	-0.79	-2.75	.006	-0.55	-2.00	.046
IQ Change From Age 12-18 ^b	-0.03	0.00	0.03	0.11	.91	-0.05	-0.17	.87
			Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a					
Discordant Twins	Non-User (N=23)	Weekly+ User (N=23)	Difference Between Discordant Twin Pairs ^a	t	p		t	p
Age 12 IQ	9.37	10.34	0.97	1.28	.21	0.91	1.33	.19

Age 18 IQ	9.10	9.06	-0.04	-0.04	.97	-0.13	-0.15	.88
IQ Change From Age 12-18 ^b	-0.27	-1.28	-1.01	-1.16	.25	-1.04	-1.20	.24

Note. Means and statistical tests are adjusted for sex. a. Negative scores indicate that adolescents who used cannabis at least weekly showed lower IQ/greater IQ decline than adolescents who did not use cannabis in the past year. b. IQ change was represented as a change score (age 18 IQ – age 12 IQ). We focused on IQ decline from age 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.

Supplemental Table 7. 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.

Executive Functions	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			
	Non-User (N=1,242)	Weekly User (N=132)	t	p	Non-User (N=1,242)	Weekly User (N=132)	t	p	Non-User (N=23)	Weekly User (N=23)	t	p	Non-User (N=23)	Weekly User (N=23)	t	p
RVP A Prime	0.06	-0.28	-3.85	<.001	0.04	-0.11	-1.74	.08	0.02	0.12	0.37	.71	0.08	0.06	-0.08	.94
RVP Total False Alarms ^a	-0.03	0.03	0.71	.48	-0.02	-0.07	-0.55	.58	-0.05	-0.31	-0.98	.34	-0.05	-0.30	-0.93	.36
SWM Total Errors ^a	-0.07	0.29	3.91	<.001	-0.05	0.14	2.33	.020	0.02	-0.12	-0.79	.44	-0.05	-0.05	-0.04	.97
SWM Strategy ^a	-0.05	0.28	3.98	<.001	-0.03	0.14	2.19	.029	0.14	0.08	-0.24	.81	0.04	0.18	0.55	.59
Spatial Span Forward	0.06	-0.48	-5.95	<.001	0.04	-0.33	-4.43	<.001	-0.10	-0.07	0.14	.89	0.00	-0.16	-0.75	.46
Spatial Span Reversed	0.07	-0.42	-5.49	<.001	0.05	-0.27	-4.01	<.001	0.14	-0.29	-1.80	.09	0.14	-0.29	-1.91	.07

Note. Means and statistical tests are adjusted for sex. Non-user=did not use cannabis in the past year at age 18. Weekly User=used cannabis weekly or more in the past year at age 18. RVP=Rapid Visual Processing. SWM=Spatial Working Memory. For the full sample, Ns ranged from 1238-1242 for the non-user group and 130-132 for the user group, as a few people from each group did not complete all executive function tests. For discordant twins, N=23 twin pairs. a. Higher scores are worse. Statistically significant differences are shown in bold.