Cannabis Use In Youth

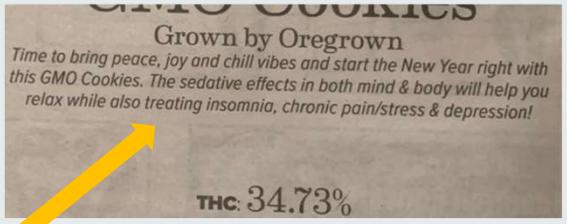
David C. Rettew, M.D.
Medical Director, Lane County Behavioral Health
Eugene, Oregon
Child & Adolescent Psychiatrist
Clinical Professor, Oregon Health and Science University
Clinical Assistant Professor, Western University of Health Sciences
David.Rettew@lanecountyor.gov

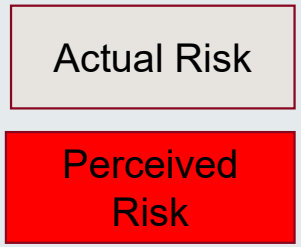
Note: Speaking on behalf of Lane County Behavioral Health but did not try to get additional clearance with OHSU or Western so not officially representing them

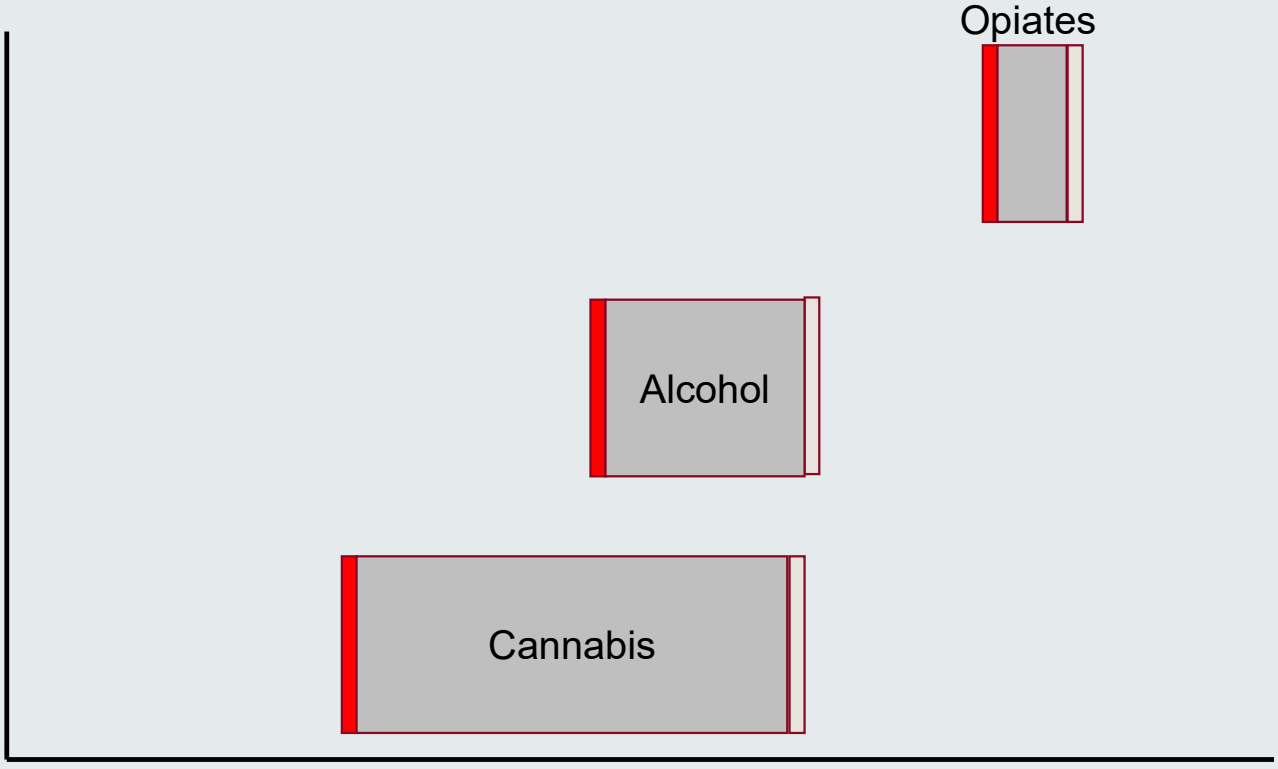
Disclosures

Source	Research Funding	Advisor/ Consultant	Employee	Speakers' Bureau	Books, Intellectual Property	In-kind Services (example: travel)	Stock or Equity	Honorarium or expenses for this presentation or meeting
PacificSource		x						
NIMH	X							
Oxford U Press					X			
Psychology Today					X			

The Big Picture

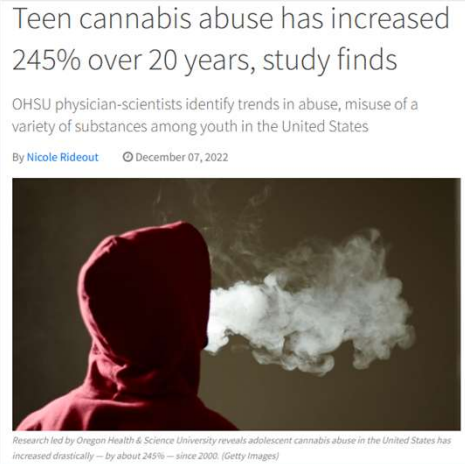






Key Statistics

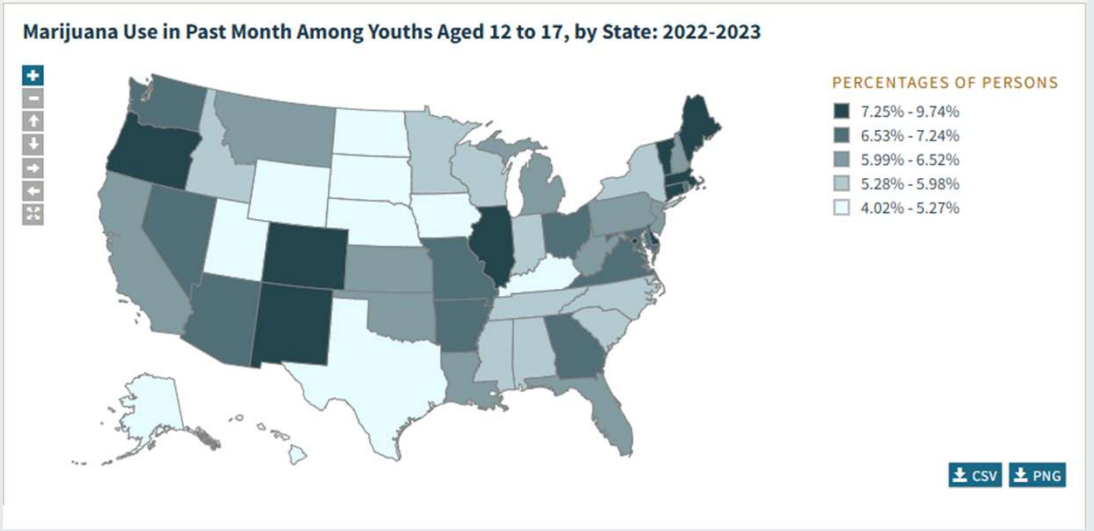
- While cannabis <u>use</u> rates among youth are relatively flat, cannabis use <u>disorder</u> rates are rising
  - Likely due to increased potency
  - Other rates of substance use dropping
- Oregon has 4th highest rates of youth cannabis use in the country
  - Past month 7.76% among ages 12-17
- Use of cannabis moves in lock step with amount of perceived risk
  - Oregon has <u>lowest youth perception of cannabis use risk in the US</u>


Teen cannabis abuse has increased 245% over 20 years, study finds

OHSU physician-scientists identify trends in abuse, misuse of a variety of substances among youth in the United States

By Nicole Rideout December 07, 2022

Research led by Oregon Health & Science University reveals adolescent cannabis abuse in the United States has increased drastically — by about 245% — since 2000. (Getty Images)



From National Survey on Drug Use and Health; Monitoring the Future Study; Oregon Student Health Survey

Cannabis Changes the Brain, Especially Young Ones

Long-term effects of marijuana use on the brain

Francesca M. Filbey[a,1], Sina Aslan[a,b], Vince D. Calhoun[c,d], Jeffrey S. Spence[a], Eswar Damaraju[c], Arvind Caprihan[c], and Judith Segall[c]

Neurobiology of Disease

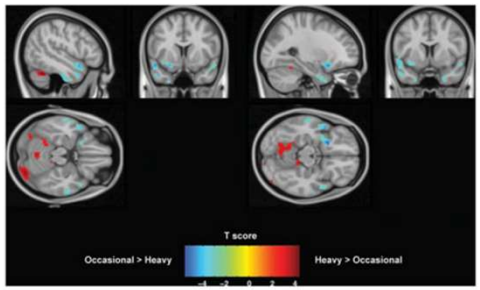
Cannabis Use Is Quantitatively Associated with Nucleus Accumbens and Amygdala Abnormalities in Young Adult Recreational Users

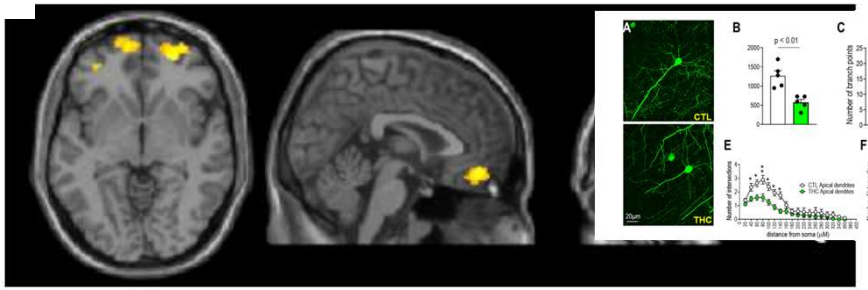
Cannabis Affects Cerebellar Volume and Sleep Differently in Men and Women

Katherine L. McPherson[1] Dardo G. Tomasi[1] Gene-Jack Wang[1] Peter Manza[1,2*] Nora D. Volkow[1,2*]

[1] National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda, MD, United States
[2] National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD, United States

npg
Long-term effects of cannabis on brain structure
G Battistella *et al*
2044





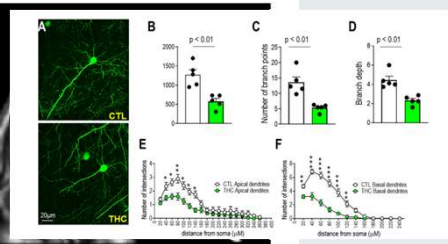


Fig. 1. Group comparison of the gray matter volume by SPM8 plus DARTEL sis demonstrates significant reduction of gray matter volume in bi- l orbitofrontal gyri (AAL atlas) in marijuana users compared with controls. side of the image represents the right hemisphere in axial view.

Psychological Medicine, Page 1 of 14. © Cambridge University Press 2015
doi:10.1017/S0033291715002342

Effect of high-potency cannabis on corpus callosum microstructure

Long-Term Cannabis Use and Cognitive Reserves and Hippocampal Volume in Midlife

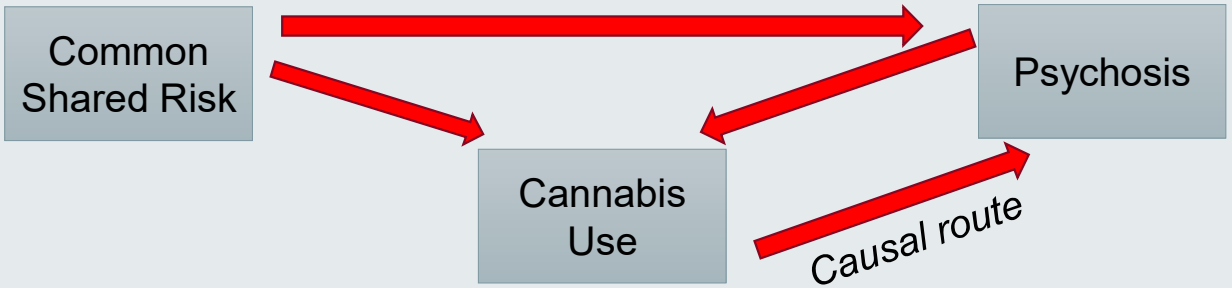
Madeline H. Meier, Ph.D., Avshalom Caspi, Ph.D., Annchen R. Knodt, M.Sc., Wayne Hall, Ph.D., Antony Ambler, M.Sc., HonaLee Harrington, B.A., Sean Hogan , B.A., Renate M. Houts, Ph.D., Richie Poulton, Ph.D., Sandhya Ramrakha, Ph.D., Ahmad R. Hariri, Ph.D., Terrie E. Moffitt, Ph.D.

Published Online: 8 Mar 2022 | https://doi.org/10.1176/appi.ajp.2021.21060664

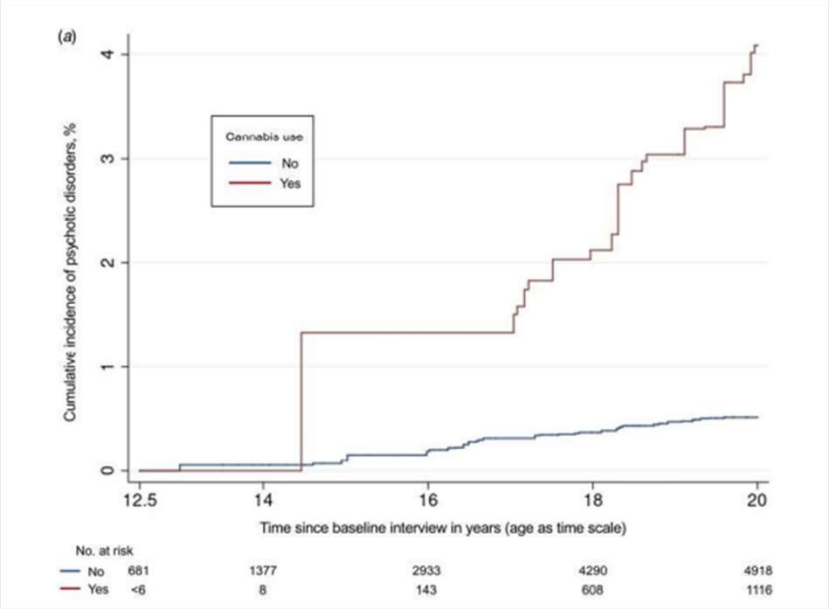
Aberrant hippocampal shape development in young adults with heavy cannabis use: Evidence from a longitudinal study

Hui Xu [a, b], Dandong Li [a], Bo Yin [a]

Cannabis and Psychotic Disorders

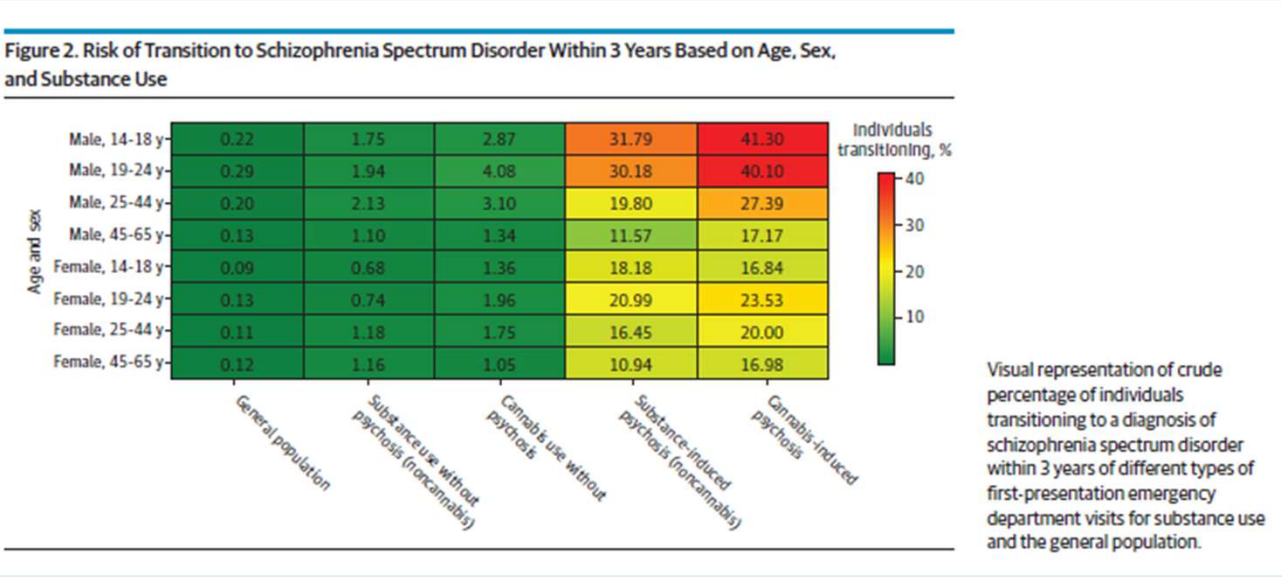


- Many studies show that cannabis use in adolescence is related up to an 11x risk of developing of psychotic disorder
  - Question is HOW these variables are related
- Best estimates are that ALL of these pathways (including causal) have a role in the association between cannabis and schizophrenia



Gillespe & Kendler, JAMA Psychiatry, 2020; McDonald et al., 2024

Cannabis and Psychotic Disorders



- Large Canadian study of nearly 10 million people
- Presenting to ED for substance use (with or without psychosis) associated with higher rates of conversion to psychotic disorder
- Cannabis had strongest link: **Over 200x** more likely to covert with substance use psychosis

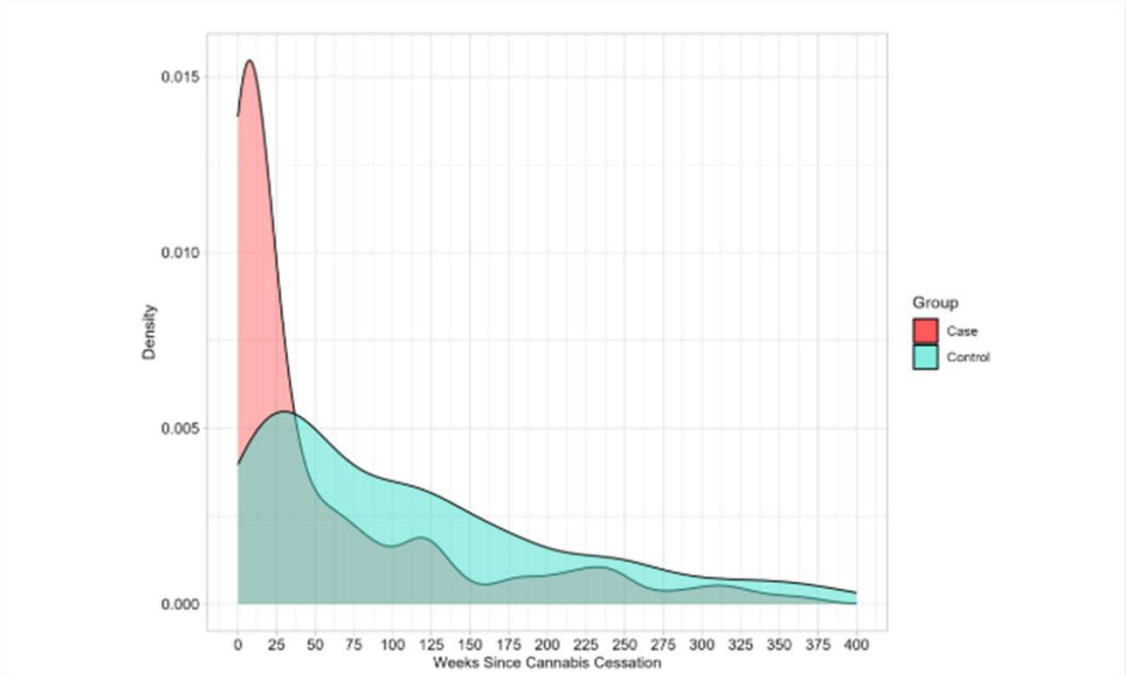
Project ECHO Oregon ECHO Network

Partner logo

Myran et al., JAMA Psychiatry, 2023

Cessation of Cannabis and Lowering Risk of Psychosis

- Case-control study from Europe and Brazil
- Risk of psychosis found to decline with duration of abstinence after cessation of cannabis use
- Risk back to population baseline after 37 weeks of abstinence
- Risk maintained for up to 3 years for those with heavy use of high potency products

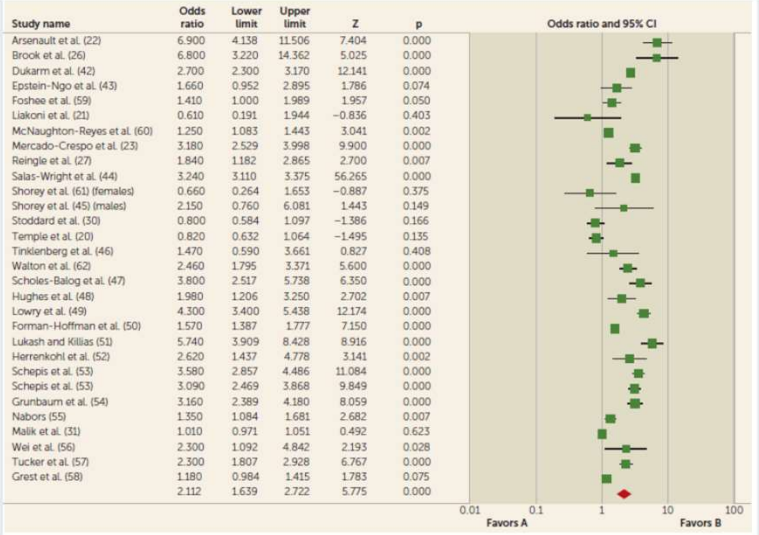


Bond et al., CJP, 2025

Cannabis and Violence

Association Between the Use of Cannabis and Physical Violence in Youths: A Meta-Analytical Investigation

Laura Dellazizzo, M.Sc., Stéphane Potvin, Ph.D., Bo Yi Dou, Mélissa Beaudoin, M.Sc., Mimosa Luigi, B.Sc., Charles-Édouard Giguère, M.Sc., Alexandre Dumais, M.D., Ph.D.



Study name	Odds ratio	Lower limit	Upper limit	Z	p
Arsenault et al. (22)	6.900	4.138	11.506	7.404	0.000
Brook et al. (26)	6.800	3.220	14.362	5.025	0.000
Dukarm et al. (42)	2.700	2.300	3.170	12.141	0.000
Epstein-Ngo et al. (43)	1.660	0.952	2.895	1.786	0.074
Foshee et al. (59)	1.410	1.000	1.989	1.957	0.050
Liakoni et al. (21)	0.610	0.191	1.944	−0.836	0.403
McNaughton-Reyes et al. (60)	1.250	1.083	1.443	3.041	0.002
Mercado-Crespo et al. (23)	3.180	2.529	3.998	9.900	0.000
Reingle et al. (27)	1.840	1.182	2.865	2.700	0.007
Salas-Wright et al. (44)	3.240	3.110	3.375	56.265	0.000
Shorey et al. (61) (females)	0.660	0.264	1.653	−0.887	0.375
Shorey et al. (45) (males)	2.150	0.760	6.081	1.443	0.149
Stoddard et al. (30)	0.800	0.584	1.097	−1.386	0.166
Temple et al. (20)	0.820	0.632	1.064	−1.495	0.135
Tinklenberg et al. (46)	1.470	0.590	3.661	0.827	0.408
Walton et al. (62)	2.460	1.795	3.371	5.600	0.000
Scholes-Balog et al. (47)	3.800	2.517	5.738	6.350	0.000
Hughes et al. (48)	1.980	1.206	3.250	2.702	0.007
Lowry et al. (49)	4.300	3.400	5.438	12.174	0.000
Forman-Hoffman et al. (50)	1.570	1.387	1.777	7.150	0.000
Lukash and Killias (51)	5.740	3.909	8.428	8.916	0.000
Herrenkohl et al. (52)	2.620	1.437	4.778	3.141	0.002
Schepis et al. (53)	3.580	2.857	4.486	11.084	0.000
Schepis et al. (53)	3.090	2.469	3.868	9.849	0.000
Grunbaum et al. (54)	3.160	2.389	4.180	8.059	0.000
Nabors (55)	1.350	1.084	1.681	2.682	0.007
Malik et al. (31)	1.010	0.971	1.051	0.492	0.623
Wei et al. (56)	2.300	1.092	4.842	2.193	0.028
Tucker et al. (57)	2.300	1.807	2.928	6.767	0.000
Grest et al. (58)	1.180	0.984	1.415	1.783	0.075
	2.112	1.639	2.722	5.775	0.000

[a] Young adults were <30 years old. One study (53) estimated the effect for boys and girls separately. Favors A=favors non-perpetration of violence, favors B=favors perpetration of violence.

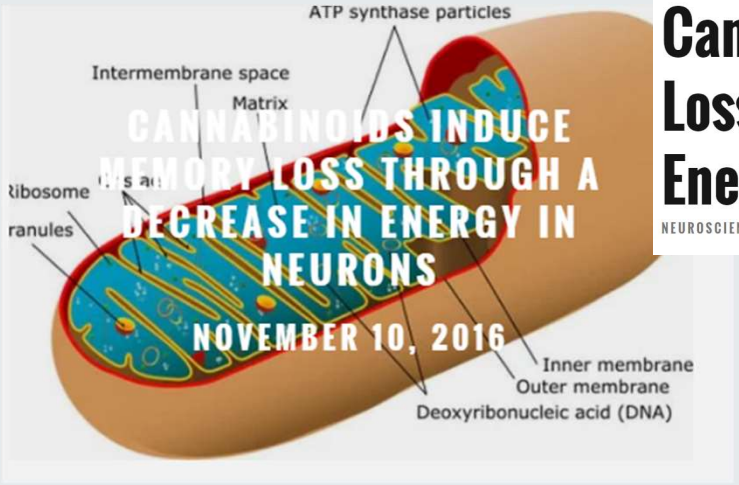
"*this study suggests that cannabis use appears to be a contributing factor in the perpetration of violence*."

Cognitive Function

Strong evidence of impairment in attention, memory, learning when intoxicated (Volkow et al., 2016)

2 Meta-analyses show evidence of poorer neuropsychological test performance (executive function, verbal ability, attention, memory) related to longer term use (Grant et al., 2003; Schreiner et al., 2012)

- Related to age on onset, frequency, length of abstinence
- BUT restricting studies to those with longer abstinence shows no differences in performance



Cannabinoids Induce Memory Loss Through a Decrease in Energy in Neurons

NEUROSCIENCE NEWS × NOVEMBER 10, 2016

Study from Nature Nov 2016

Cannabis bind to mitochondria (energy factories) in hippocampus brain cells (area highly involved in memory) leading to less activation

Cannabis and IQ

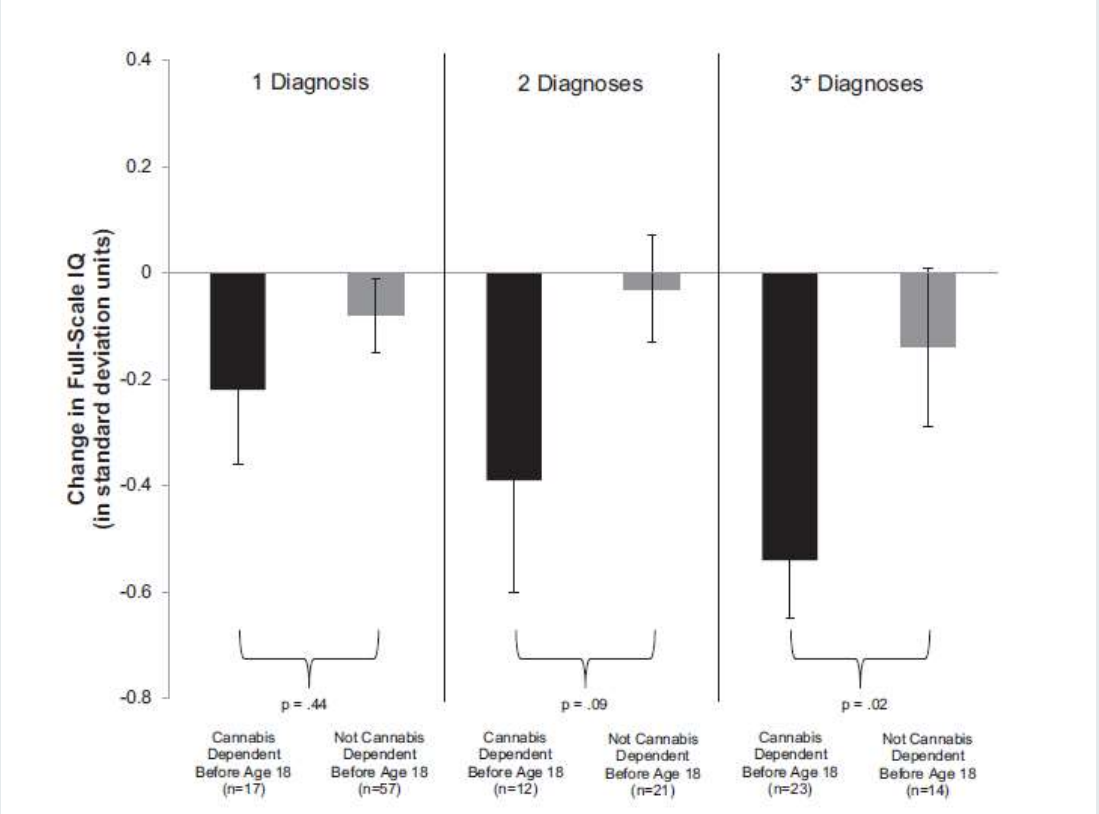
Dunedin study found IQ drop of 8 points from adolescence to adulthood among heavy users who started in adolescence

Deficits related to frequency and duration of use and age of initiation (adolescence)

Recovery after quitting inconsistently found

Subsequent study did not find evidence of IQ drop after controlling for other factors (Jackson et al., 2016)

- Much lower threshold for use



Meier et al., PNAS, 2012

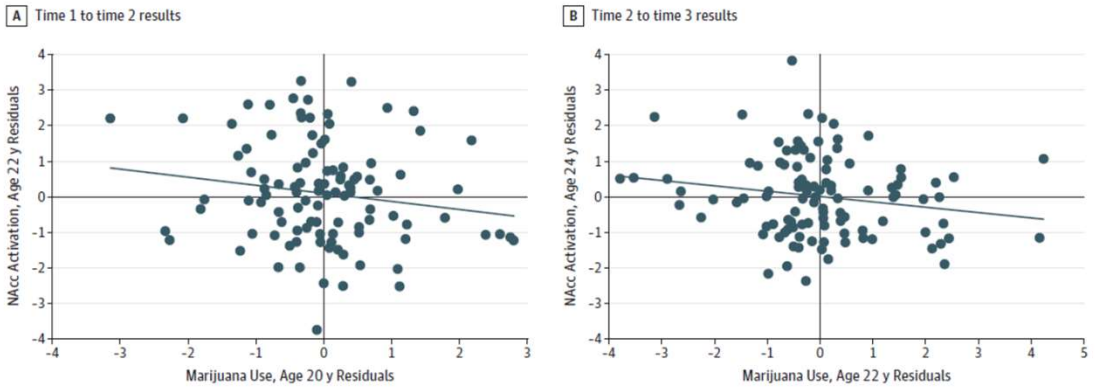
Cannabis and Motivation

JAMA Psychiatry | Original Investigation

Association of Marijuana Use With Blunted Nucleus Accumbens Response to Reward Anticipation

Meghan E. Martz, MS; Elisa M. Trucco, PhD; Lora M. Cope, PhD; Jillian E. Hardee, PhD; Jennifer M. Jester, PhD; Robert A. Zucker, PhD; Mary M. Heitzeg, PhD

Figure 2. Prospective Associations Between Marijuana Use and Nucleus Accumbens (NAcc) Activation During Reward Anticipation

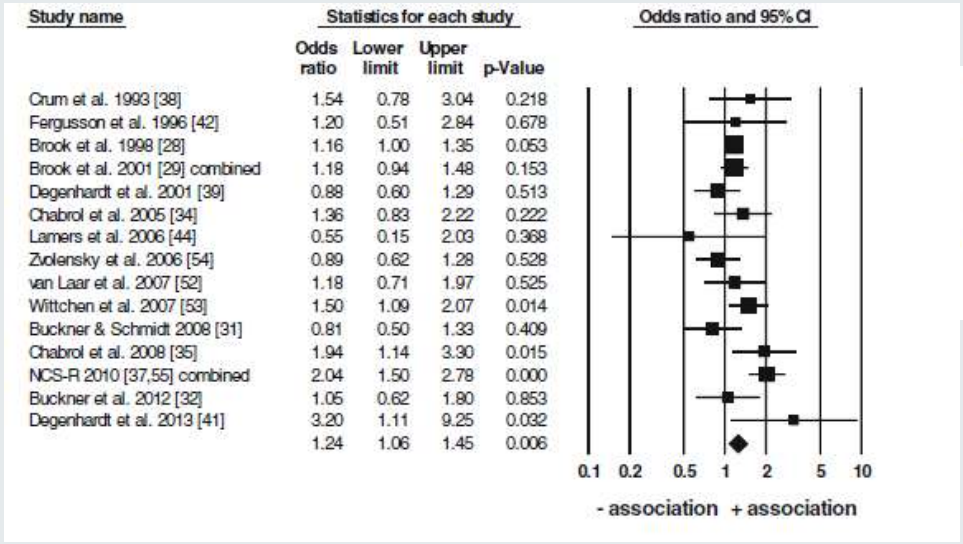


A, Past-year marijuana use at age 20 years (time 1) and NAcc activation during reward anticipation at 22 years (time 2). B, Past-year marijuana use at 22 years (time 2) and NAcc activation during reward anticipation at 24 years (time 3). Both partial regression plots controlled for all covariates included in cross-lagged analyses. Circles indicate data points for each participant; horizontal line, coefficient line.

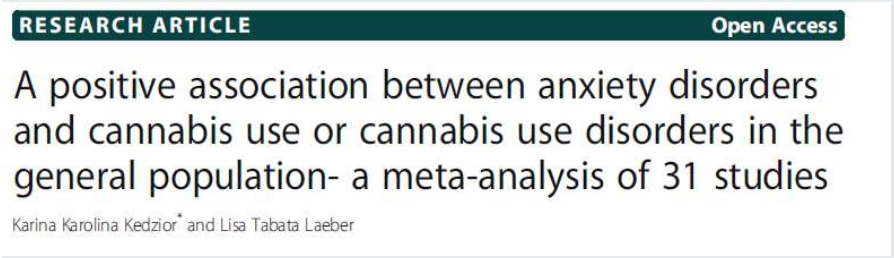
Cannabis use related to decreased future activity in major reward center of the brain

Martz et al., 2016

Cannabis and Anxiety



Study name	Odds ratio	Lower limit	Upper limit	p-Value
Crum et al. 1993 [38]	1.54	0.78	3.04	0.218
Fergusson et al. 1996 [42]	1.20	0.51	2.84	0.678
Brook et al. 1998 [28]	1.16	1.00	1.35	0.053
Brook et al. 2001 [29] combined	1.18	0.94	1.48	0.153
Degenhardt et al. 2001 [39]	0.88	0.60	1.29	0.513
Chabrol et al. 2005 [34]	1.36	0.83	2.22	0.222
Lamers et al. 2006 [44]	0.55	0.15	2.03	0.368
Zvolensky et al. 2006 [54]	0.89	0.62	1.28	0.528
van Laar et al. 2007 [52]	1.18	0.71	1.97	0.525
Wittchen et al. 2007 [53]	1.50	1.09	2.07	0.014
Buckner & Schmidt 2008 [31]	0.81	0.50	1.33	0.409
Chabrol et al. 2008 [35]	1.94	1.14	3.30	0.015
NCS-R 2010 [37,55] combined	2.04	1.50	2.78	0.000
Buckner et al. 2012 [32]	1.05	0.62	1.80	0.853
Degenhardt et al. 2013 [41]	3.20	1.11	9.25	0.032
	1.24	1.06	1.45	0.006



RESEARCH ARTICLE Open Access

A positive association between anxiety disorders and cannabis use or cannabis use disorders in the general population- a meta-analysis of 31 studies

Karina Karolina Kedzior* and Lisa Tabata Laeber

- Overall association between cannabis use and increased anxiety disorders
- Clinically, often observe initial decrease followed by later increase
- Another meta-analysis did not find significant effect in young adults (Gobi et al., 2019)

Cannabis and Suicide

- Large meta-analysis that included study of over 23,000 adolescents found that cannabis use was related to over a tripling of the risk of a future suicide attempt during young adulthood
- Study found 37% increased risk of developing depression
- "*This translates to some 413 326 young adult cases of depression potentially attributable to cannabis exposure, considering that the population of young people between 18 and 34 years in the United States*."

Gobi et al., JAMA Psychiatry, 2019

Table 3. Toxicology test results among non-natural, non-homicide deaths, Colorado residents younger than 25 years (population of interest), 2010-2022‡

Toxicology result	Frequency	Percent (%) (n=2,233)
Toxicology test results available	2,223	
No substance	713	31.9%
Marijuana present	651	29.2%
Alcohol present	560	25.1%
Opioid present	558	25.0%
Amphetamine present	255	11.4%
Cocaine present	254	11.4%
Benzodiazepines present	185	8.3%
Antidepressant present	180	8.1%
Anticonvulsants present	72	3.2%
Antipsychotic present	51	2.3%
Carbon monoxide present	38	1.7%
Muscle relaxant present	9	0.4%
Barbiturates present	6	0.3%

Future Drug Use

- Most cannabis users do not go on to have drug problems with opiates, meth, etc.
- However, there is evidence that cannabis use increases likelihood of using even more dangerous drugs
- Studies that have attempted to control for potential confounds and genetic influences (discordant twin designs) continue to support this pathway (Lynskey et al., 2003, 2006)
- Evidence of “reverse gateway” with regard to tobacco smoking (Patton et al., 2005)
- Not specific to cannabis (alcohol too) and may be partially attributable to shared genetic risk, as in psychosis.

Offramps can also be
Used as onramps when it
Comes to substances

Parental THC Exposure Leads to Compulsive Heroin-Seeking and Altered Striatal Synaptic Plasticity in the Subsequent Generation

Henrietta Szutorisz[1,2], Jennifer A DiNieri[1,2], Eric Sweet[3], Gabor Egervari[1,2], Michael Michaelides[1,2], Jenna M Carter[1,2], Yanhua Ren[1,2], Michael L Miller[1,2], Robert D Blitzer[1,4] and Yasmin L Hurd*[,1,2,5]

[1]Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [4]Department of Pharmacology and Systems Therapeutics, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [5]James J Peters Veterans Medical Center, Bronx, NY, USA

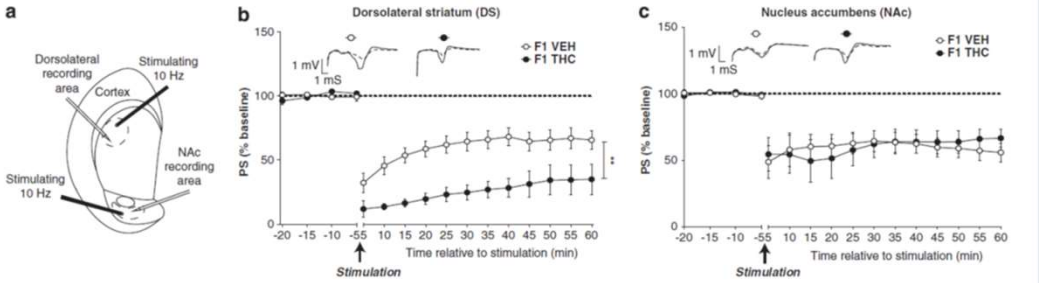
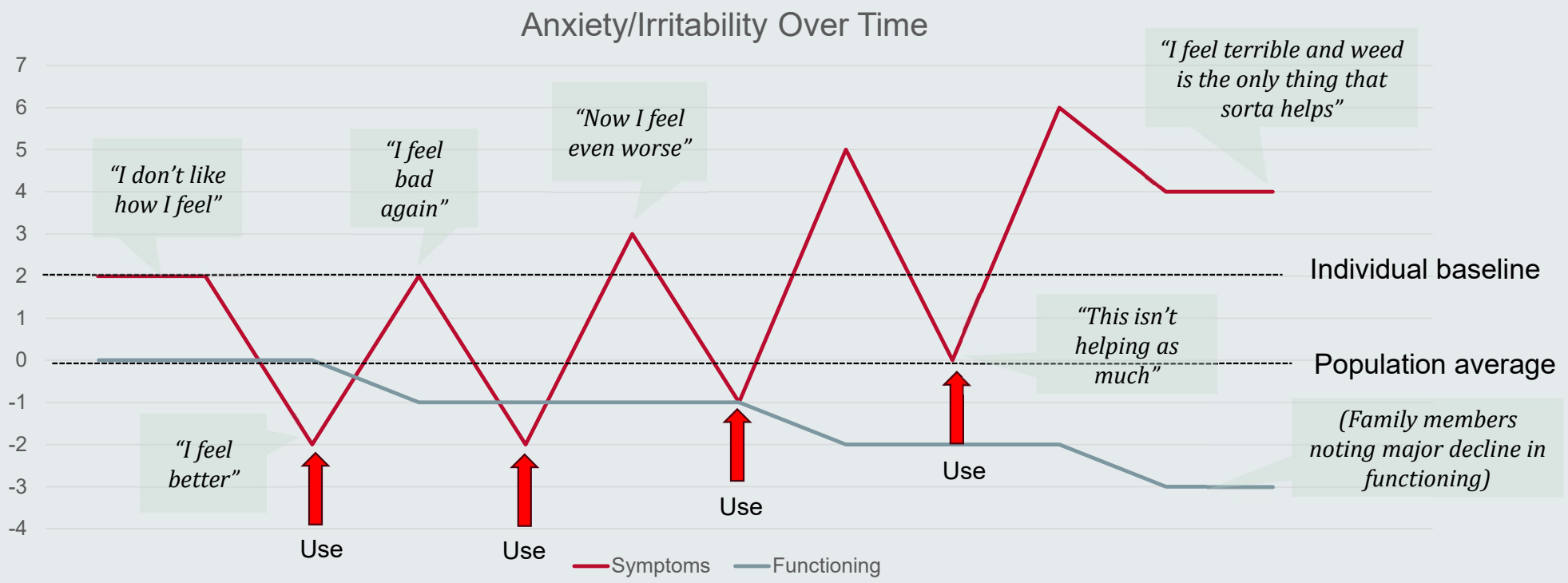


Figure 5 Parental THC exposure leads to increased LTD in the dorsal striatum of F1 offspring with parental germline THC exposure. (a) Schematic of a coronal striatal slice showing the general placement of the stimulating (filled symbol) and recording (open symbol) electrodes in the dorsolateral striatum (DS) and nucleus accumbens (NAc). (b) LTD in the dorsal striatum of rats in the THC group (filled symbols, $N = 4$) was enhanced relative to the vehicle control group (open symbols, $N = 9$; ** indicates $p < 0.01$ as a main effect of THC exposure; there was no significant interaction between time and group. Inset shows samples of superimposed averaged sample PSs recorded during the baseline period (solid line) and during the final 5 min of the experiment (dashed line). (c) LTD induced in NAc was unaffected by parental THC exposure ($N = 4$ THC group; $N = 9$ vehicle group). Sample traces as described in b.

- Exposure of THC to adolescent rats was associated not only with increased opiate use of the exposed rat but <u>also in their offspring</u>.
- Found to be related to changes in the activation of brain area called the dorsolateral striatum
- "*Evidence garnered in our current study now imply a 'cross-generational gateway' state in F1 offspring*."

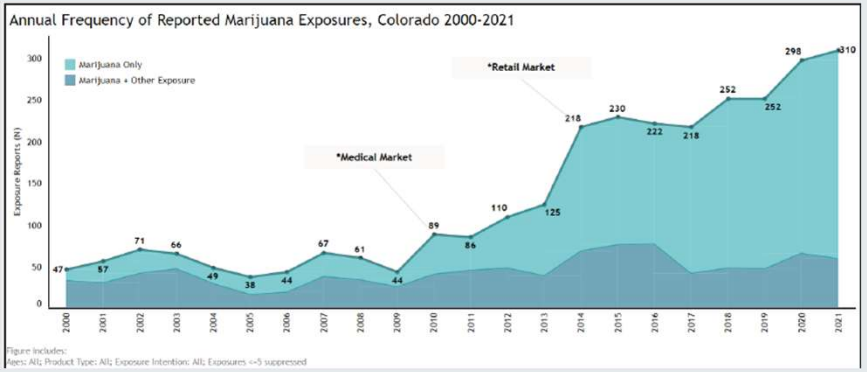
Course of Cannabis Use

A composite of many cases



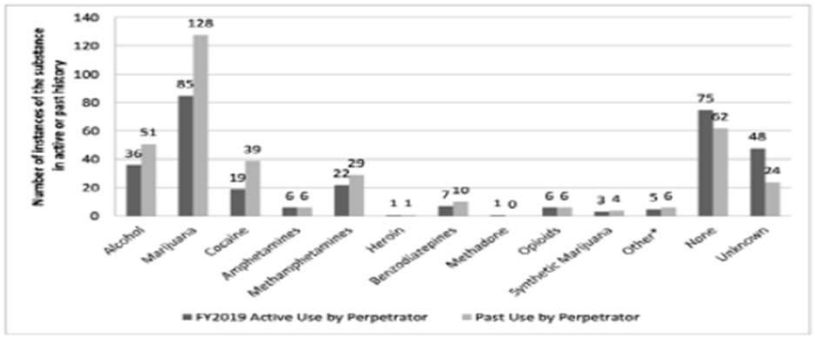
How Cannabis Hurts Youth

- Direct medical/psychiatric effects from youth use
- Indirect effects (car crashes)
- Parental use leading to neglect and abuse
- Parental use during pregnancy
- Accidental poisonings



Cannabis and Child Maltreatment statistics

Figure 11. Confirmed Child Abuse or Neglect Fatality by Substance Abuse by Perpetrator



*Other includes lighter fluid, Kratom, ecstasy, morphine and Benadryl.

https://www.dfps.state.tx.us/About_DFPS/Reports_and_Presentations/PEI/documents/2020/2020-03-01_FY2019_Child_Fatality_and_Near_Fatality_Annual_Report.pdf

Potential Steps to Decrease Public Health Impact of Cannabis Use

- Public health campaign to fight against misinformation
  - Incorporate strategies similar to successful tobacco campaign
- Increased availability of evidence-based treatment
  - e.g. contingency management
- Prevention programs
  - Planet Youth Program from Iceland and others
- Better data on use in Oregon
  - OR one of only states that does not participate in national Youth Risk Behavior Survey
- Regulation
  - Potency limits
- Stronger use of legal system
  - Enforcement of false advertising
  - Using court system more effectively for repeat youth users