American Journal of Epidemiology
Vol. 175, No. 3
DOI: 10.1093/aje/kwr315
Advance Access publication:
December 21, 2011

Original Contribution

Is Illicit Drug Use Harmful to Cognitive Functioning in the Midadult Years? A Cohort-based Investigation

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Initially submitted June 2, 2011; accepted for publication August 15, 2011.

From March to July of 2011, the authors investigated the prospective association between illicit drug use and cognitive functioning during the midadult years. A total of 8,992 participants who were surveyed at 42 years of age in the National Child Development Study (1999–2000) were included. The authors analyzed data on 3 cognitive functioning measures (memory index, executive functioning index, and overall cognitive index) when the participants were 50 years of age (2008–2009). Illicit drug use at 42 years of age was based on self-reported current or past use of any of 12 illicit drugs. Multivariable regression analyses were performed to estimate the association between different illicit drug use measures at 42 years of age and cognitive functioning at 50 years of age. A positive association was observed between ever (past or current) illicit drug use and cognitive functioning ($\beta = 0.62$, $P < 0.001$), although the effect size was small. Even though there was no clear evidence against the null hypothesis, drug dependence ($\beta = -0.27$, $P = 0.58$) and long-term illicit drug use ($\beta = -0.04$, $P = 0.87$) tended to be negatively associated with cognitive functioning. At the population level, it does not appear that current illicit drug use is associated with impaired cognitive functioning in early middle age. However, the authors cannot exclude the possibility that some individuals and groups, such as those with heavier or more prolonged use, could be harmed.

cognition; cohort studies; memory; prospective studies; street drugs

Abbreviation: OR, odds ratio.

In the context of an aging world population, the preservation of cognitive functioning represents a major public health concern. In past decades, there has been increasing interest from researchers and health professionals in understanding risk factors and identifying protective factors for cognitive decline (1). Several risk factors for cognitive decline have been proposed, including diabetes, hypertension, stroke, alcohol abuse, smoking, and hypercholesterolemia (2–5). It has also been suggested that illicit drug use might be associated with impaired cognitive functioning; however, this relation has not been thoroughly investigated, and the evidence is rather inconclusive. Some investigators have found that long-term illicit drug use may be associated with impaired short-term and working memory (6, 7), word fluency (8), attention span (9), and cognitive flexibility (10). In other studies, no association between illicit drug use and executive functioning and working memory was found (11–14). Comparison between the different studies is complicated by methodological differences in sampling methods, the types of drugs studied, cognitive outcome measures, and length of follow-up. Additionally, most studies were focused on adolescence and young adulthood, resulting in a dearth of information about the potential consequences of adult illicit drug use for long-term cognitive functioning.

One of the main reasons for the dearth of longitudinal studies of cognitive functioning is the cost of these studies in terms of both resources and time. An alternative solution is to examine existing cohorts in which cognitive functioning and illicit drug use have been recorded over time. The United Kingdom-based National Child Development Study has followed 17,415 people born in the United Kingdom between March 3 and March 9, 1958. To date, there have been 8 surveys of all members of the birth cohort at ages 7, 11, 16, 23, 33, 42, 46, and 50 years, and in the latest sweep,

Table 1. Illicit Drug Use at 42 Years of Age in the Study Population, National Child Development Study, 1999–2009

Drug	Currently Using		Ever Used		Never Used	
	No.	%	No.	%	No.	%
Cannabis	736	6	2,674	24	7,863	70
Ecstasy	67	1	214	2	10,991	97
Cocaine	124	1	417	4	10,731	95
Crack cocaine	12	0	55	1	11,206	99
Heroin	15	0	113	1	11,145	99
Amphetamines	92	1	840	7	10,341	92
Hallucinogenic mushrooms	34	0	693	6	10,545	94
LSD	16	0	527	5	10,730	95
Temazepam	100	1	305	3	10,867	96
Methadone	13	0	60	1	11,200	99
Amyl nitrates (poppers)	53	1	502	4	10,717	95
Ketamine	9	0	29	0	11,234	100
Other drugs[a]	0	0	243	2	11,030	98

Abbreviation: LSD, lysergic acid diethylamide.
[a] The question about other drugs asked participants whether they had tried any other illegal drug.

several measures of memory and executive functioning were included to assess participants' cognitive functioning. At age 42 years, participants were asked several questions about their past and current illicit drug use. In the present study, we aimed to use data from these 2 survey rounds of the National Child Development Study cohort to explore the long-term impact of illicit drug use on cognitive functioning.

MATERIALS AND METHODS

Study data

For the 1999–2000 survey of the National Child Development Study (which occurred when participants were 42 years of age), information on illicit drug use was collected via interview together with self-completion of the survey using computer-assisted personal interviewing. At 42 years of age, 11,419 of the original participants were surveyed, representing a response rate of 75% of the eligible target population. Inability to contact a participant (moved and new address not obtained) represented the main reason for loss of participants from the initial sample (13%). Data for cognitive measures were collected approximately 8 years later in 2008–2009, when participants were 50 years of age.

Memory

Participants were asked to learn 10 unrelated words and perform 2 recall tasks, one immediate and one delayed. The delayed task was performed after the executive functioning tests were performed. Immediate and delayed recall tests have been used in previous studies and across different ethnic groups (15, 16). Participants' performance on the 2 memory tests was given an equal weighting toward an overall memory index.

Executive functioning

The verbal fluency task involved the participants naming as many different animals as possible within 1 minute. The reliability and validity of the animal-naming test has been well documented (17). A letter-cancellation test was used to measure individuals' attention spans, mental speeds, and visual scanning abilities. The participants were given a page of random letters of the alphabet and asked to cross out as many P's and W's as possible within 1 minute. Independent scores were calculated for speed and accuracy. The speed score was measured as the total number of letters scanned, and the accuracy score was measured as the number of P's and W's that were scanned but missed. The 2 scores were likely to be related, as scanning a greater number of letters would increase the number of letters that could potentially be missed. Participants' performances on animal-naming, speed, and accuracy tasks were given equal weighting toward an overall executive functioning index.

Cognitive index

A continuous measure of overall cognitive functioning was derived by combining participants' scores on the overall memory and executive functioning indexes. Each test received equal weighting toward the combined cognitive index. These tests were similar to those used in other population and community surveys (18, 19). The development of these variables was based on the work of Nunn et al. (20).

Illicit drug use

Information on illicit drug use at 42 years of age was available for 99% of the participants and was collected from responses to a set of questions asking whether the respondent had ever used or was still using any of the 12 different illicit

Table 2. Predictors of Illicit Drug Use at 42 Years of Age in the Study Population, National Child Development Study, 1999–2009

Variable	Total No. of Participants	Current Drug Use[a]				Ever Drug Use[b]			
		Frequency	%	OR	95% CI	Frequency	%	OR	95% CI
Gender									
Male	5,519	562	10	1	Referent	2,224	40		Referent
Female	5,734	313	5	0.52	0.44, 0.61	1,499	26	0.52	0.47, 0.57
Marital status									
Married	7,951	377	5		Referent	2,208	28		Referent
Single	3,299	498	15	2.55	2.18, 2.98	1,515	46	1.95	1.77, 2.16
Social class									
High	4,712	343	7		Referent	1,723	37		Referent
Middle	4,485	350	8	0.99	0.82, 1.20	1,390	31	0.86	0.77, 0.96
Low	1,708	123	7	0.86	0.67, 1.11	475	28	0.72	0.66, 0.90
Qualification level									
No qualifications	2,211	218	10		Referent	701	32		Referent
CSE 2–5	1,691	106	6	0.85	0.66, 1.11	465	28	1.05	0.90, 1.23
O-level certificate	4,077	284	7	1.12	0.91, 1.38	1,249	31	1.45	1.27, 1.65
A-level certificate	1,435	104	7	1.35	1.02, 1.80	483	34	1.90	1.60, 2.25
College degree	1,838	163	9	1.87	1.43, 2.46	825	45	3.31	2.80, 3.92
Health status in the previous year									
Good	10,128	709	7		Referent	3,281	32		Referent
Poor	1,125	166	15	1.54	1.21, 1.96	442	39	1.12	0.95, 1.32
Long-standing illness									
No	9,757	683	7		Referent	3,150	32		Referent
Yes	1,492	191	13	1.26	1.00, 1.57	571	38	1.12	0.97, 1.30
Depressive symptoms									
No	9,268	616	7		Referent	2,927	32		Referent
Yes	1,985	259	13	1.42	1.17, 1.74	796	40	1.30	1.14, 1.48

Table continues

drugs listed in Table 1. The response options to these items were never, yes (not in the last 12 months), and yes (in the last 12 months).

Participants were grouped into those who had ever taken at least 1 of the 12 illicit drugs mentioned and those who had never taken illicit drugs. Participants were also classified according to whether they had tried any of the 12 illicit drugs over the preceding 12 months, which was referred to as current use. A third measure was used to assess the length of illicit drug use, and based on that measure, we grouped participants into 3 categories: those who were currently using and had in the past used any illicit drug, those who had used any illicit drug in the past but were not using at present, and those who had never used any drug.

The potential for harm from current and ever usage was classified as high, intermediate, and lower. High-risk drugs include heroin, cocaine, crack cocaine, ecstasy, hallucinogenic mushrooms, methadone, and LSD (lysergic acid diethylamide). Intermediate-risk drugs include amphetamines and cannabis. Lower-risk drugs, which were considered to have the least capacity to harm, include ketamine, temazine, and amyl nitrates (poppers). For the present study, other drugs were classified as lower risk. This classification was based on the controlled drugs classes set out in the United Kingdom Misuse of Dugs Act (1971) and the US Controlled Substances Act of 1970, although cannabis was rated as high risk in the latter.

Data on illicit drug use were also obtained from answers to 2 questions about whether participants had seen a specialist for illicit drug dependency. Because of the small number ($n = 51$) of participants who reported dependence on an illicit drug on the survey at 42 years of age, this information was completed with data from previous surveys (at ages 16, 23, and 33 years) that questioned the participants about whether they had ever had a drug-dependency problem.

Covariates

Social class was measured by using the Registrar General's scale (21), and this measure classified participants into high (classes I and II of the Registrar's scale), medium (class III of the Registrar's scale), or low (classes IV and V of the Registrar's scale) social class. Educational level was based on participants' highest educational qualifications obtained: no qualification, Certificate of Secondary Education, O-level

Table 2. Continued

Variable	Total No. of Participants	Current Drug Use[a]				Ever Drug Use[b]			
		Frequency	%	OR	95% CI	Frequency	%	OR	95% CI
Physical exercise									
Weekly	7,382	531	7		Referent	2,494	40		Referent
Less than weekly	2,897	250	9	1.44	1.10, 1.90	877	30	1.35	1.14, 1.61
None at all	972	94	10	1.07	0.90, 1.28	351	36	1.35	1.21, 1.51
Smoking status									
Never smoker	5,016	148	3		Referent	870	17		Referent
Ex-smoker	3,011	151	5	1.79	1.41, 2.27	1,141	38	3.66	3.26, 4.09
Occasional smoker	484	89	18	6.21	4.61, 8.36	265	55	6.09	4.94, 7.49
<10 cigarettes/day	794	134	17	6.23	4.79, 8.11	398	50	6.40	5.39, 7.61
11–20 cigarettes/day	1,595	257	16	5.37	4.27, 6.75	760	48	5.65	4.42, 6.49
>20 cigarettes/day	512	92	18	4.33	3.17, 5.92	283	55	6.26	5.05, 7.74
Drinking problem (CAGE score ≥2)									
No	9,652	603	6		Referent	2,878	30		Referent
Yes	1,443	266	18	1.96	1.64, 2.33	823	57	2.03	1.79, 2.30
Criminal convictions									
No	10,737	761	7		Referent	3,439	32		Referent
Yes	515	114	22	1.89	1.47, 2.44	283	55	1.58	1.29, 1.94
Self-reported body mass index[c]									
Normal	3,781	349	9		Referent	1,275	34		Referent
Underweight	518	71	14	0.90	0.66, 1.22	206	40	0.89	0.72, 1.11
Overweight	5,440	373	7	0.78	0.66, 0.92	1,768	33	0.96	0.86, 1.06
Obese	1,603	80	5	0.53	0.40, 0.69	470	29	0.91	0.79, 1.05
Life satisfaction scale	11,249	875	8	1.07	1.03, 1.12	3,724	33	1.08	1.05, 1.11
Nagelkerke's R^2					22				26

Abbreviations: A-level, advanced level; CI, confidence interval; CSE, Certificate of Secondary Education; O-level, ordinary level; OR, odds ratio.
[a] Current drug use referred to any illicit drug use during the previous year at 42 years of age.
[b] Ever drug use referred to any illicit drug use up to and including the age of 42 years.
[c] Weight (kg)/height $(m)^2$.

certificate (ordinary), A-level certificate (advanced), and college degree or higher. The information on partnership status was used to group participants into persons who were married or living with a partner and persons who were single. Participants were classified into 6 categories according to their smoking behavior: never smoker, ex-smoker, occasional smoker, and smoker, which was further divided into categories of <10 cigarettes per day, 10–20 cigarettes per day, and >20 cigarettes per day. Alcohol drinking behavior was used to group participants into those who had a CAGE score (22) of 2 or more and those who had a score of less than 2. The CAGE scale is based on 4 questions that ask about a participant's alcohol-related habits (i.e., ''had to have a drink first thing in the morning to steady hands''). Based on participants' physical exercise habits, 3 groups were created: no physical exercise, less than weekly/occasional exercise, and weekly physical exercise. Participants were grouped by category of criminal convictions as persons who reported at least 1 court conviction since the previous survey and those who had never been convicted in a court of law. According to participants' body mass index (weight in kilograms divided by height in meters squared) at 42 years of age, participants were grouped into 4 categories: underweight (<18.5), normal (18.5–24.9), overweight (25–29.9), and obese (≥30). The Malaise Inventory (20) was used to group participants into persons with depressive symptoms (a score ≥7) and those with no depressive symptoms (a score <7). Participants' self-efficacy was assessed by using a scale comprising 3 dichotomous questions that focused on how much participants felt in control of their lives. Two categories were developed: poor self-efficacy skills (scores ≥5) and good self-efficacy skills (scores <5). A continuous life-dissatisfaction measure was included based on a single question that asked participants to report how satisfied they were with their life in general (scores ranged from 0 to 8). Two global physical health measures were used: long-standing illness (coded as 1 if a long-standing illness was reported and 0 otherwise) and physical health status (coded as 1 if the participant reported poor health status

over the previous year and 0 if good health status was reported). A gender factor was constructed; women were assigned a value of 1 and men were assigned a value of 0. Participants were classified by ethnicity as being of white origin, black origin, or Asian origin.

Statistical analysis

Because the most disadvantaged participants were likely to be missing from surveys conducted when they were adults (23), restricting the study sample to those cohort members for whom we had complete information on all factors could have resulted in sampling bias. Following the method of White and Thompson (24), we included an indicator variable for missing data in categories. Specifically, a dummy variable was created to indicate missing data for each relevant variable and was set to 1 for respondents for whom we were missing the data and 0 for participants for whom the data were present.

Logistic regression models were fitted to estimate predictors of current use and ever use of illicit drugs at 42 years of age, as well as high-risk, intermediate-risk, and lower-risk drug use. Multivariable linear regression models were fitted to estimate the association of illicit drug use at age 42 years with cognitive functioning at age 50 years. All predictors were treated as categorical, with an explicitly defined category for missing data. Only life dissatisfaction was included as a continuous variable. The most advantaged group represented the reference category for all predictors in both linear and logistic regressions. These predictors were social class, highest qualification level, poor physical health, long-standing illness, gender, ethnicity, smoking, drinking, body mass index, life dissatisfaction, low self-efficacy, physical exercise routine, partnership status, and depression. All predictors were entered into the equation at the same step. All analyses were carried out using SPSS, version 14 (SPSS, Inc., Chicago, Illinois).

RESULTS

Of the 11,419 persons who participated in the survey at 42 years of age, 11,253 (99%) of them reported information on illicit drug use in the survey. A total of 8,992 (80%) who reported information on illicit drug use at age 42 years took part in the survey at age 50 years. There were 8,871 (78%) participants who responded to the memory questions and 8,756 (77%) who answered the questions on executive functioning. In a logistic regression model (data not shown), illicit drug use among participants at 42 years of age was not associated with cognitive functioning nonresponse at 50 years of age (odds ratio (OR) = 0.93, 95% confidence interval: 0.79, 1.11).

Table 2 shows data on the distribution of illicit drug use. Illicit drug use was greater among males and among persons who were single at the time of the survey, reported poor health status (including long-standing illness), reported depressive symptoms, and had a drinking problem or previous criminal conviction. These associations were similar for current use and ever use. Among ever drug users, illicit drug use tended to be greater in respondents from higher social classes and persons who reported higher educational qualifications (45% among participants with degree-level qualifications vs. 32% among participants with no qualifications). Compared with having no educational qualifications, having a degree-level qualification was associated with greater odds of drug use among both current (OR = 1.87) and ever (OR = 3.31) drug users. Poor health (both physical and psychological) was associated with greater odds of illicit drug use than was good health.

A similar pattern of association was observed when use of illicit drugs was classified by the potential for harm (Table 3). Specifically, there were greater odds of illicit drug use for men, single persons, and participants with degree-level qualifications for each of the 3 classes of illicit drugs. Poor health, however, was associated with greater odds of lower-risk and intermediate-risk illicit drug use but not high-risk drug use. Depression was associated with greater odds of high-risk and lower-risk drug use (OR = 1.74 and OR = 3.10, respectively). In all analyses, smoking was strongly associated with illicit drug use. Similar results were observed for ever drug users and when classifying cannabis as high risk (data not shown).

Table 4 shows descriptive statistics for the 3 cognitive measures at age 50 years. Table 5 shows adjusted mean differences from the regression model for cognitive measures between illicit drug users and nonusers. As noted above, illicit drug use at 42 years of age was not predictive of survey drop-out at the 8-year follow-up. Current illicit drug use at 42 years of age was not associated with any of the 3 cognitive functioning outcomes at 50 years of age. Ever use of illicit drugs, however, was associated with marginally higher cognitive functioning at age 50 years in all 3 indexes. The differences in all 3 cognitive outcomes (range, 0.23–0.62) tended to be small and of doubtful clinical significance. This pattern of association was generally apparent with respect to intermediate-risk and lower-risk drugs but not high-risk drugs. Participants who reported ever use of intermediate-risk drugs tended to score higher than never users on overall cognitive functioning ($\beta = 0.63$, $P < 0.001$), memory ($\beta = 0.36$, $P < 0.001$), and executive functioning ($\beta = 0.26$, $P < 0.001$) tests. Also, ever use of lower-risk drugs was associated with higher scores on overall cognitive functioning ($\beta = 0.40$, $P = 0.30$) and memory ($\beta = 0.39$, $P < 0.001$) tests.

When illicit drug use was broken down by its severity (Table 5), analyses tended to point toward a possible long-term negative association between overall and executive cognitive functioning and drug-dependency problems and/or lengthier drug use. However, none of the main effects reached conventional levels of statistical significance. Participants who reported seeing a health professional for a drug-dependence problem had lower overall cognitive functioning at age 50 years ($\beta = -0.27$, $P = 0.58$). Similar negative coefficients were observed with respect to memory ($\beta = -0.04$, $P = 0.97$) and executive functioning ($\beta = -0.17$, $P = 0.57$). Long-term illicit drug use was associated with lower overall cognitive functioning scores ($\beta = -0.04$, $P = 0.87$), as well as lower executive functioning scores ($\beta = -0.19$, $P = 0.19$).

Regression analyses (shown in Table 6) revealed a positive association between all 3 cognitive measures and ever use of cannabis and between memory and ever use of cocaine or amphetamines. However, no such associations were observed for current use of specific drugs.

Table 3. Predictors of the Use of Different Groups of Illicit Drugs at 42 Years of Age in the Study Population, National Child Development Study, 1999–2009

Covariate[a]	High-Risk Drugs[b]		Intermediate-Risk Drugs[c]		Lower-Risk Drugs[d]	
	OR	95% CI	OR	95% CI	OR	95% CI
Female gender	0.36	0.25, 0.52	0.49	0.41, 0.58	0.71	0.50, 1.02
Single marital status	2.52	1.77, 3.59	2.44	2.07, 2.88	2.91	2.02, 4.19
Social class						
Middle	1.51	0.99, 2.28	0.99	0.81, 1.21	0.95	0.61, 1.47
Low	1.12	0.63, 1.96	0.84	0.64, 1.10	1.06	0.61, 1.85
Qualification level						
CSE 2–5	0.87	0.50, 1.51	0.85	0.64, 1.12	0.72	0.39, 1.31
O-level certificate	1.22	0.79, 1.89	1.08	0.86, 1.35	1.11	0.71, 1.75
A-level certificate	1.41	0.77, 2.60	1.42	1.05, 1.91	1.24	0.65, 2.35
College degree	2.22	1.25, 3.92	1.77	1.32, 2.36	1.72	0.93, 3.19
Criminal convictions	2.46	1.63, 3.73	1.75	1.34, 2.29	2.66	1.66, 4.26
Long-standing illness	1.02	0.64, 1.62	1.20	0.94, 1.53	1.88	1.23, 2.89
Poor health status	1.07	0.64, 1.77	1.39	1.07, 1.90	2.27	1.46, 3.53
Smoking status						
Ex-smoker	1.40	0.83, 2.36	2.15	1.65, 2.79	1.10	0.66, 1.87
Occasional smoker	3.48	1.84, 6.56	7.52	5.47, 10.33	2.35	1.19, 4.66
<10 cigarettes/day	3.67	2.11, 6.40	7.88	5.93, 10.46	1.39	0.71, 2.76
11–20 cigarettes/day	3.01	1.86, 4.89	6.59	5.12, 8.48	2.07	1.29, 3.35
>20 cigarettes/day	2.51	1.35, 4.66	5.20	3.71, 7.28	2.09	1.13, 3.87
Drinking problem (CAGE score ≥2)	2.52	1.79, 3.54	1.92	1.60, 2.32	1.14	0.76, 1.70
Physical exercise routine						
None	0.99	0.69, 1.43	1.12	0.92, 1.35	0.84	0.58, 1.23
Less than weekly	1.20	0.67, 2.16	1.34	0.99, 1.80	1.58	0.90, 2.79
Low self-efficacy	1.41	0.90, 2.22	0.80	0.61, 1.06	0.93	0.58, 1.48
Life dissatisfaction scale	1.11	1.02, 1.22	1.06	1.01, 1.11	1.05	0.96, 1.15
Depressive symptoms	1.74	1.17, 2.58	1.23	0.99, 1.53	3.10	2.07, 4.65
Self-reported body mass index[e]						
Underweight	1.14	0.67, 1.93	0.92	0.67, 1.26	0.77	0.37, 1.37
Overweight	0.68	0.48, 0.96	0.75	0.63, 0.90	0.78	0.53, 1.14
Obese	0.34	0.17, 0.68	0.57	0.43, 0.76	0.60	0.34, 1.03
Nagelkerke's R^2	21		21		19	

Abbreviations: A-level, advanced level; CI, confidence interval; CSE, Certificate of Secondary Education; O-level, ordinary level; OR, odds ratio.

[a] The reference covariates were as follows: male gender, married marital status, high social class, no qualifications, no criminal convictions, no long-standing illness, good health status, never smoker, CAGE score <2 for drinking problems, weekly physical exercise routine, high self-efficacy, no depression, and normal body mass index.

[b] High-risk drugs included heroin, cocaine, crack cocaine, ecstasy, hallucinogenic mushrooms, methadone, and LSD (lysergic acid diethylamide).

[c] Intermediate-risk drugs included amphetamines and cannabis.

[d] Lower-risk drugs included ketamine, temazine, amyl nitrates, and other drugs.

[e] Weight (kg)/height $(m)^2$.

DISCUSSION

The aim of the present study was to estimate long-term cognitive functioning in the midlife of adults with varying patterns of illicit drug use. The findings differed between participants who had ever used drugs and those who currently used them. No association was observed between current illicit drug use at age 42 years and cognitive functioning at a 10-year follow-up. However, current or past illicit drug use was associated with marginally higher cognitive functioning

Table 4. Descriptive Indexes for Cognitive Measures at 50 Years of Age in the Study Population, National Child Development Study, 1999–2009

Index	Sample Size	Mean (SD)	Range
Cognitive[a]	9,385	26.94 (4.78)	6–41
Memory[b]	9,592	11.98 (2.94)	5–23
Executive[c]	9,442	14.94 (2.90)	5–20

Abbreviation: SD, standard deviation.

[a] The cognitive index measured combined participants' scores on memory and executive functioning indexes.

[b] The memory index combined participants' scores on immediate- and delayed-recall tasks.

[c] The executive functioning index combined participants' scores on the animal naming and letter-cancellation tasks.

scores than was no illicit drug use. Similar results were obtained for all 3 cognitive function measures investigated and across different groups and types of illicit drugs after adjusting for a wide range of confounding factors.

The positive association between ever use of illicit drugs and cognitive functioning suggests that any cognitive deficits associated with immediate illicit drug use (7, 9) might dissipate with time. Cognitive impairment due to persistent intoxication (25) might not be present among past recreational illicit drug users. Thus, the association between past use and cognitive function might be explained by residual confounding with higher educational level among ever illicit drug users, leading to higher cognitive abilities or increased familiarity with cognitive tests. In the present study, prevalence rates of ever illicit drug use were considerably higher among degree-qualified participants (48%) than among participants without an educational qualification (32%). The ever illicit drug use group could include persons with mild or moderate past use of less harmful drugs (26) who had a lower risk of drug dependence (27). Although models in the present study were adjusted for differences in educational qualifications, it is nonetheless possible that other education-related characteristics (e.g., higher cognitively skilled jobs or greater access to health care) might account for the better cognitive performance among ever illicit drug users. Indeed, when analyses were stratified by educational level, the association between ever illicit drug use and cognitive functioning was not statistically significant for the participants with degree-level qualifications (data not shown).

The lack of association between current illicit drug use and subsequent cognitive functioning might be due to selective attrition of participants who reported illicit drug use at 42 years

Table 5. Association Between Illicit Drug Use at 42 Years of Age and Cognitive Functioning at 50 Years of Age in Participants in the National Child Development Study, 1999–2009[a]

	Cognitive Index		Memory Index		Executive Functioning Index	
	β	95% CI	β	95% CI	β	95% CI
Current drug use[b]						
Any drug	0.27	−0.10, 0.63	0.14	−0.09, 0.37	0.12	−0.12, 0.34
High-risk drugs[c]	0.49	−0.30, 1.37	0.33	−0.16, 0.82	0.16	−0.34, 0.65
Intermediate-risk drugs[d]	0.31	−0.08, 0.69	0.18	−0.06, 0.42	0.14	−0.10, 0.38
Lower-risk drugs[e]	−0.07	−0.92, 0.78	−0.06	−0.59, 0.48	−0.09	−0.63, 0.44
Ever drug use[f]						
Any drug	0.62	0.41, 0.83	0.37	0.24, 0.50	0.23	0.10, 0.37
High-risk drugs	0.08	−0.23, 0.40	0.13	−0.06, 0.33	−0.08	−0.27, 0.12
Intermediate-risk drugs	0.63	0.41, 0.85	0.36	0.23, 0.50	0.26	0.12, 0.39
Lower-risk drugs	0.40	0.04, 0.76	0.39	0.16, 0.62	0.02	−0.20, 0.25
Severity of drug use[a]						
Never had a drug dependency	0.25	0.10, 0.39	−0.27	0.12, 0.42	0.25	0.10, 0.39
Had a drug dependency	−0.27	−1.23, 0.69	−0.04	−0.70, 0.62	−0.17	−0.78, 0.43
Time period of drug use[g]						
Both before and at 42 years of age	−0.04	−0.50, 0.42	0.11	−0.17, 0.40	−0.19	−0.48, 0.10
Before 42 years of age only	0.53	0.31, 0.74	0.35	0.22, 0.49	0.16	0.02, 0.29

Abbreviation: CI, confidence interval.

[a] Adjusted for social class, educational level, physical health, long-standing illness, gender, ethnicity, smoking status, alcohol drinking, body mass index (weight (kg)/height $(m)^2$), life dissatisfaction, self-efficacy, physical exercise, partnership status, and depression. The reference category for drug predictors was no drug use.

[b] Any illicit drug use over the previous year at age 42 years.

[c] High-risk drugs included heroin, cocaine, crack cocaine, ecstasy, hallucinogenic mushrooms, methadone, and LSD (lysergic acid diethylamide).

[d] Intermediate-risk drugs included amphetamines and cannabis.

[e] Lower-risk drugs included ketamine, temazine, amyl nitrates, and other drugs.

[f] Any illicit drug use before the age of 42 years. The reference category for drug predictors was no drug use.

[g] Main effect tests.

Table 6. Associations Between Specific Illicit Drug Use and Cognitive Functioning Among Participants in the National Child Development Study, 1999–2009[a]

	Cognitive Index		Memory Index		Executive Functioning Index	
	β	95% CI	β	95% CI	β	95% CI
Current drug use[b]						
Cannabis	0.28	−0.10, 0.41	0.16	−0.10, 0.41	0.11	−0.14, 0.36
Ecstasy	0.70	−0.61, 2.01	0.40	−0.43, 1.22	0.14	−0.70, 0.97
Cocaine or crack cocaine	0.78	−0.15, 1.72	0.46	−0.14, 1.05	0.34	−0.26, 0.93
Amphetamine	0.58	−0.55, 1.71	−0.06	−0.78, 0.66	0.48	−0.24, 1.20
Ever drug use[c]						
Cannabis	0.69	0.47, 0.92	0.40	0.26, 0.54	0.28	0.14, 0.43
Ecstasy	0.58	−0.08, 1.23	0.37	−0.04, 0.77	0.15	−0.27, 0.56
Cocaine	0.43	−0.06, 0.91	0.36	0.05, 0.67	0.01	−0.30, 0.32
Amphetamine	0.49	0.11, 0.86	0.41	0.17, 0.64	0.07	−0.17, 0.30
Heroin	−0.023	−0.94, 0.90	0.34	−0.24, 0.92	−0.43	−1.018, 0.16

Abbreviation: CI, confidence interval.

[a] Adjusted for social class, educational level, physical health, long-standing illness, gender, ethnicity, smoking status, drinking, body mass index (weight (kg)/height $(m)^2$), life dissatisfaction, self efficacy, physical exercise, partnership status, and depression. The reference category for drug predictors was no drug use.

[b] Any illicit drug use over the previous year at age 42 years.

[c] Any illicit drug use before the age of 42 years.

of age. However, illicit drug use at the age of 42 years was not predictive of nonresponse at the age of 50 years. A more plausible explanation is that any effects of illicit drug use on cognition are generally temporary and might disappear after a short period of time (25). This is likely to be true among people for whom illicit drug use is constrained to early life periods, such as adolescence or young adulthood, and does not become a long-term severe habit. This suggestion is supported to a certain extent by the observed, albeit not statistically significant, negative association between drug dependency and long-term illicit drug use and subsequent cognitive functioning. Further investigations using cohort studies and with better recording of data on drug dependency and length of illicit drug use are warranted to confirm this suggestion.

The positive association between illicit drug use and long-term cognitive performance seems to be consistent with previous studies based on clinical populations (28–30). The lack of association between current illegal drug use and cognitive functioning also appears to be congruent with previous evidence showing the absence of a long-term residual effect of illicit drug use on cognition (9, 11, 31). In contrast, the present findings disagree with other evidence that linked cannabis use to impaired cognition and memory (6, 8, 32, 33). This apparently contrasting finding could be accounted for by methodological limitations of previous studies, such as small sample sizes, different age groups, limited drug types (usually only cannabis), and a focus on short-term immediate effect (32, 33). By exploring the influence of illicit drug use over a longer period of time, we were able to avoid the bias caused by false cognitive impairment noted above (25). In addition, the findings of the present study allowed us to document the possibility of a reversible effect of illicit drug use on cognition, probably among participants without severe chronic drug-dependency problems.

The accuracy of information about the history of illicit drug use may be questioned in this study, as it relied on self-reporting. Future studies using multiple approaches, such as self-report, clinical assessment, and biologic techniques, could further substantiate the findings described here. It is likely that frequent illicit drug use has a greater impact on cognitive function than does occasional use. This information was not collected in the data; however, our measure of drug dependency could be seen as a legitimate proxy measure for frequency of drug use. The findings for use of specific drugs need further confirmation from similar studies with superior data, including information about the reasons for drug use, which may vary with age (e.g., medical reasons could be more common in older adults than in younger adults). Although the missing-indicator method used in the present study to adjust for attrition is prone to bias (34), multiple imputations for outcome variables led to similar results, particularly a significant correlation between ever drug use and long-term cognitive functioning (OR = 0.55, confidence interval: 034, 0.77).

Another important shortcoming of the present study relates to the lack of relevant cognitive functioning measures at baseline (age 42 years) to allow for adjustment for possible imbalances in cognitive ability associated with illicit drug use. However, we were able to adjust for differences in educational qualifications, which represent a valid marker for cognitive ability (35). Reverse causality may also account for the observed findings in the participants who had ever used illicit drugs. In the present data, the most highly educated participants reported higher rates of illicit drug use, which could account for the positive association between illicit drug use and better cognitive performance. Also, the present study included a large number of different illicit drugs, and each drug might have a different impact on cognitive functioning. The present study explored the possibility of different patterning

of illicit drugs according to their potential for harm. The results pointed toward the possibility of different outcomes associated with specific groups of drugs, but the findings need further confirmation. Notwithstanding data shortcomings, the prospective, nationally representative adult sample and the use of standardized measures of cognitive functioning and multiple illicit drug measures represent major strengths of the present study.

In conclusion, the relation between illicit drug use and cognitive impairment is a complex one, and the present data confirm this. At the population level, it does not appear that past or even current illicit drug use is associated with impaired cognitive functioning in early middle age. This is true for different groups of illicit drugs considered separately. However, we cannot exclude the possibility that some individuals and groups, such as those with heavier or more prolonged use, could be harmed.

ACKNOWLEDGMENTS

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Conflict of interest: none declared.

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