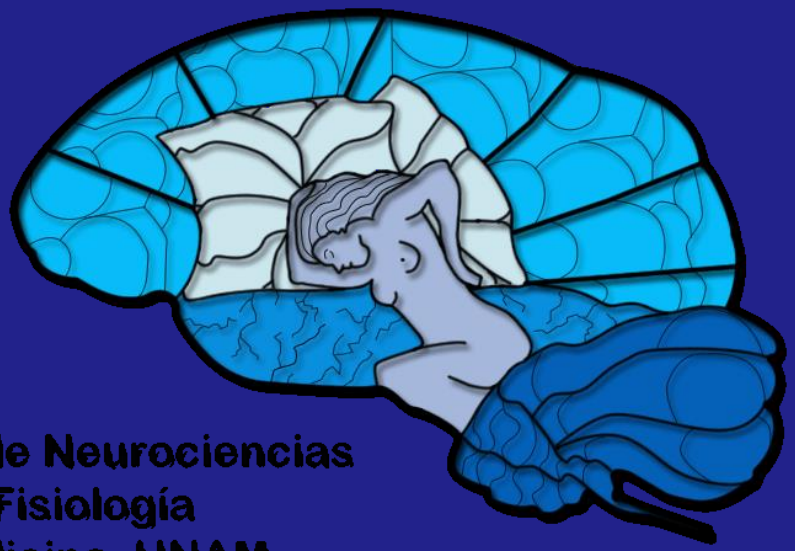
CONSIDERACIONES MÉDICAS DEL USO DE MARIHUANA



Grupo de Neurociencias
Fisiología
Medicina, UNAM

Dr. Oscar Prospéro García

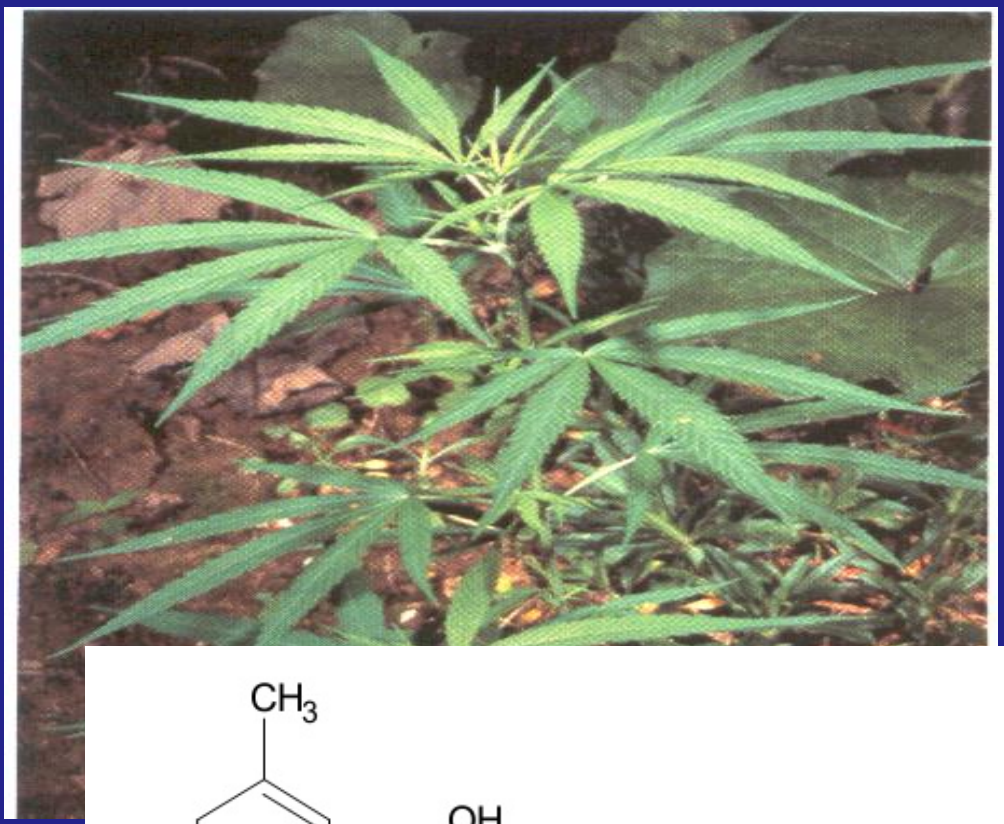
Laboratorio de Canabinoides. Grupo de Neurociencias, Departamento de Fisiología

Facultad de Medicina, UNAM

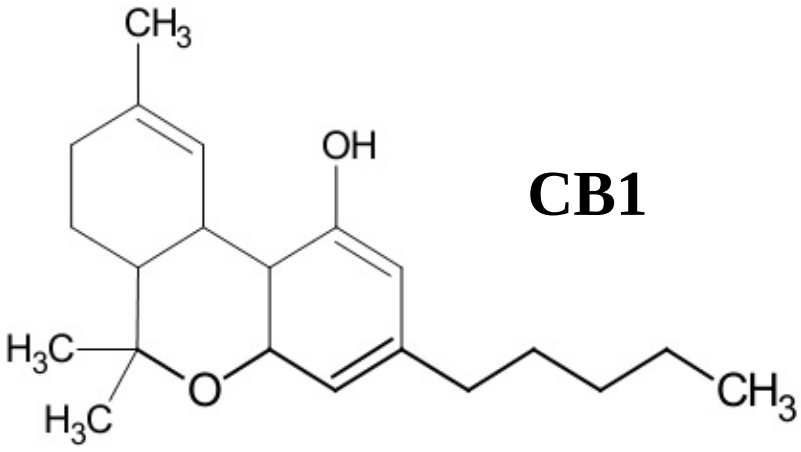
UNIVERSIDAD NACIONAL

AUTÓNOMADE MÉXICO

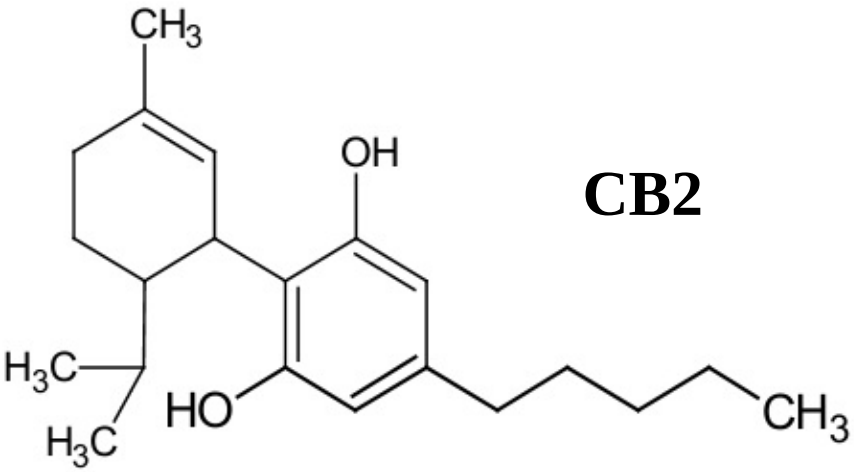
Cannabis sativa



Fabrica más de 400 compuestos
La mayoría no estudiados.
2 compuestos son los más estudiados:
El Delta-9-Tetrahidrocannabinol (THC)
Y el cannabidiol (CBD)



Tetrahydrocannabinol (THC)



Cannabidiol (CBD)

ENDOCANNABINOIDES

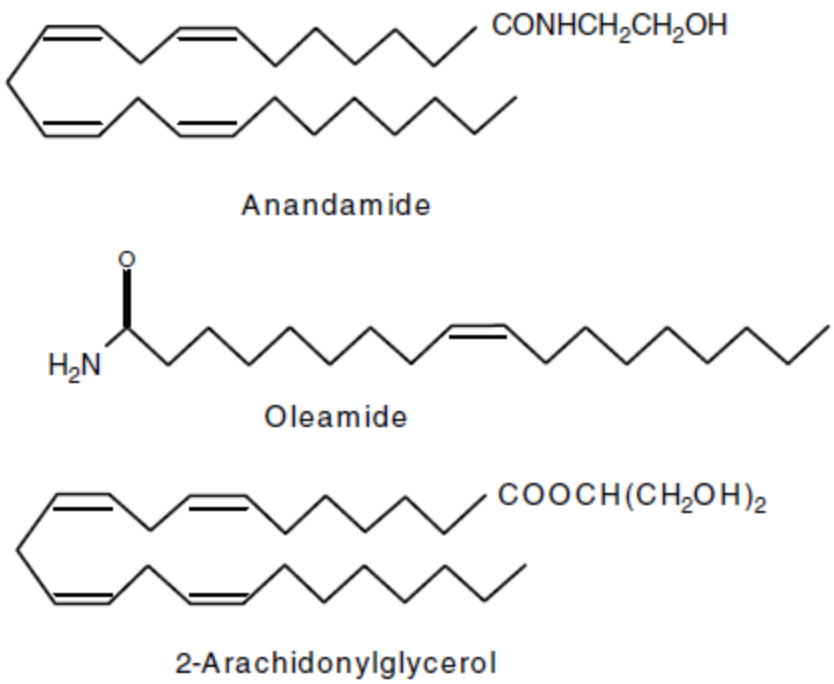


Figure 25.1 Molecular structure of some endocannabinoids.

Drug harms in the UK: a multicriteria decision analysis

David J Nutt, Leslie A King, Lawrence D Phillips, on behalf of the Independent Scientific Committee on Drugs

Lancet 2010; 376: 1558–65
Published Online November 1, 2010
DOI:10.1016/S0140-6736(10)61462-6

Summary

Background Proper assessment of the harms caused by the misuse of drugs can inform policy makers in health, policing, and social care. We aimed to apply multicriteria decision analysis (MCDA) modelling to a range of drug harms in the UK.

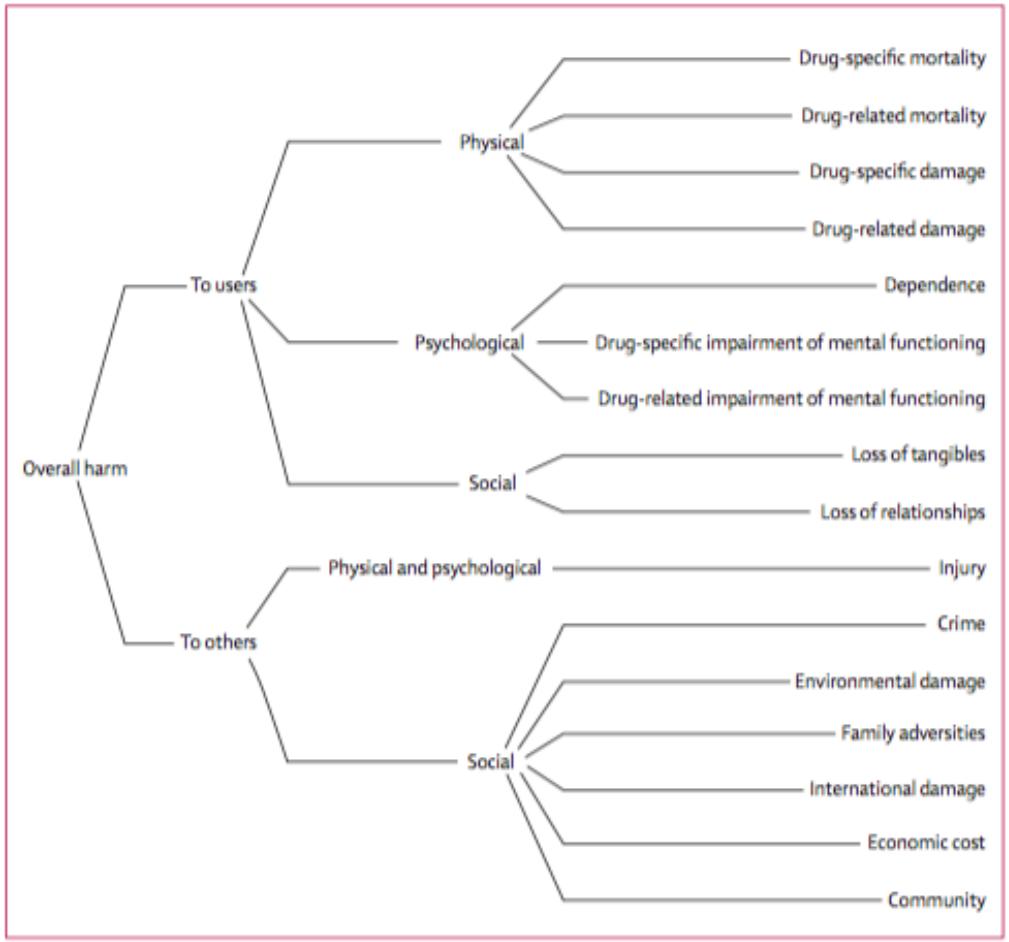


Figure 1: Evaluation criteria organised by harms to users and harms to others, and clustered under physical, psychological, and social effects

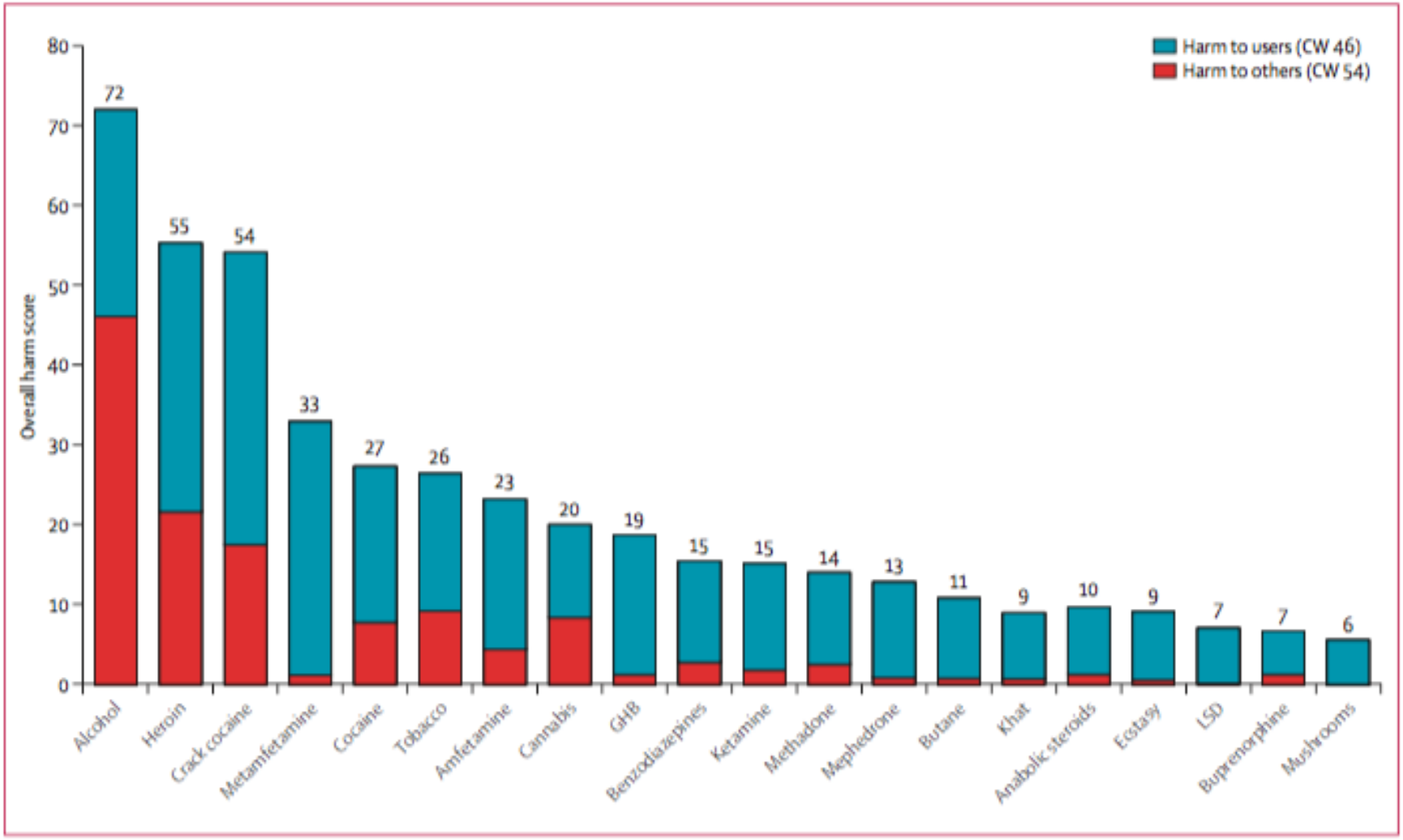
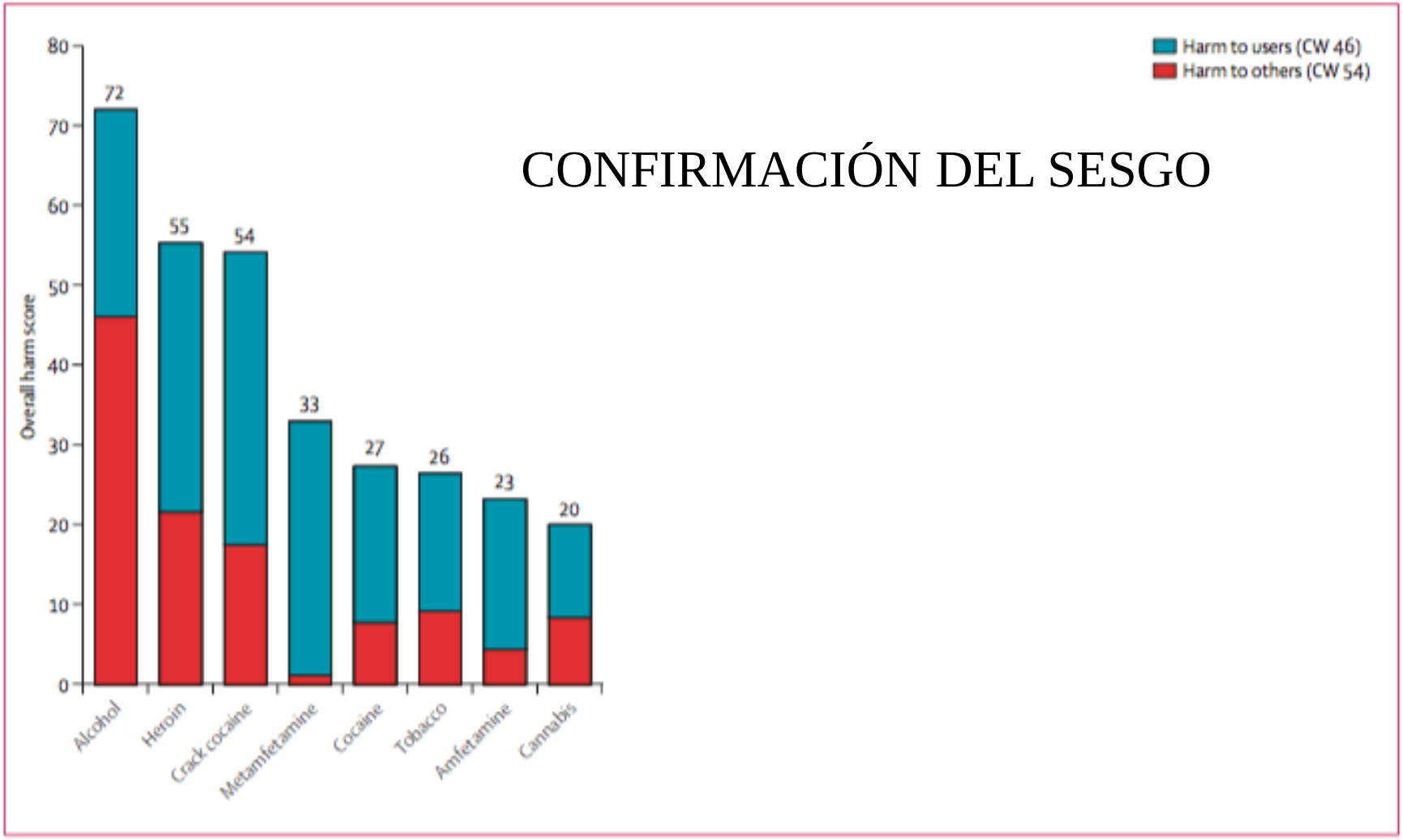


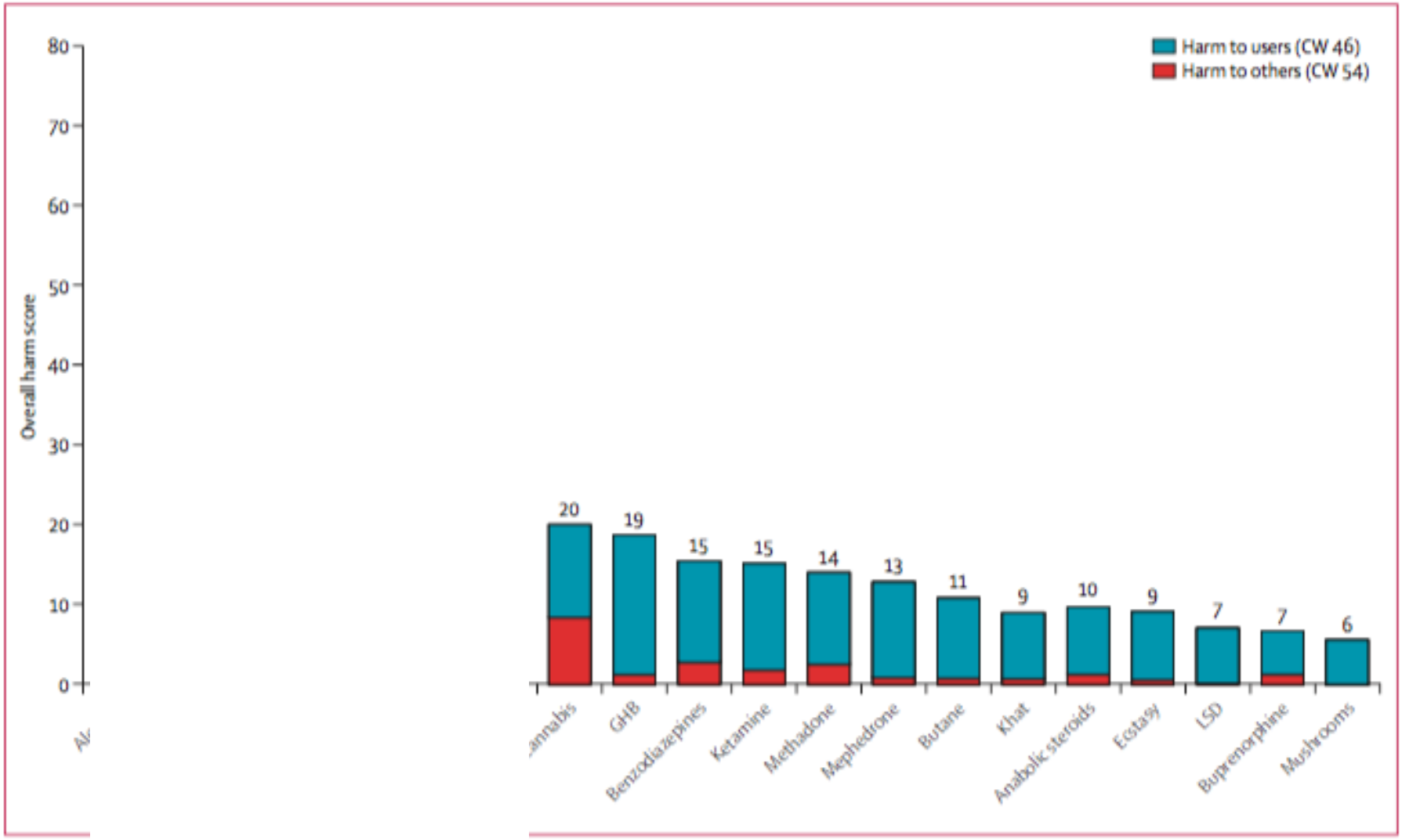
Figure 2: **Drugs ordered by their overall harm scores, showing the separate contributions to the overall scores of harms to users and harm to others**

The weights after normalisation (0–100) are shown in the key (cumulative in the sense of the sum of all the normalised weights for all the criteria to users, 46; and for all the criteria to others, 54). CW=cumulative weight. GHB=γ hydroxybutyric acid. LSD=lysergic acid diethylamide.



CONFIRMACIÓN DEL SESGO

Figure 2: **Drugs ordered by their overall harm scores, showing the separate contributions to the overall scores of harms to users and harm to others**
The weights after normalisation (0–100) are shown in the key (cumulative in the sense of the sum of all the normalised weights for all the criteria to users, 46; and for all the criteria to others, 54). CW=cumulative weight. GHB=γ hydroxybutyric acid. LSD=lysergic acid diethylamide.



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In conclusion, we have used MCDA to analyse the harms of a range of drugs in relation to the UK (panel 2). Our findings lend support to previous work in the UK and the Netherlands, confirming that the present drug classification systems have little relation to the evidence of harm. They also accord with the conclusions of previous expert reports[11,18] that aggressively targeting alcohol harms is a valid and necessary public health strategy.

Estas (conclusiones) están de acuerdo con conclusiones de reportes
Previos en los que se dice que hay que poner agresivamente en la mira
a los daños producidos por el alcohol es
una estrategia de salud válida y necesaria

Drug and Alcohol Dependence 140 (2014) 145–155

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

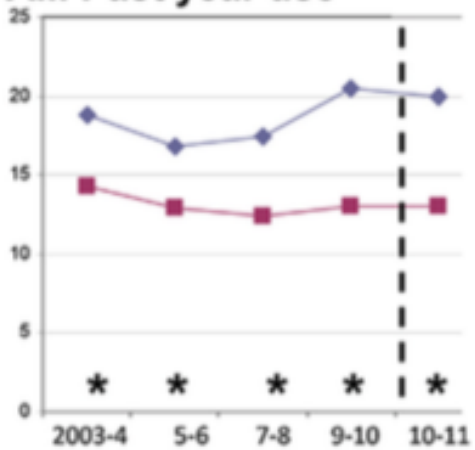
Temporal trends in marijuana attitudes, availability and use in Colorado compared to non-medical marijuana states: 2003–11☆

Joseph Schuermeyer[a], Stacy Salomonsen-Sautel[a], Rumi Kato Price[b], Sundari Balan[b], Christian Thurstone[a,c], Sung-Joon Min[d], Joseph T. Sakai[a,*]

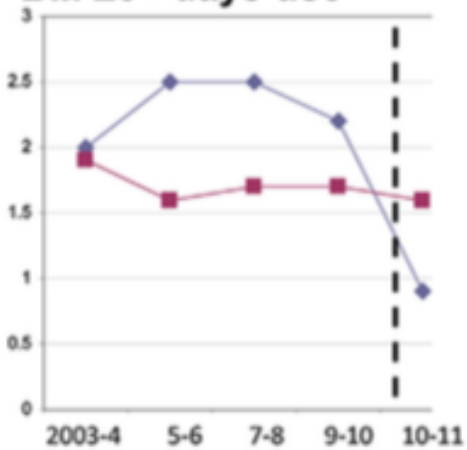
[a] Department of Psychiatry, University of Colorado Anschutz Medical Campus, Aurora, CO, United States
[b] Department of Psychiatry, Washington University School of Medicine, St. Louis, MO, United States
[c] Denver Health and Hospital Authority, Denver, Colorado, United States
[d] Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

Row 1. Adolescents (12-17 year olds)

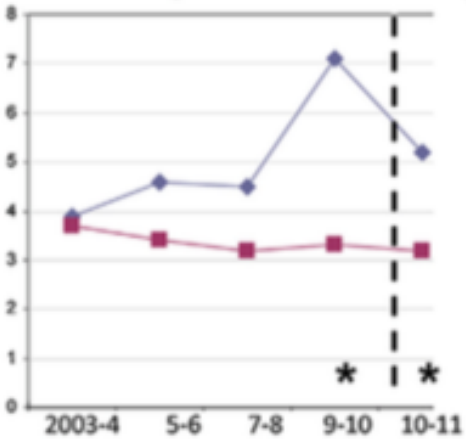
A.i. Past year use



B.i. 20+ days use

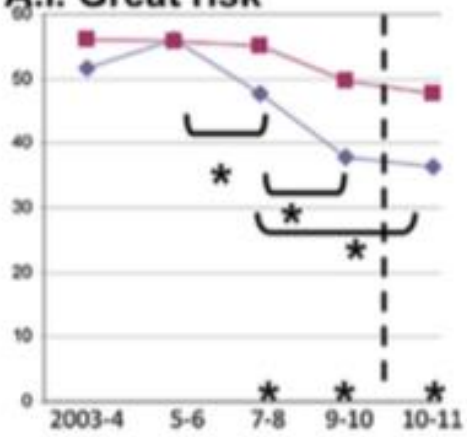


C.i. Marijuana abuse/dependence

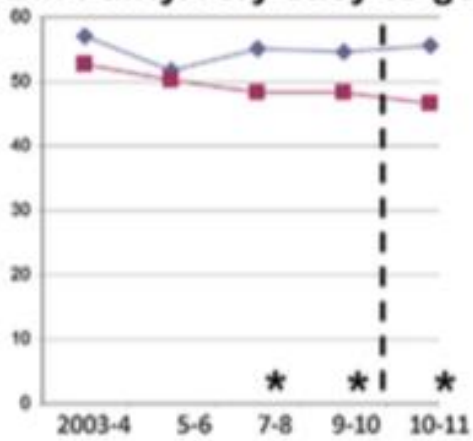


Row 1. Adolescents (12-17 year olds)

A.i. Great risk



B.i. Fairly/very easy to get

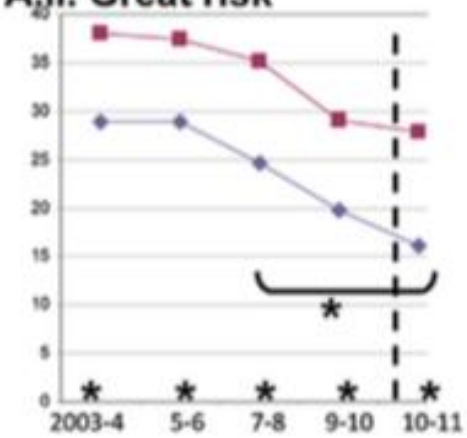


C.i. Somewhat/strongly disapprove

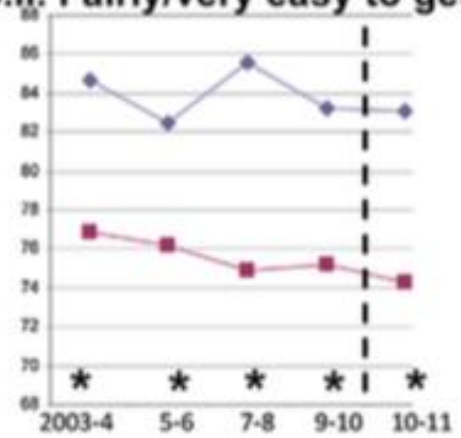
This item was not asked of adolescents

Row 2. Young adults ((18-25 year olds)

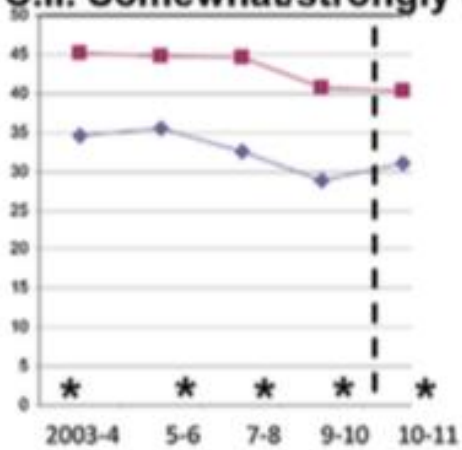
A.ii. Great risk



B.ii. Fairly/very easy to get



C.ii. Somewhat/strongly disapprove



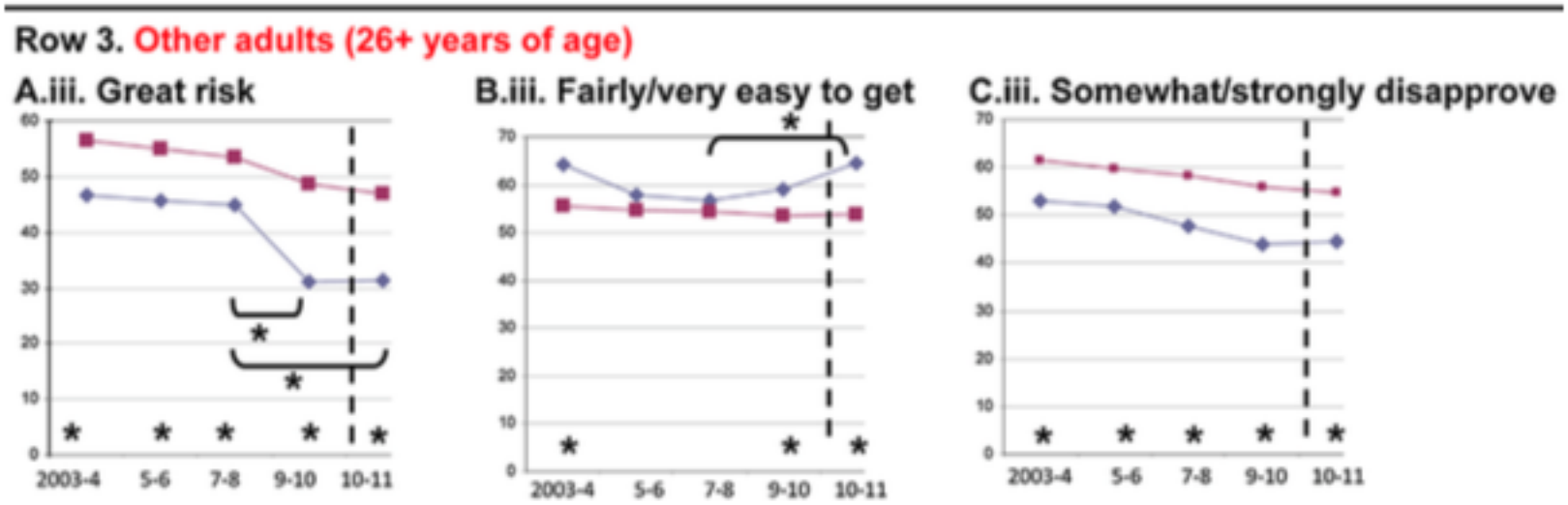
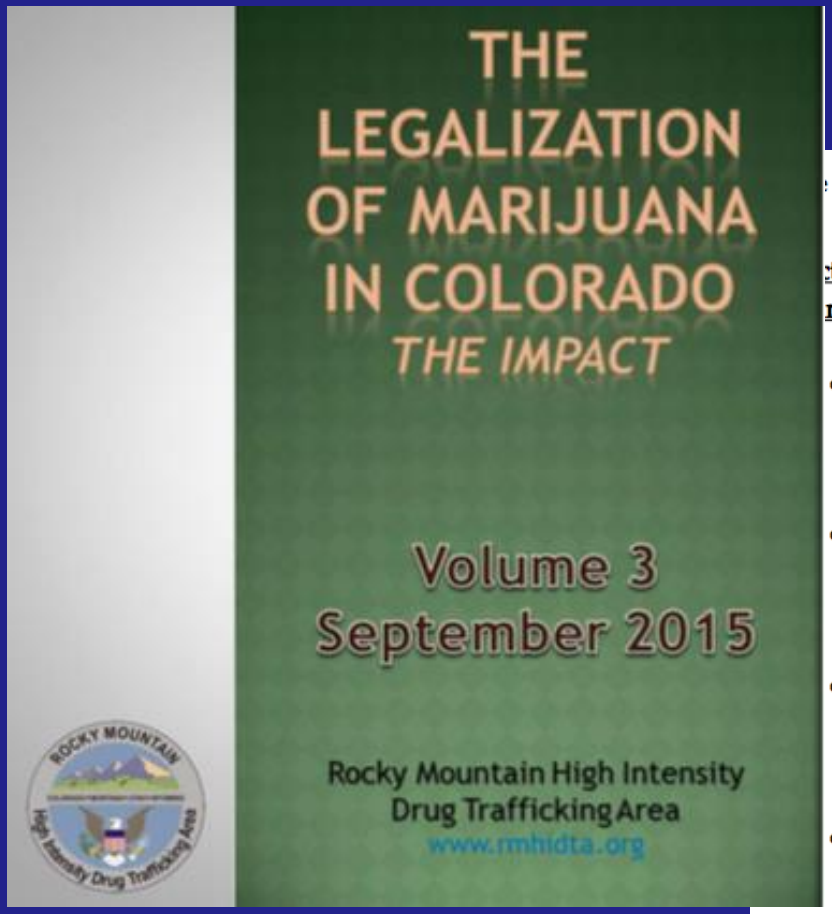


Fig. 1. Measures of marijuana-related attitudes, change across time (2003–4 to 2010–11) within Colorado (blue; diamond markers) and within 34 states without medical marijuana laws (NMMS, red; square markers). (A) Great risk to smoking marijuana 1–2 times per week. (B) Fairly/very easy to obtain marijuana. (C) Somewhat or strongly disapprove of adults trying. Row 1 represents 12–17 year olds, row 2 represents 18–25 year olds and row 3 represents those 26+ years. *x*-Axis indicates year, while *y*-axis indicates percent of respondents endorsing an item. Dashed line indicates that years 2009–10 and 2010–11 are not independent. Brackets and associated asterisk(s) indicate a significant change within-Colorado across years. Asterisk below lines, just above the years (*x*-axis) indicate that Colorado and 34 non-medical marijuana states significantly differed (*<0.05) (For interpretation of the color information in this figure legend, the reader is referred to the web version of the article.).

4.7. *Conclusions*

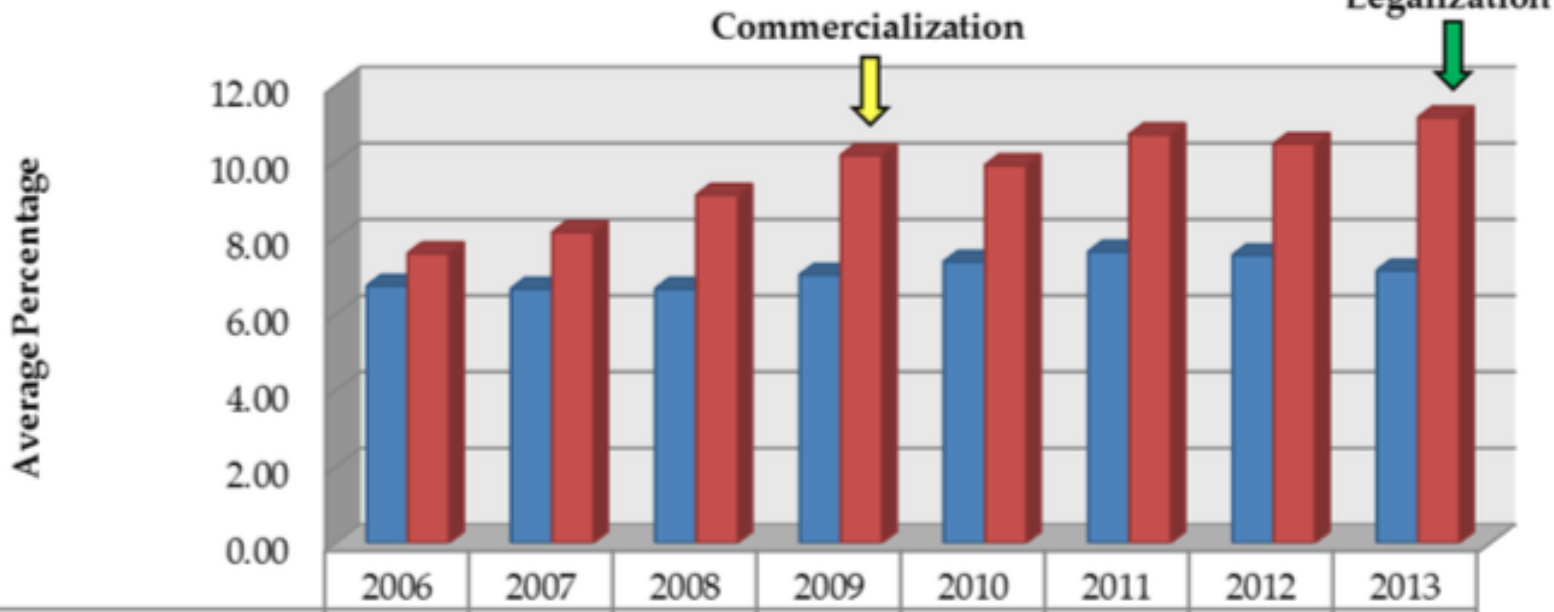
While the current study showed relatively consistent differences between Colorado and other states without medical marijuana laws on measures of marijuana attitudes and use-related-outcomes, results in some measures indicate the differences are widening in more recent years, especially since 2009. Those include risk perception, and trend for differences in changes in availability and abuse/dependence in some age groups, even after controlling for demographic differences. Data taken together provide suggestive evidence of diverging changes in marijuana risk perception and some use practices specific to Colorado in 2009 and after. Even though causality cannot be established, Colorado would be wise to implement prevention efforts regarding marijuana and make treatment for those with marijuana use disorders more broadly available in the state.



:tion 4 – Emergency Room Marijuana and Hospital Marijuana-Related missions:

- In 2014, when retail marijuana businesses began operating, there was a **29 percent** increase in the number of marijuana-related emergency room visits in only one year.
- In 2014, when retail marijuana businesses began operating, there was a **38 percent** increase in the number of marijuana-related hospitalizations in only one year.
- In the three years after medical marijuana was commercialized, compared to the three years prior, there was a **46 percent** increase in hospitalizations related to marijuana.
- Children's Hospital Colorado reported **2** marijuana ingestions among children under 12 in 2009 compared to **16** in 2014.

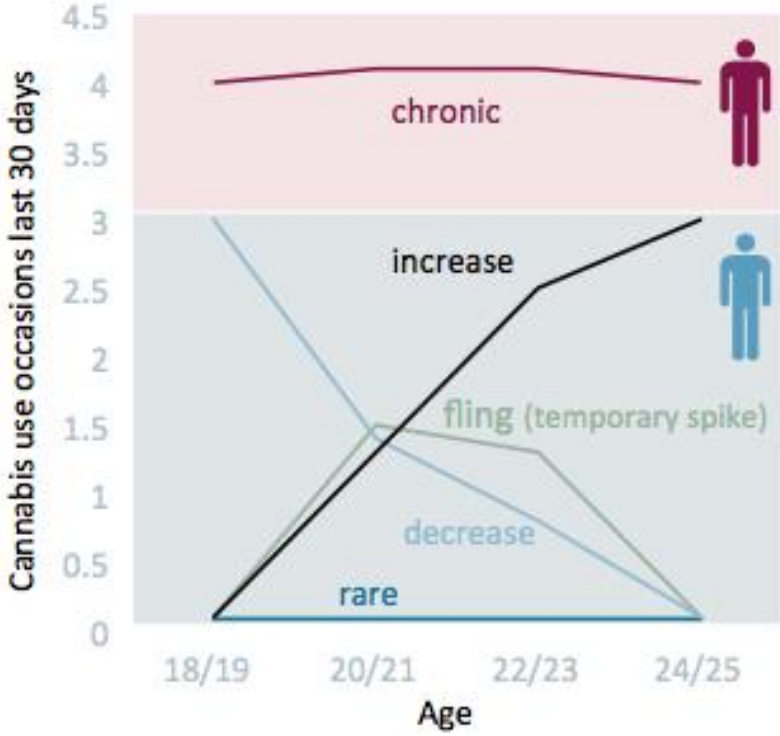
Youth (Ages 12 to 17 Years Old) Past Month Marijuana Use National vs. Colorado



	2006	2007	2008	2009	2010	2011	2012	2013
National Average	6.74	6.67	6.67	7.03	7.38	7.64	7.55	7.15
Colorado Average	7.60	8.15	9.13	10.17	9.91	10.72	10.47	11.16

SOURCE: **SAMHSA.gov, National Survey on Drug Use and Health, 2006-2013**

FIG. 16. Different trajectories of cannabis use in late adolescence and young adulthood



In adolescence chronic cannabis users had
- lower grades and school attendance
- lower college aspirations

In early adulthood chronic cannabis users were
- highest on problematic substance use
- less likely to be married and have children
- less likely to have graduated from college
- more likely to experience unemployment

Chronic users

Non-chronic users

Source: Schulenberg and others, "Trajectories of marijuana use" (2005).

The Journal of Neuroscience, April 16, 2014 • 34(16):5529–5538 • 5529

Neurobiology of Disease

Cannabis Use Is Quantitatively Associated with Nucleus Accumbens and Amygdala Abnormalities in Young Adult Recreational Users

Jodi M. Gilman,[1,4,5] John K. Kuster,[1,2]* Sang Lee,[1,6]* Myung Joo Lee,[1,6]* Byoung Woo Kim,[1,6] Nikos Makris,[3,5] Andre van der Kouwe,[4,5] Anne J. Blood,[1,2,4,5]† and Hans C. Breiter[1,2,4,6]†

[1]Laboratory of Neuroimaging and Genetics, Department of Psychiatry, [2]Mood and Motor Control Laboratory, [3]Center for Morphometric Analysis, Department of Psychiatry, and [4]Athinoula A. Martinos Center in Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown, Massachusetts 02129, [5]Harvard Medical School, Boston, Massachusetts 02115, and [6]Warren Wright Adolescent Center, Department of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, Chicago, Illinois 06011

Table 1. Participant demographics

	CON ($n = 20$)	MJ ($n = 20$)	p-value
Sex (M/F)	9 M/11 F	9 M/11 F	N/A
Age	20.7 (1.9)	21.3 (1.9)	0.30
Years of education	14.3 (3.4)	12.6 (4.8)	0.20
STAI[a]			
State	28.9 (7.94)	27.7 (7.38)	0.65
Trait	29.8 (7.32)	29.5 (5.56)	0.89
HAM-D[b]	0.80 (1.40) [range: 0–5]	1.10 (1.37) [range: 0–5]	0.50
TIPI[c]			
Extroversion	10.9 (2.36)	10.7 (2.13)	0.78
Agreeableness	10.8 (2.47)	10.7 (1.81)	0.94
Conscientiousness	11.9 (2.08)	11.7 (2.13)	0.76
Emotional stability	10.5 (2.52)	11.4 (2.64)	0.27
Openness	12.1 (1.90)	12.4 (1.61)	0.57
Substance use			
Alcohol			
No. alcoholic drinks/week	2.64 (2.38)	5.09 (4.69)	0.10
AUDIT score	3.30 (1.78)	5.50 (2.21)	0.05
Cigarettes			
No. of occasional smokers[d]	0	7	N/A
No. of daily smokers	0	1	N/A
Marijuana			
No. days/week	0	3.83 (2.36)	N/A
No. joints/week	0	11.2 (9.61)	N/A
No. joints/occasion	0	1.80 (0.77)	N/A
No. smoking occasions/day	0	1.80 (0.70)	N/A
Age of onset (years)	—	16.6 (2.13)	N/A
Duration of use (years)	—	6.21 (3.43)	N/A

All values are expressed in means and SDs. CON, controls; MJ, marijuana users.

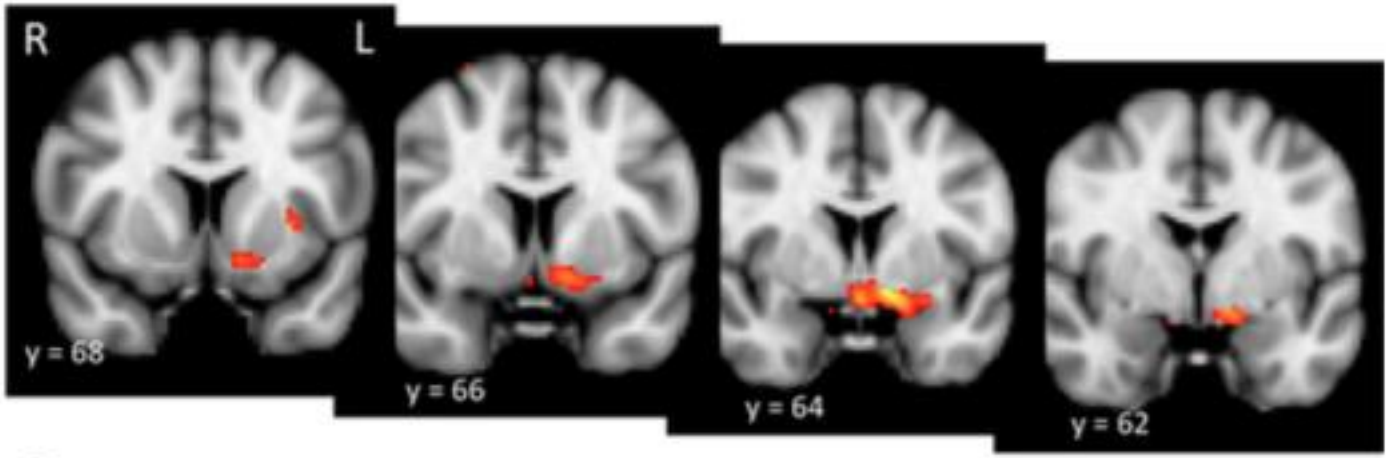
[a]State Trait Anxiety Inventory Form (Spielberger et al., 1983).

[b]Hamilton Depression Rating Scale (Hamilton, 1960).

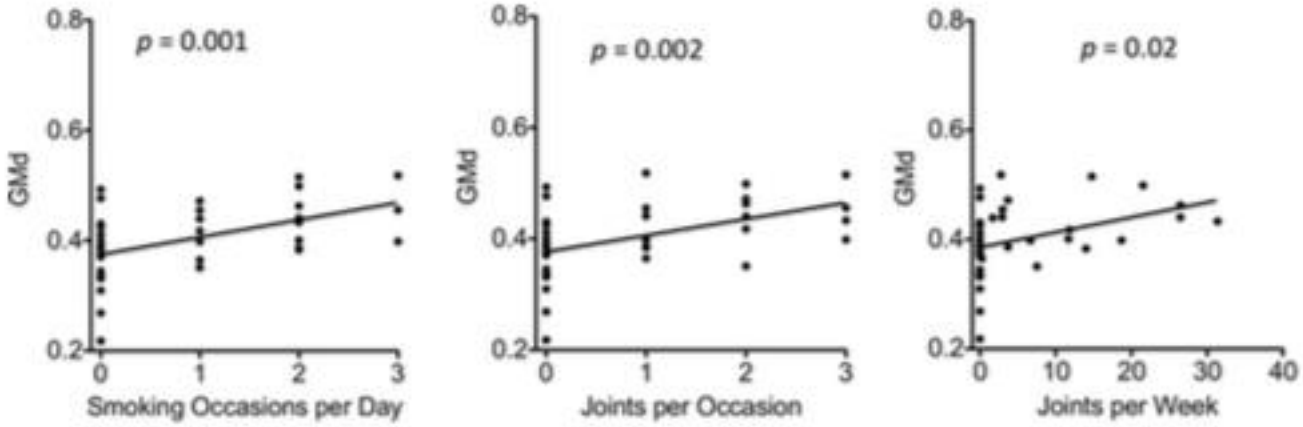
[c]Ten-Item Personality Inventory (Gosling et al., 2003).

[d]Occasional smokers reported from 1 cigarette/week to 1 cigarette every 3 months.

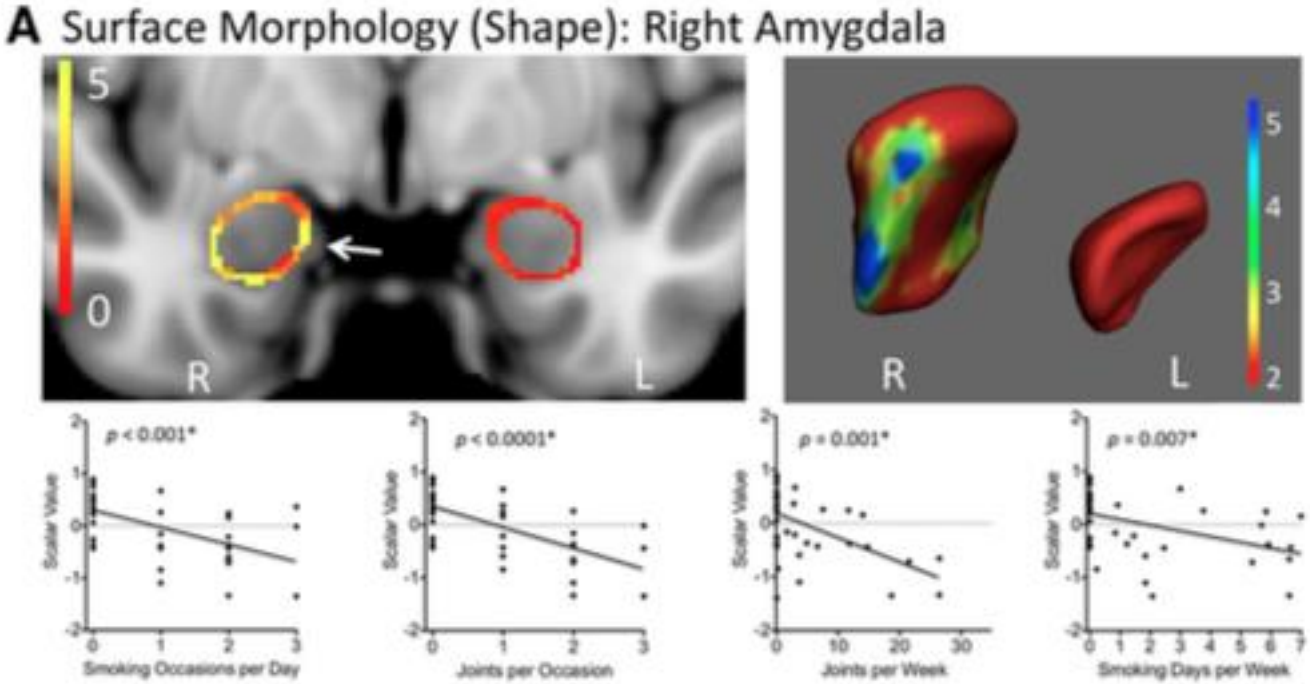
A Gray Matter Density: Marijuana > Control Participants



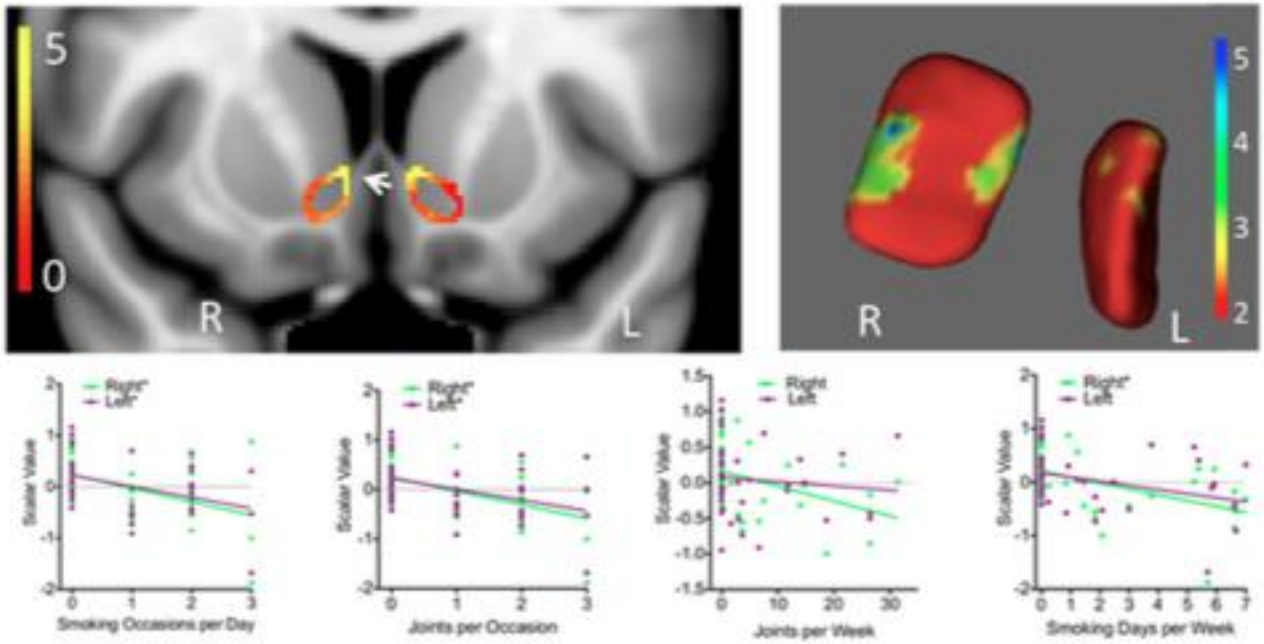
B Associations Drug Use Behavior and Gray Matter Density in Left Nucleus Accumbens



Gilman et al. • Cannabis Use Abnormalities



B Surface Morphology (Shape): Nucleus Accumbens



Psychiatry Research: Neuroimaging 173 (2009) 228–237

Contents lists available at ScienceDirect

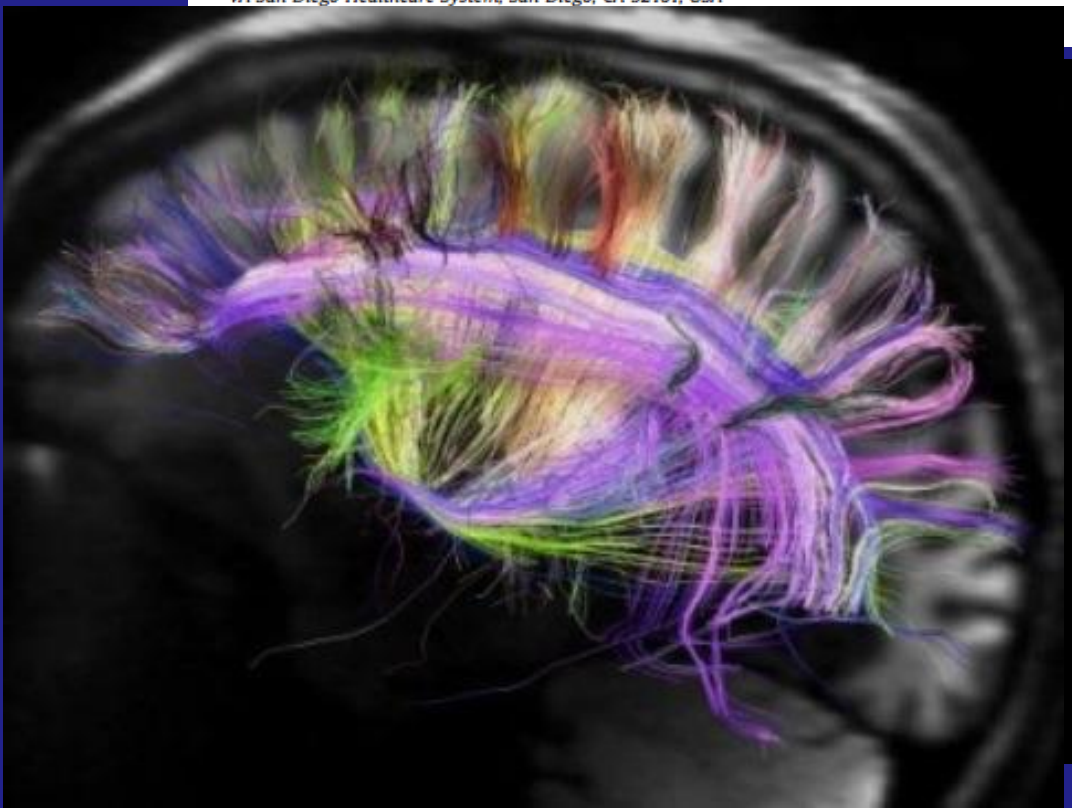
Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Altered white matter microstructure in adolescent substance users

Sunita Bava[a,b], Lawrence R. Frank[b,c], Tim McQueeny[c], Brian C. Schweinsburg[a,d], Alecia D. Schweinsburg[d], Susan F. Tapert[a,c,*]

[a]Department of Psychiatry, University of California, San Diego, La Jolla, CA 92093, USA
[b]Department of Radiology, University of California, San Diego, La Jolla, CA 92093, USA
[c]VA San Diego Healthcare System, San Diego, CA 92161, USA



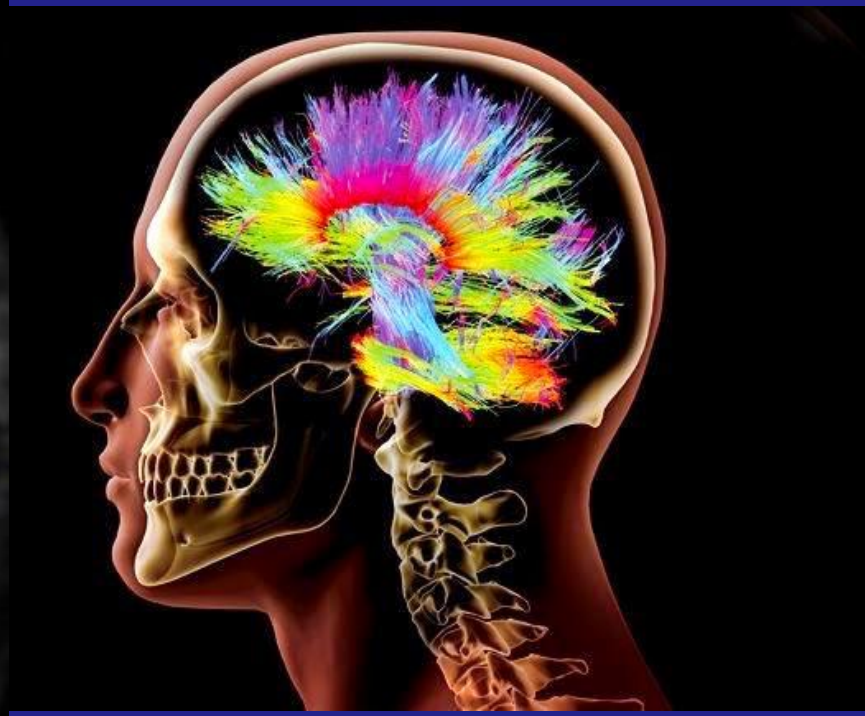
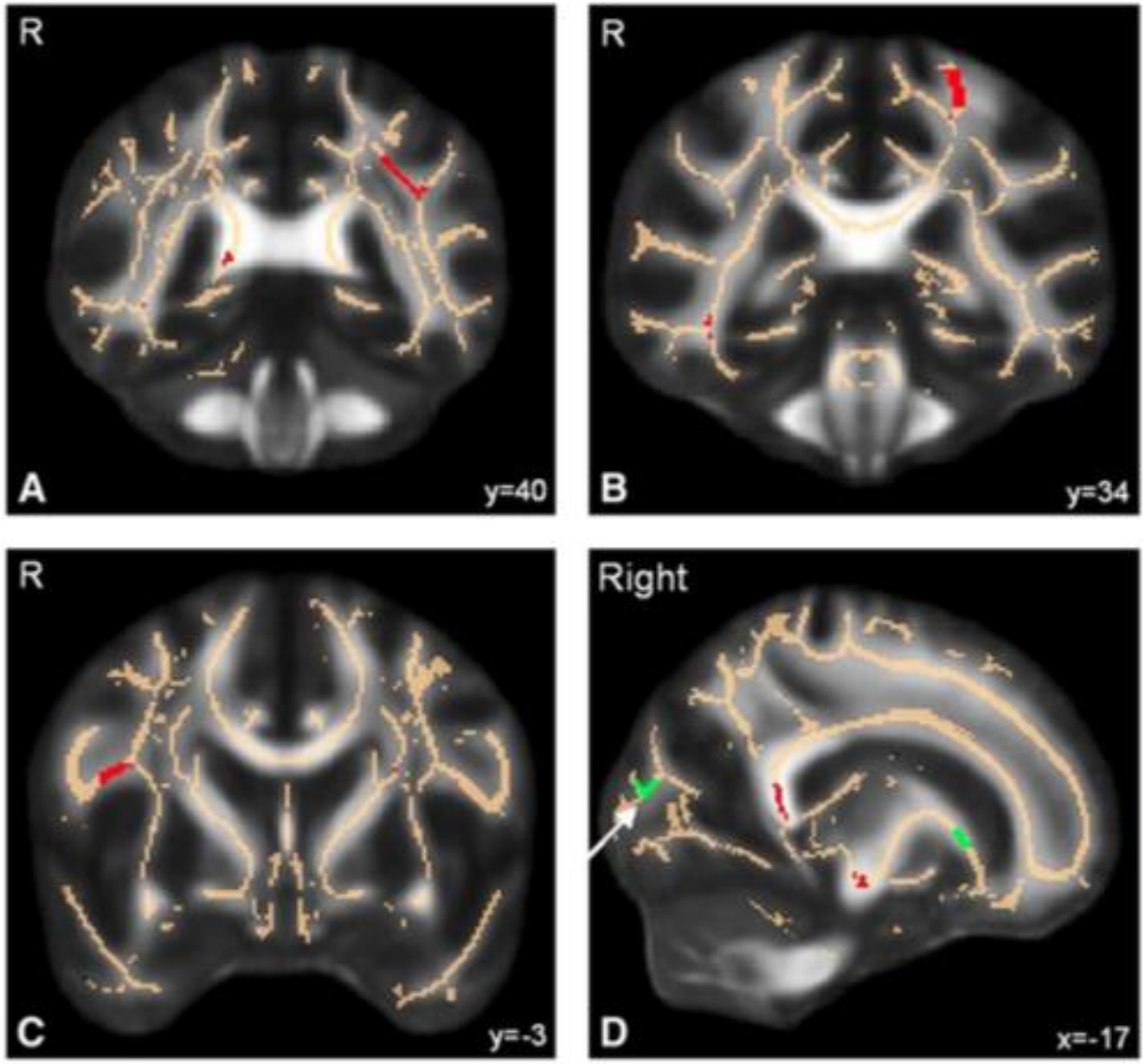


Table 1
Demographic and substance use characteristics of participants.

	MJ + ALC ($n = 36$) M (S.D.) or %	Controls ($n = 36$) M (S.D.) or %
Years of age (range 16.3–19.0)	17.9 (0.9)	17.8 (0.8)
Female	27.8%	27.8%
Caucasian	61.1%	62.9%
Annual household income (thousands)	141.7 (128.3)	115.9 (60.2)
Hollingshead socioeconomic level	28.8 (13.7)	30.4 (16.2)
Parental history of a substance use disorder*[a]	41.7%	11.4%
WASI vocabulary T-score[b]	58.4 (8.7)	58.7 (8.7)
WRAT-3 reading standard score[c]	106.7 (8.0)	109.7 (6.6)
Spielberger state anxiety T-score	39.5 (6.7)	37.7 (7.0)
Beck depression inventory total	3.2 (3.2)	2.6 (2.7)
Child behavior checklist internalizing T-score	46.1 (10.0)	44.8 (7.9)
Child behavior checklist externalizing T-score	49.7 (9.4)	45.2 (10.3)
Age of first marijuana use*	13.9 (2.0)	15.4 (1.7)[d]
Age of first weekly marijuana use	14.7 (3.1)	-
Lifetime marijuana use episodes**	551.7 (481.2)	1.4 (2.3)
Marijuana use days per month (past 3 months)**	11.6 (8.4)	0.1 (0.3)
Days between last marijuana use and DTI study**	52.1 (69.6)	355.4 (330.3)[d]
Age of first alcohol use*	13.1 (1.9)	14.6 (1.7)[d]
Age of first weekly alcohol use	15.5 (1.7)	16.0[e]
Lifetime alcohol drinks**	195.3 (152.7)	25.0 (38.6)
Drinks per month (past 3 months)**	52.9 (52.4)	8.2 (12.4)
Days between last alcohol use and DTI study	43.0 (68.6)	86.9 (118.2)[d]
Cigarettes per smoking day*	1.2 (3.8)	0.0 (0.2)
Fagerstrom test for nicotine dependence score*	0.3 (0.7)	0.0 (0.0)
Lifetime other drug use instances**	10.5 (11.2)	0.5 (2.2)

*$P<0.05$.
**$P<0.001$.
MJ + ALC = marijuana and alcohol user.
[a] Parent with DSM-IV alcohol or drug abuse or dependence.
[b] From Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999).
[c] From Wechsler Wide Range Achievement Test (Wilkinson, 1993).
[d] For controls with history of any marijuana ($n = 14$) or alcohol ($n = 12$) use.
[e] ($n = 1$).


R
A
y=40
R
B
y=34
R
C
y=-3
Right
D
x=-17

Persistent cannabis users show neuropsychological decline from childhood to midlife

Madeline H. Meier[a,b,1], Avshalom Caspi[a,b,c,d,e], Antony Ambler[e,f], HonaLee Harrington[b,c,d], Renate Houts[b,c,d], Richard S. E. Keefe[d], Kay McDonald[f], Aimee Ward[f], Richie Poulton[f], and Terrie E. Moffitt[a,b,c,d,e]

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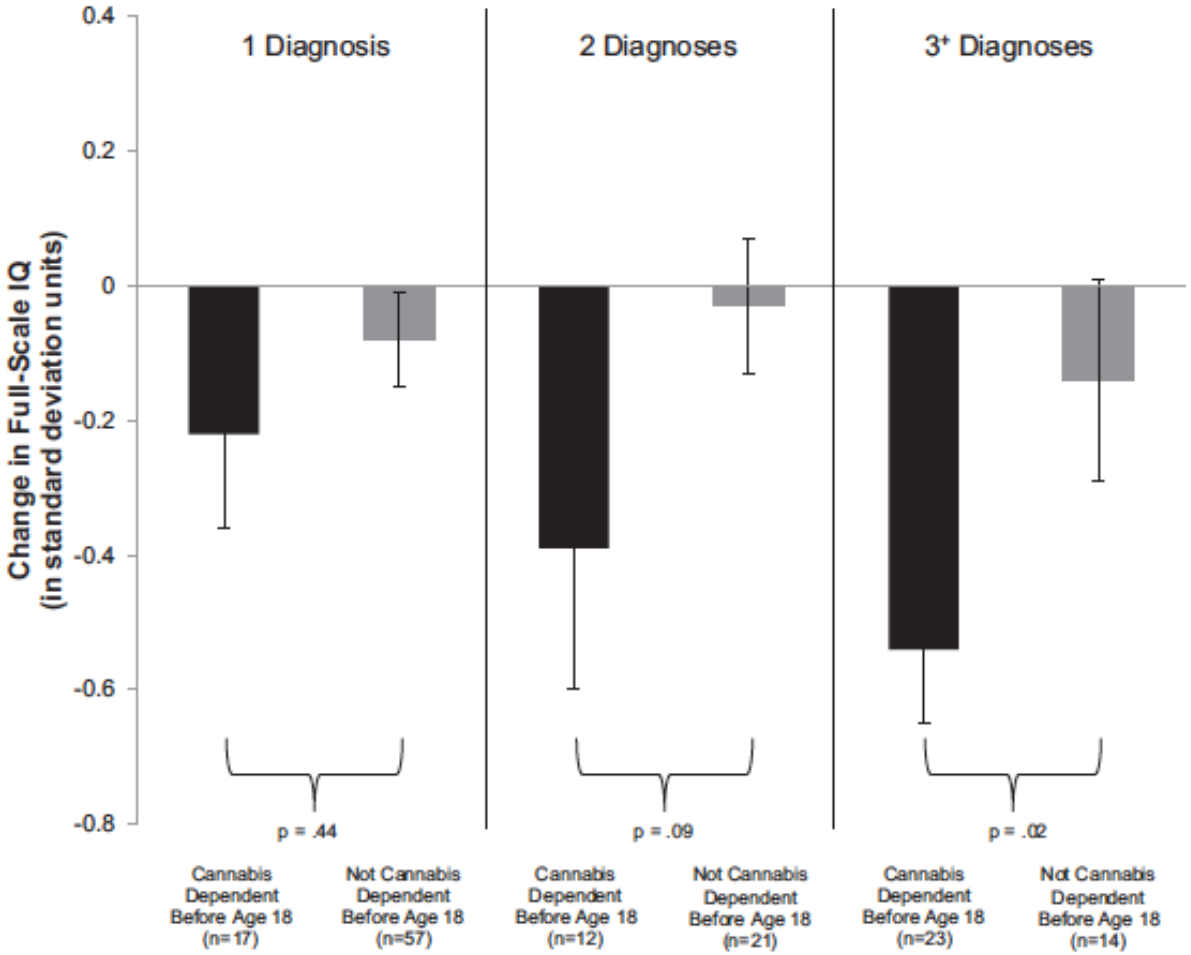

Fig. 2. Adolescent vulnerability. Shown is change in full-scale IQ (in SD units) from childhood to adulthood among study members with 1, 2, or 3+ diagnoses of cannabis dependence as a function of age of onset of cannabis dependence. Individuals with adolescent-onset cannabis dependence (black bars) experienced greater IQ decline than individuals with adult-onset cannabis dependence (gray bars). IQ decline of approximately –0.55 SD units among individuals with adolescent-onset cannabis dependence in the 3+ group represents a decline of 8 IQ points. Error bars = SEs.

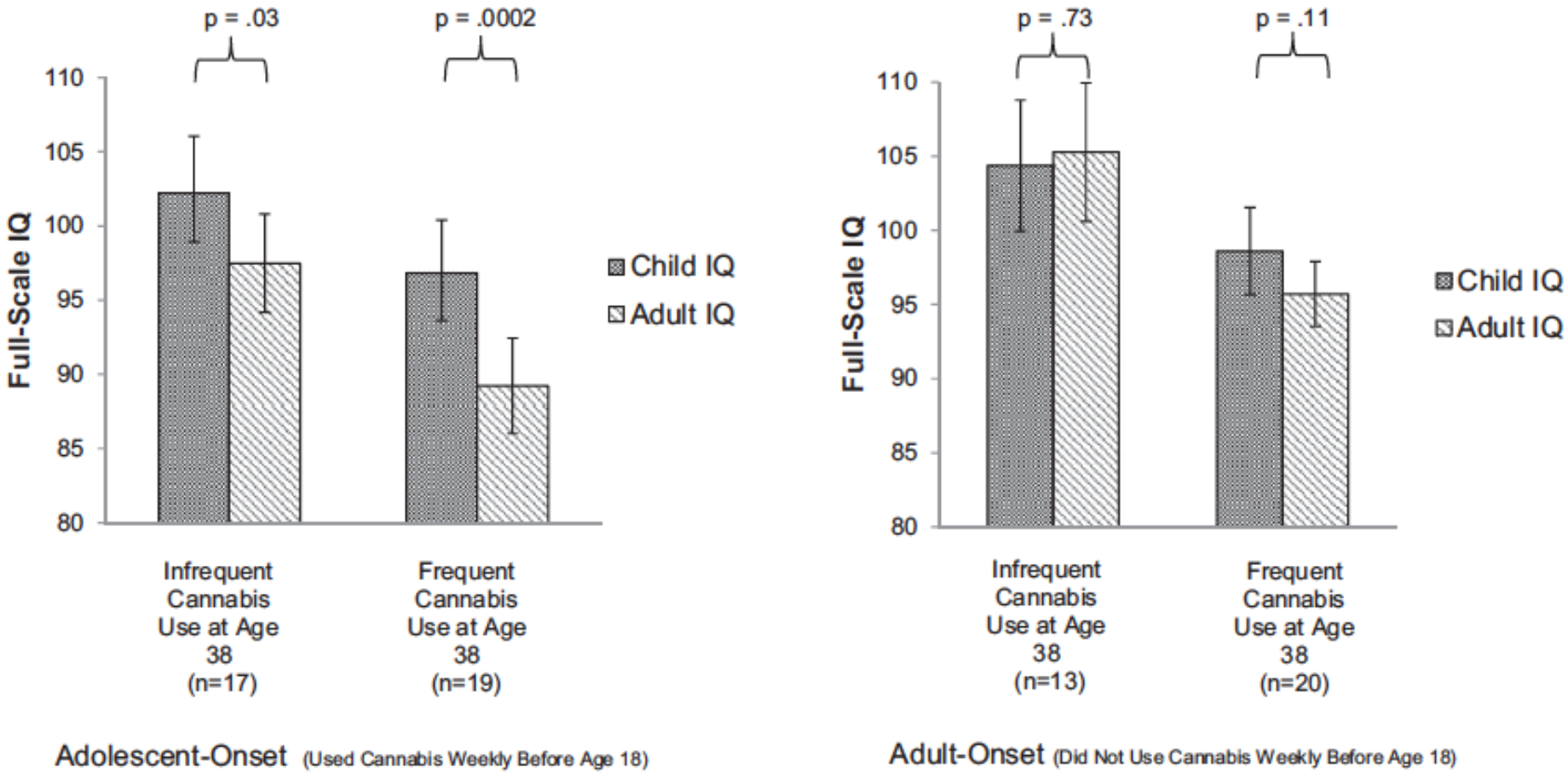

Fig. 3. Postcessation IQ among former persistent cannabis users. This figure is restricted to persistent cannabis users, defined as study members with two or more diagnoses of cannabis dependence. Shown is full-scale IQ in childhood and adulthood. IQ is plotted as a function of (*i*) age of onset of at least weekly cannabis use and (*ii*) the frequency of cannabis use at age 38 y. Infrequent use was defined as weekly or less frequent use in the year preceding testing at age 38 y. Median use among infrequent and frequent adolescent-onset cannabis users was 14 (range: 0–52) and 365 (range: 100–365) d, respectively. Median use among infrequent and frequent adult-onset cannabis users was 6 (range: 0–52) and 365 (range: 100–365) d, respectively. IQ decline was apparent even after cessation of cannabis use for adolescent-onset former persistent cannabis users. Error bars = SEs.

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A controlled family study of cannabis users with and without psychosis

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Table 1
Number of subjects and relatives by sample.

	Sample 1 (n = 87)	Sample 2 (n = 84)	Sample 3 (n = 32)	Sample 4 (n = 79)
Probands	m = 42; f = 45	m = 40; f = 44	m = 15; f = 17	m = 60; f = 16
First degree relatives	338	333	137	360
Total relatives	1234	1517	460	1080

Chi^2 tests found no significant sex differences between groups.

Table 2
Lifetime morbid risk of psychiatric illnesses for first degree relatives (FDR) of probands with schizophrenia and controls, with regard to cannabis use.

	FDR of sample 1			FDR of sample 2			FDR of sample 3			FDR of sample 4		
	n = 338			n = 333			n = 137			n = 360		
Diagnosis	A	BZ	MR%	A	BZ	MR%	A	BZ	MR%	A	BZ	MR%
Schizophrenia	3	265	1.4	2	200.5	1.0	8	88	9.1	14	215	6.5
Bipolar disorder	3	215.5	1.4	6	203.5	3.0	3	87	3.4	13	216	6.0
Depression	18	201	9.1	29	187.5	15.5	9	84.5	10.7	28	201	13.9
Drug abuse	12	219.5	5.5	47	213.5	22.0	10	90	11.1	23	219	10.5

A is number of affected relatives; BZ is age-corrected number of relatives; MR% is morbid risk.
Significant between sample comparisons:
Samples 1 vs 2: Drug abuse $X^2 = 25.17$, $p < .001$.
Samples 1 vs 3: Schizophrenia, $p < .001$.
Samples 1 vs 4: Schizophrenia, $p = .001$; Bipolar, $p = .008$.
Samples 2 vs 3: Schizophrenia, $p = .001$; Drug abuse $X^2 = 4.90$, $p = .03$.
Samples 2 vs 4: Schizophrenia, $p = .002$; Drug abuse $X^2 = 10.49$, $p = .002$.

Table 3
Lifetime morbid risk of psychiatric illnesses for all relatives of probands with schizophrenia and controls, with regard to cannabis use.

	All relatives of sample 1			All relatives of sample 2			All relatives of sample 3			All relatives of sample 4		
	n = 1234			n = 1517			n = 460			n = 1080		
Diagnosis	A	BZ	MR%	A	BZ	MR%	A	BZ	MR%	A	BZ	MR%
Schizophrenia	7	794.5	0.9	12	874	1.4	13	315.5	4.1	38	718.5	5.3
Bipolar disorder	9	803	1.1	12	876.5	1.4	7	315.5	2.2	26	718	3.6
Depression	27	687.5	3.4	42	779.5	5.4	21	273.5	7.7	64	615	10.4
Drug abuse	36	811	4.4	87	897.5	9.7	21	317.5	6.6	50	724.5	6.9

A is number of affected relatives; BZ is age-corrected number of relatives; MR% is morbid risk.
Significant between sample comparisons:
Samples 1 vs 2: Drug Abuse $X^2 = 17.58$, $p < .001$.
Samples 1 vs 3: Schizophrenia $X^2 = 13.37$, $p < .001$; Depression $X^2 = 5.78$, $p = .01$.
Samples 1 vs 4: Schizophrenia $X^2 = 25.40$, $p < .001$; Bipolar $X^2 = 13.04$, $p < .001$; Depression $X^2 = 21.00$, $p < .001$; Drug Abuse $X^2 = 4.37$, $p = .04$.
Samples 2 vs 3: Schizophrenia $X^2 = 8.48$, $p = .004$.
Samples 2 vs 4: Schizophrenia $X^2 = 19.86$, $p < .001$; Bipolar $X^2 = 8.62$, $p = .003$; Depression $X^2 = 12.35$, $p < .001$; Drug Abuse $X^2 = 4.05$, $p = .04$.

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ORIGINAL ARTICLE

Genetic predisposition to schizophrenia associated with increased use of cannabis

RA Power[1,2], KJH Verweij[3], M Zuhair[1], GW Montgomery[4], AK Henders[4], AC Heath[5], PAF Madden[5], SE Medland[4], NR Wray[2] and NG Martin[4]

Table 1. Summary statistics of sample for cannabis use traits

	Users	*Non-users*
N	1011	1071
Mean age (s.e.)	41.3 (0.23)	53.0 (0.37)
Percentage female (%)	46.5	56.0
Mean age at initiation (s.e.)	19.6 (0.06)	—
Mean number of uses over lifetime (s.e.)	62.7 (4.56)	—

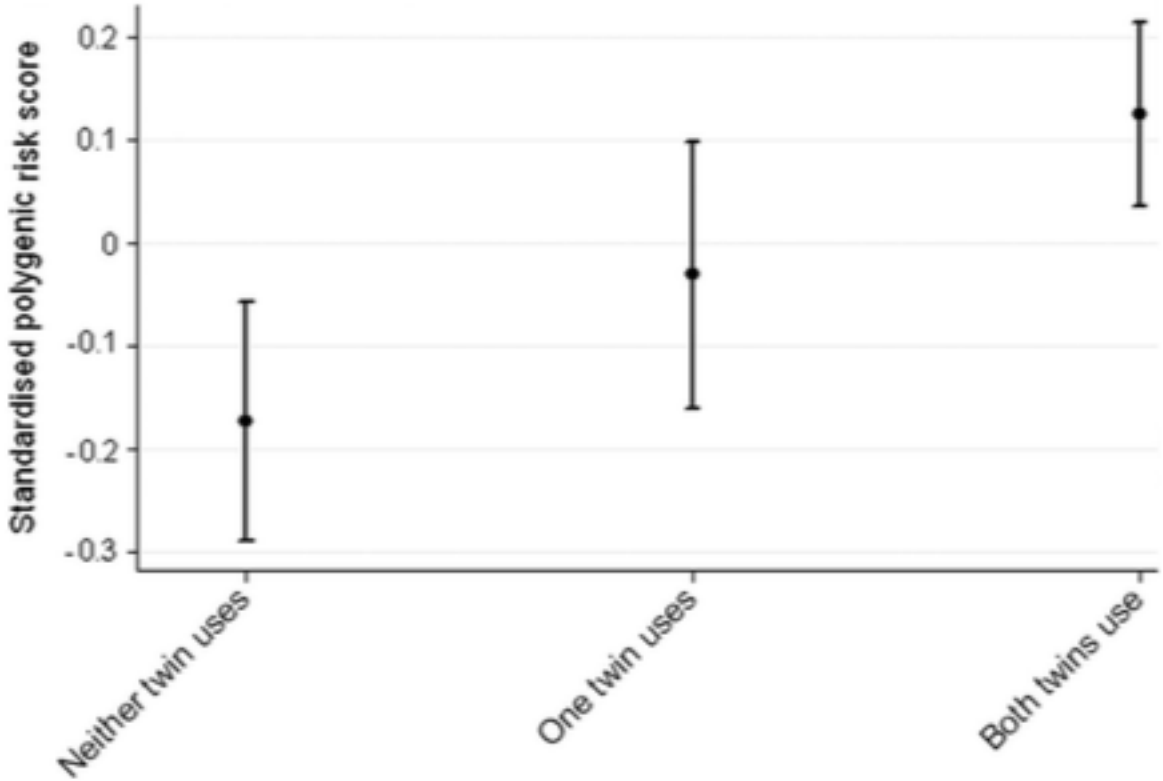

Figure 2. Mean standardized schizophrenia polygenic risk scores for pairs of twins when neither ($n = 272$), one ($n = 273$) or both twins ($n = 445$) had reported use of cannabis. An ordinal regression reported a significant association ($P = 0.001$).

Table 4
Families with first degree relatives affected by psychiatric illnesses.

	Families of sample 1		Families of sample 2		Families of sample 3		Families of sample 4	
	n = 87		n = 84		n = 32		n = 76	
Diagnosis	A	%	A	%	A	%	A	%
Schizophrenia	3	3.4	2	2.4	5	15.6	9	11.8
Bipolar disorder	3	3.4	6	7.1	3	9.4	12	15.8
Depression	17	19.5	23	27.4	7	21.9	22	29.0
Drug abuse	11	12.6	30	35.7	7	21.9	16	21.1

A is number of affected families; % is percentage of affected families.
Significant between sample comparisons:
Samples 1 vs 2: Drug Abuse $X^2 = 12.75$, $p < .001$.
Samples 1 vs 3: Schizophrenia, $p = .03$.
Samples 1 vs 4: Schizophrenia, $p < .001$; Bipolar $p = .001$.
Samples 2 vs 3: Schizophrenia, $p = .02$.
Samples 2 vs 4: Schizophrenia, $p = .02$; Drug Abuse $X^2 = 4.19$, $p = .04$.

Table 5
Families with any degree relative affected by psychiatric illnesses.

	Families of sample 1		Families of sample 2		Families of sample 3		Families of sample 4	
	n = 87		n = 84		n = 32		n = 76	
Diagnosis	A	%	A	%	A	%	A	%
Schizophrenia	5	5.8	10	11.9	8	25.0	24	31.2
Bipolar disorder	8	9.2	11	13.1	6	18.8	20	26.0
Depression	24	27.6	31	36.9	12	37.5	29	37.7
Drug abuse	21	24.1	35	41.7	11	34.4	25	32.5

A is number of affected families; % is percentage of affected families.
Significant between sample comparisons:
Samples 1 vs 2: Drug Abuse $X^2 = 6.20$, $p = .02$.
Samples 1 vs 3: Schizophrenia $X^2 = 9.07$, $p = .003$.
Samples 1 vs 4: Schizophrenia $X^2 = 18.79$, $p < .001$; Bipolar $X^2 = 8.55$, $p = .004$.
Samples 2 vs 4: Schizophrenia $X^2 = 9.23$, $p = .002$.

Conclusiones:
La marihuana causa daños irreversibles en el cerebro y
En el coeficiente intelectual del individuo
Cuando la consume antes de los 20 años.
Puede facilitar psicosis, esquizofrenia y trastorno bipolar
Su uso frecuente causa dependencia
También causa síndrome amotivacional

Los principios activos de la marihuana como con el delta-9-THC,
El canabidiol y la tetrahidrocanabivarina
pueden ser utilizados en medicina con potencial uso en el control
Del dolor, de la ansiedad, el insomnio y algún tipo de epilepsia