From Pavlov to Placebos: Implications from Research for Traffic Safety

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Overview of today's webinar

- **From Pavlov to Placebos: Implications from Research for Traffic Safety**
  - Why does alcohol affect people differently at different times?
  - Why is it that someone who is sober says they would never drive after drinking, but make a different decision after they've been drinking?
  - How come someone's ability to "hold their liquor" can disappear in an instant?
  - How can cannabis impact attention, concentration, and memory?

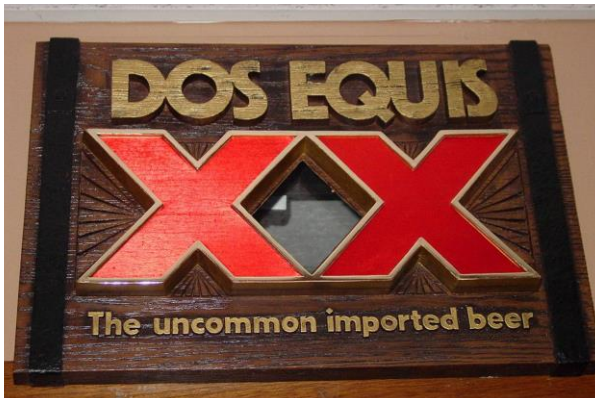
There are huge placebo and expectancy effects at play

Expectancies

- What are ways alcohol affects you positively in social situations?
- What are ways alcohol affects you in "not-so-good" ways in social situations?
- Have you ever had alcohol do different things for you at different times?

EXPECT

GET	Alcohol	No Alcohol
Alcohol		
No Alcohol		



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Taylor & Francis

Check for updates

Placebo Effects of Edible Cannabis: Reported Intoxication Effects at a 30-Minute Delay

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[a]Fellow, National Center for PTSD Training and Dissemination Division, VA Palo Alto Health Care System, Menlo Park, CA, USA; [b]Professor, Department of Psychology, University at Albany SUNY, Albany, NY, USA; [c]Graduate Student, Department of Psychology, University at Albany SUNY, Albany, NY, USA; [d]Adjunct Assistant Professor, Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

ABSTRACT

Previous research has demonstrated the ability of non-active smoked cannabis cigarettes to induce subjective effects of intoxication (i.e., placebo effect). No studies have been conduced to test whether edible forms of cannabis, which are associated with a significant delay in onset of effect, are able to induce a placebo effect. In the present study, 20 participants were told that they would receive an edible cannabis lollipop containing a high dose of tetrahydrocannabinol (THC), but were instead given a placebo control. Measures of intoxication and mood were taken at baseline, 30 minutes, and 60 minutes post-ingestion of the placebo lollipop. Results of four repeated-measures ANOVAs found significant and quadratic changes across time in cannabis (ARCI m-scale) intoxication ($F(2,18) = 4.90$, $p = .01$, $\eta^2 = .22$) and negative mood ($F(2,18) = 3.99$, $p = .05$, $\eta^2 = .19$). Changes in positive mood and the overall measure of general intoxication (ARCI) failed to reach significance. The present study provides preliminary evidence that a placebo effect can be induced with inert edible agents when participants are told that they are receiving active THC. This is the first known study to demonstrate an edible cannabis intoxication placebo effect.

ARTICLE HISTORY
Received 12 January 2017
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KEYWORDS
Cannabis; edibles; expectancy; marijuana; placebo

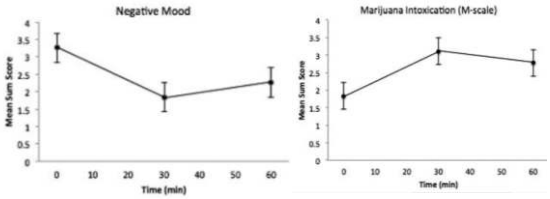
Loflin, et al., 2017

Loflin, et al. (2017)

- **Asked participants to refrain at least 8 hours before study**
- **Told to plan for a variable end (1.5-6 hours depending on dose they would receive)**
- **Told they would be in one of three rooms (no dose, low THC, high THC)**
- **Cubicles (no interaction), and had to rate music and comedy clips, color designs, and compute math problems**

Loflin, et al. (2017)

- **Used Hemp Pops**
  - **Hemp seed oil (no active elements of THC or CBD), glucose syrup, citric acid, sugar, natural flavors, and colors #2 and #5**



Placebo effects need to be explored

- **For example…**
  - **Sativa – typically described as uplifting and energetic**
  - **Indica – typically described as relaxing and calming**
- **"We would all prefer simple nostrums to explain complex systems, but this is futile and even potentially dangerous in the context of a psychoactive drug such as cannabis" (Piomelli & Russo, 2016, *Cannabis and Cannabinoid Research*)**
- **Differences in observed effects could be due to other content (which is rarely assayed) or what is reported to potential consumers**

The science on how (and why) decision making is affected by alcohol is well established

Alcohol-Related Consequences

n =26,139 students in the undergraduate reference group from Fall 2017

- Among undergraduate students who drink, within the past 12 months as a consequence of drinking…
  - 33.0% did something they later regretted
  - 28.6% forgot where they were/what they did
  - 21.0% had unprotected sex
  - 13.2% physically injured themselves

American College Health Association, 2018

Blood Alcohol Level

- .02% Relaxed
- .04% Relaxation continues, Buzz develops
- .06% Cognitive judgment is impaired

"Alcohol Myopia"

Impelling Cues

Alcohol impairs information processing, **narrowing attention** to only the most salient internal and environmental cues.

?

Inhibiting Cues

If a person feels like they can "hold their liquor," that likely could "disappear" in a new setting

Tolerance

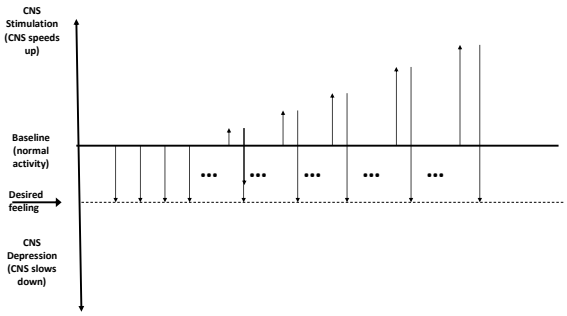
Applying Laboratory Research:
Drug Anticipation and the Treatment of Drug Addiction

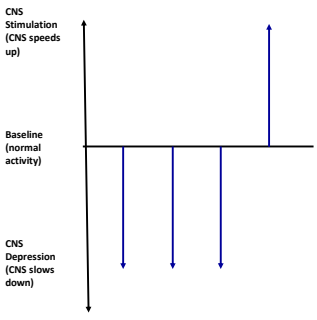
Shepard Siegel and Barbara M. C. Ramos
McMaster University

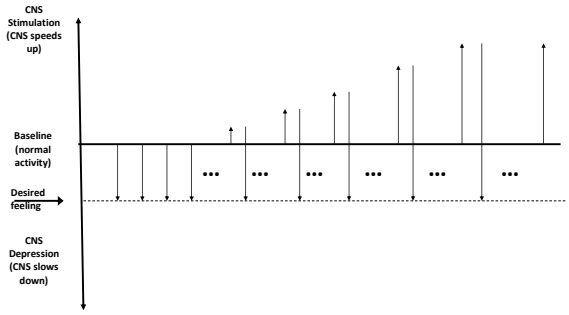
Siegel, S. & Ramos, B.M.C. (2002) Applying laboratory research: Drug anticipation and the treatment of drug addiction. *Experimental and Clinical Psychopharmacology, 10,* 162-183.

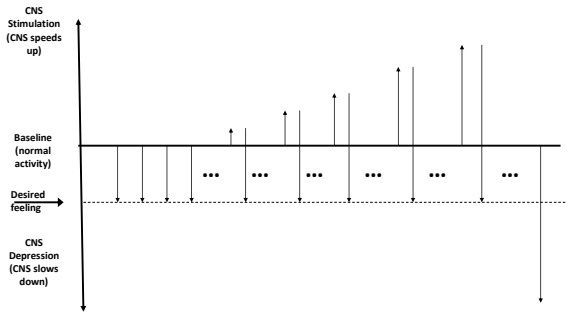
Types of learning

- **Classical Conditioning**
  - Pavlov
    - Association of two events such that one event acquires the ability to elicit responses formerly associated with the other event









Considering cues

- **Even taste can be a cue**
  - Siegel (2011) noted that college students who consume alcohol in the presence of usual taste cues (e.g., a beer flavored beverage) display greater tolerance to intoxicating effects than when consumed in a novel blue, peppermint-flavored beverage of the same strength.

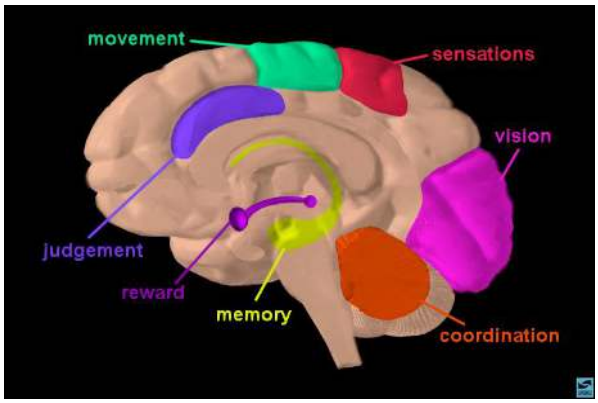
Conclusion

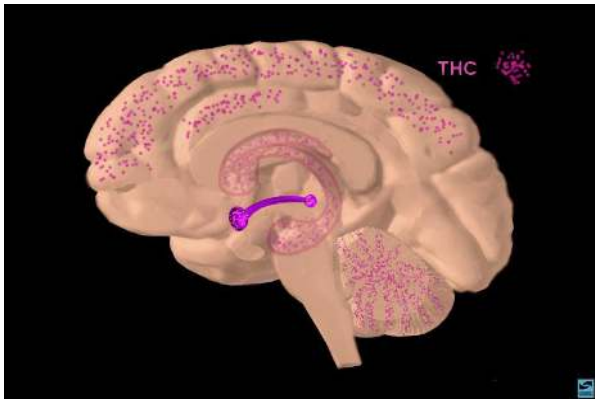
- **"The situational specificity of tolerance"**
  - **If alcohol is presented "in a manner divorced from the usual alcohol-associated stimuli, the effects of the alcohol are enhanced (Siegel, 2011, p. 358)."**

Implications for the college setting

- **Consider high-risk events that can be associated with changes in cues:**
  - **Spring Break**
  - **21st birthdays**
  - **Halloween**
  - **Formals/dances**
- **Students studying abroad**
- **As a field, we still need to research ways to incorporate this information into prevention/intervention efforts, both for those who make the choice to drink and for those who may be bystanders intervening on someone's behalf**

There's some good research on marijuana's effects (with clear relevance to young adults) – here are some highlights.





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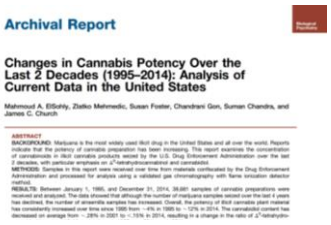
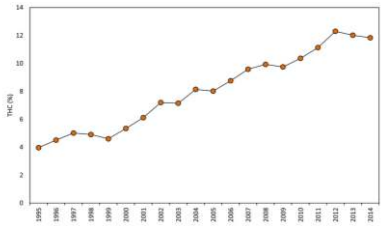


Archival Report

Changes in Cannabis Potency Over the Last 2 Decades (1995–2014): Analysis of Current Data in the United States

Mahmoud A. ElSohly, Zlatko Mehmedic, Susan Foster, Chandrani Gon, Suman Chandra, and James C. Church



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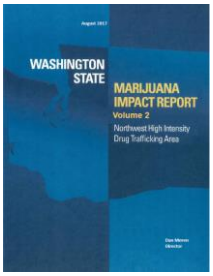
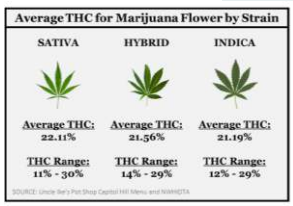
Washington State Impact Report

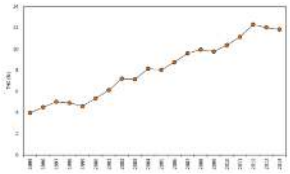


www.mfiles.org



Average potency (nation) = 13.18%
Average potency (Seattle) = 21.62%

Concentrates average potency (nation) = 55.85%
Concentrates average potency (Seattle) = 71.71%



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Cross-sectional comparisons from Young Adult Health Survey

Source: DBHR/CSHRB Young Adult Health Survey Year 4 data report

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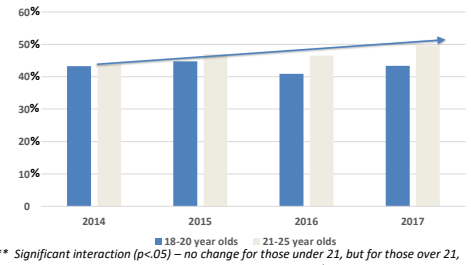
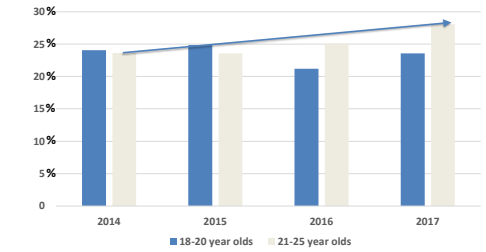
Past year personal marijuana use by age group



*** Significant interaction (p<.05) – no change for those under 21, but for those over 21, there is an increasing linear trend in marijuana use over time/cohort (p<.05); additionally, the difference is statistically significant for cohort 4 vs. cohort 1 (p<.01).***

Source: DBHR/CSHRB Young Adult Health Survey Year 4 data report

Past month personal marijuana use by age group



*** no linear trend over time for those 18-20; among those 21-25, we see a significant increasing trend over time in at least monthly use (p<.05) and, when treating cohort as a dummy variable, we also see a significant difference between Cohort 4 and Cohort 1 (p<.05) ****

Longitudinal comparisons

Cohort 1

Personal marijuana use in past year

	% reporting any personal use
2014	37.80%
2015	39.81%
2016	39.30%
2017	46.07%

*** trend for increasing likelihood of personal marijuana use over time, p<.001****
*** 2017 is significantly higher than 2014, p<.001****

Personal marijuana use – weekly use

	% reporting any personal – weekly
2014	12.03%
2015	12.17%
2016	13.84%
2017	16.59%

*** trend for increasing likelihood of personal marijuana use over time, p<.001****
*** 2017 is significantly higher than 2014, p<.001****

Source: DBHR/CSHRB Young Adult Health Survey Year 4 data report

Longitudinal comparisons

Cohort 2

Personal marijuana use

Personal marijuana use in past year

	% reporting any personal use
2015	46.74%
2016	48.08%
2017	52.16%

*** trend for increasing likelihood of personal marijuana use over time, p<.01***
*** 2017 is significantly higher than 2015, p<.01***

Personal marijuana use – weekly use

	% reporting any personal – weekly
2015	13.72%
2016	18.43%
2017	18.46%

*** trend for increasing likelihood of personal marijuana use over time, p<.001***
*** 2016 is significantly higher than 2015, p<.001; 2017 is significantly higher than 2015, p<.001***

Source: DBHR/CSHRB Young Adult Health Survey Year 4 data report

Published guidelines on "lower risk" use

AJPH POLICY

Lower-Risk Cannabis Use Guidelines: A Comprehensive Update of Evidence and Recommendations

Benedikt Fischer, PhD, Cayley Russell, MA, Pamela Sabioni, PhD, Wim van den Brink, MD, PhD, Bernard Le Foll, MD, PhD, Wayne Hall, PhD, Jürgen Rehm, PhD, and Robin Room, PhD

Background. Cannabis use is common in North America, especially among young people, and is associated with a risk of various acute and chronic adverse health outcomes. Cannabis control regimes are evolving, for example toward a national legalization policy in Canada, with the aim to improve public health, and thus require evidence-based interventions. As cannabis-related health outcomes may be influenced by behaviors that are modifiable by the user, evidence-based Lower-Risk Cannabis Use Guidelines (LRCUG)—akin to similar guidelines in other health fields—offer a valuable, targeted prevention tool to improve public health outcomes.

Objectives. To systematically review, update, and quality-grade evidence on behavioral factors determining adverse health outcomes from cannabis that may be

Main results. For most recommendations, there was at least "substantial" (i.e., good-quality) evidence. We developed 10 major recommendations for lower-risk use: (1) the most effective way to avoid cannabis use–related health risks is abstinence, (2) avoid early age initiation of cannabis use (i.e., definitively before the age of 16 years), (3) choose low-potency tetrahydrocannabinol (THC) or balanced THC-to-cannabidiol (CBD)–ratio cannabis products, (4) abstain from using synthetic cannabinoids, (5) avoid combusted cannabis inhalation and give preference to nonsmoking use methods, (6) avoid deep or other risky inhalation practices, (7) avoid high-frequency (e.g., daily or near-daily) cannabis use, (8) abstain from cannabis-impaired driving, (9) populations at higher risk for cannabis use–related health problems should avoid use altogether, and

RECOMMENDATIONS

Recommendation 1: The most effective way to avoid any risks of cannabis use is to abstain from use. Those who decide to use need to recognize that they incur risks of a variety of—acute and long-term—adverse health and social outcomes. These risks will vary in their likelihood and severity with user characteristics, use patterns, and product qualities, and so may not be the same from user to user or use episode to another. *[Evidence Grade: Have received.]*

Recommendation 2: Early initiation of cannabis use (i.e., most clearly that which begins before age 16 years) is associated with multiple subsequent adverse health and social effects in young adult life. These effects are particularly pronounced in early-onset users who also engage in intensive and frequent use. This may be in part because frequent cannabis use affects the developing brain. Prevention messages should emphasize that, the later cannabis use is initiated, the lower the risks will be for adverse effects on the user's general health and welfare throughout later life. *[Evidence Grade: Substantial.]*

Recommendation 3: High THC-content products are generally associated with higher risks of various (acute and chronic) mental and behavioral problem outcomes. Users should know the nature and composition of the cannabis products that they use, and ideally use cannabis products with low THC content. Given the evidence of CBD's attenuating effects on some THC-related outcomes, it is advisable to use cannabis containing high CBD:THC ratios. *[Evidence Grade: Substantial.]*

Recommendation 4: Recent reviews on synthetic cannabinoids indicate markedly more acute and severe adverse health effects from the use of these products (including instances of death). The use of these products should be avoided. *[Evidence Grade: Limited.]*

Recommendation 5: Regular inhalation of combusted cannabis adversely affects respiratory health outcomes. While alternative delivery methods come with their own risks, it is generally preferable to avoid routes of administration that involve smoking combusted cannabis material (e.g., by using vaporizers or edibles). Use of edibles eliminates respiratory risks, but the delayed onset of psychoactive effect may result in the use of larger than intended doses and subsequently increased (mainly acute, e.g., from impairment) adverse effects. *[Evidence Grade: Substantial.]*

Recommendation 6: Users should avoid practices such as "deep inhalation," breath-holding, or the Valsalva maneuver to increase psychoactive ingredient absorption when smoking cannabis, as these practices disproportionately increase the intake of toxic material into the pulmonary system. *[Evidence Grade: Limited.]*

Recommendation 7: Frequent or intensive (e.g., daily or near-daily) cannabis use is strongly associated with higher risks of experiencing adverse health and social outcomes related to cannabis use. Users should be aware and vigilant to keep their own cannabis use—and that of friends, peers, or fellow users—occasional (e.g., use only on 1 day/week, weekend use only, etc.) at most. *[Evidence Grade: Substantial.]*

Recommendation 8: Driving while impaired from cannabis is associated with an increased risk of involvement in motor-vehicle accidents. It is recommended that users categorically refrain from driving (or operating other machinery or mobility devices) for at least 6 hours after using cannabis. This wait time may need to be longer, depending on the user and the properties of the specific cannabis product used. Besides these behavioral recommendations, users are bound by locally applicable legal limits concerning cannabis impairment and driving. The use of both cannabis and alcohol results in multiply increased impairment and risks for driving, and categorically should be avoided. *[Evidence Grade: Substantial.]*

Recommendation 9: There are some populations at probable higher risk for cannabis-related adverse effects who should refrain from using cannabis. These include individuals with predisposition for, or a first-degree family history of, psychosis and substance use disorders, as well as pregnant women (primarily to avoid adverse effects on the fetus or newborn). These recommendations, in part, are based on precautionary principles. *[Evidence Grade: Substantial.]*

Recommendation 10: While data are sparse, it is likely that the combination of some of the risk behaviors listed above will magnify the risk of adverse outcomes from cannabis use. For example, early-onset use involving frequent use of high-potency cannabis is likely to disproportionately increase the risks of experiencing acute or chronic problems. Preventing these combined high-risk patterns of use should be avoided by the user and a policy focus. *[Evidence Grade: Limited.]*

Impact on attention, concentration, and memory

Marijuana and cognitive abilities

- **Effects on the brain**
  - Hippocampus
    - Attention, concentration, and memory
  - Research with college students shows impact on these even 24 hours after last use (Pope & Yurgelun-Todd, 1996)
  - After daily use, takes 28 days for impact on attention, concentration, and memory to go away (Pope, et al., 2001)
  - Hanson et al. (2010):
    - Deficits in verbal learning (takes 2 weeks to improve)
    - Deficits in verbal working memory (takes 3 weeks to improve)
    - Deficits in attention (still present at 3 weeks)

Relationship Between Cannabis Use and Academic Success

- More frequent marijuana use is associate with more discontinuous enrollment, skipping more classes, and lower GPAs (Arria, et al., 2013, 2015)
- Any marijuana use is associated with lower GPA, and decreasing and frequent marijuana use over time is associated with less current enrollment and being less likely to graduate on time (Sureken, et al., 2016)

Relationship Between Cannabis Use, Alcohol Use, and Academic Success

- Alcohol and marijuana are both associated with lower GPA; when entered in same regression, effects of alcohol became non-significant (Bolin, Pate, McClintock, 2017)
- Students using both marijuana and alcohol at moderate to high levels have significantly lower GPAs over two years (Meda, et al., 2017)
  - Students who moderate or curtail substance use improved GPA (Meda, et al., 2017)

Considering withdrawal (and management of withdrawal)

Motivations for Use

- Research team utilized qualitative open-ended responses for using marijuana among incoming first year college students to identify which motivations were most salient to this population

Lee, Neighbors, & Woods (2007)

Motivations for Use

Motive Category	Proportion of participants endorsing motive	Proportion of primary motives
Enjoyment/fun (e.g., be happy, get high, enjoy feeling)	52.14%	24.03%
Conformity (e.g., peer pressure, friends do it)	42.81%	16.40%
Experimentation (e.g., new experience, curiosity)	41.25%	29.36%
Social enhancement (e.g., bonding with friends, hang out)	25.71%	8.66%
Boredom (e.g., something to do, nothing better to do)	25.08%	4.15%
Relaxation (e.g., to relax, helps me sleep)	24.64%	6.97%
Coping (e.g., depressed, relieve stress)	18.14%	5.10%
Availability (e.g., easy to get, it was offered)	13.74%	2.23%
Relative low risk (e.g., low health risk, no hangover)	10.88%	0.95%
Altered perception or perspectives (e.g., to enhance experiences, makes things more fun)	10.58%	1.81%
Activity enhancement (e.g., music sounds better, every day activities more interesting)	5.68%	0.80%
Rebellion (e.g., rebelling against parents, thrill of something illegal)	5.21%	0.32%
Alcohol intoxication (e.g., I was drunk)	4.42%	0.47%
Food enhancement (e.g., enjoy good food, food tastes better)	3.79%	0.00%
Anxiety reduction (e.g., be less shy, feel less insecure)	3.31%	0.00%
Image enhancement (e.g., to be cool, to feel cool)	2.85%	0.32%
Celebration (e.g., special occasion, to celebrate)	1.26%	0.16%
Medical use (e.g., alleviate physical pain, have a headache)	1.26%	0.16%
Habit (e.g., feeling was addictive, became a habit)	0.95%	0.00%

Lee, Neighbors & Woods (2007)

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Enjoyment/fun
Social enhancement
Boredom
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Image enhancement
Celebration

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Food motives
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Rebellion (e.g., rebelling against parents, thrill of something illegal)	5.21%	0.32%
Alcohol intoxication (e.g., I was drunk)	4.42%	0.47%
Food enhancement (e.g., enjoy good food, food tastes better)	3.79%	0.00%
Anxiety reduction (e.g., be less shy, feel less insecure)	3.31%	0.00%
Image enhancement (e.g., to be cool, to feel cool)	2.85%	0.32%
Celebration (e.g., special occasion, to celebrate)	1.26%	0.16%
Medical use (e.g., alleviate physical pain, have a headache)	1.26%	0.16%
Habit (e.g., feeling was addictive, became a habit)	0.95%	0.00%

Lee, Neighbors & Woods (2007)

Withdrawal: Cannabis

Diagnostic Criteria **292.0 (F12.288)**

A. Cessation of cannabis use that has been heavy and prolonged (i.e., usually daily or almost daily use over a period of at least a few months).

B. Three (or more) of the following signs and symptoms develop within approximately 1 week after Criterion A:

1. Irritability, anger, or aggression.
2. Nervousness or anxiety.
3. Sleep difficulty (e.g., insomnia, disturbing dreams).
4. Decreased appetite or weight loss.
5. Restlessness.
6. Depressed mood.
7. At least one of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache.

C. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

Cross-sectional comparisons from Young Adult Health Survey

Source: DBHR/CSHRB Young Adult Health Survey Year 4 data report

Driving within 3 hours of use

Driving after marijuana use

"During the past 30 days, how many times did you drive a car or other vehicle within three hours after using cannabis (e.g., marijuana, hashish, edibles)?"

	2014	2015	2016	2017
Never	50.59%	55.29%	58.19%	58.56%
1 time	14.13%	13.13%	12.50%	12.85%
2-3 times	13.28%	12.34%	11.97%	11.98%
4-5 times	6.43%	4.35%	3.48%	4.48%
6 or more times	15.57%	14.88%	13.85%	12.12%

There are declines in driving after marijuana use between cohort 3 and cohort 1 ($p<.05$) and between cohort 4 and cohort 1 ($p<.01$), as well as a significant linear trend ($p<.01$).

Source: DBHR/CSHRB Young Adult Health Survey Year 4 data report

AMONG 21-25 YEAR OLDS ONLY

"During the past 30 days, how many times did you drive a car or other vehicle within three hours after using cannabis (e.g., marijuana, hashish, edibles)?"

	2014	2015	2016	2017
Never	50.79%	59.61%	57.99%	61.00%
1 time	13.90%	10.26%	11.60%	11.81%
2-3 times	13.18%	15.08%	11.30%	13.02%
4-5 times	7.11%	3.41%	2.28%	4.68%
6 or more times	14.86%	15.78%	15.89%	11.03%

For those 21+, there are declines in driving after marijuana use between cohort 4 and cohort 1 (p<.01), as well as a significant linear trend (p<.01).

Source: DBHR/CSHRB Young Adult Health Survey Year 4 data report

Longitudinal comparisons

Cohort 1

Driving after marijuana use

"During the past 30 days, how many times did you drive a car or other vehicle within three hours after using cannabis (e.g., marijuana, hashish, edibles)?"

	2014	2015	2016	2017
Never	54.84%	62.93%	59.15%	59.46%
1 time	15.77%	11.49%	12.41%	15.50%
2-3 times	11.19%	12.65%	8.94%	7.31%
4-5 times	3.59%	2.47%	6.31%	3.75%
6 or more times	14.62%	10.46%	13.18%	13.97%

***No significant trend, and no significant differences between years compared to year 1 ***

Source: DBHR/CSHRB Young Adult Health Survey Year 4 data report

April 2018

The April 20 Cannabis Celebration and Fatal Traffic Crashes in the United States

John A. Staples, MD, MPH[1,2,3], Donald A. Redelmeier, MD, MSHR[4,5,6]

> Author Affiliations | Article Information

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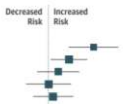
On April 20 each year, thousands of Americans celebrate the intoxicating properties of marijuana on a popular countercultural holiday known as "4/20." Legal marijuana sales surge in anticipation of the "High Holiday," and college students report increased cannabis consumption on 4/20 itself.[1] In many cities,

Staples & Redelmeier (2018)

- **Obtained data from US NHTSA's Fatality Analysis Reporting System**
- **Began first full year after High Times popularized 4/20 up to most recent year with complete data (1992 through 2016)**
- **Analyzed drivers involved in fatal crashes between 4:20 p.m. and 11:59 p.m. on 4/20 compared to same interval on 4/13 and 4/27**
  - **Controlled for weekday, season, year, and minimized bias from changes in vehicle design, travel distances, medical care, etc.**

Subgroup	Drivers in Crashes on April 20	Drivers in Crashes on Control Days
Age, y		
≤20	207	300
21-30	353	610
31-40	265	494
41-50	223	446
≥50	287	554



- **Drivers involved in fatal crashes on 4/20: 1,369 (7.1 per hour)**
- **Drivers involved in fatal crashes on control days: 2,453 (6.4 per hour)**

- **The risk of a fatal crash was significantly higher on April 20 (relative risk 1.12, p<.001)**

Staples & Redelmeier (2018)

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