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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

# CHRONIC AND ACUTE EFFECTS OF HIGH-POTENCY CANNABIS ON COGNITION


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project ECHO

# SPEAKER DISCLOSURES

I have no conflicts of interest

## Planner disclosures

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

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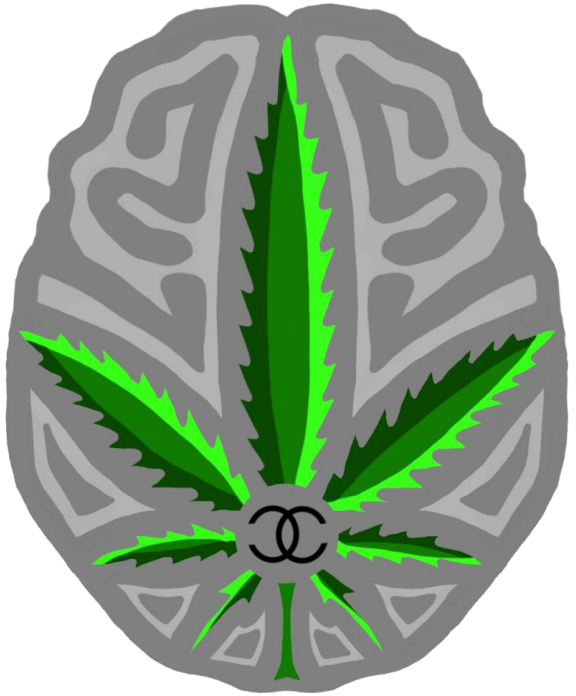
# OBJECTIVES

1. Background on cannabis use and legal issues to studying cannabis
2. Effects of chronic cannabis use on cognition
3. Effects of acute cannabis use on cognition



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# Part I: Introduction to Cannabis

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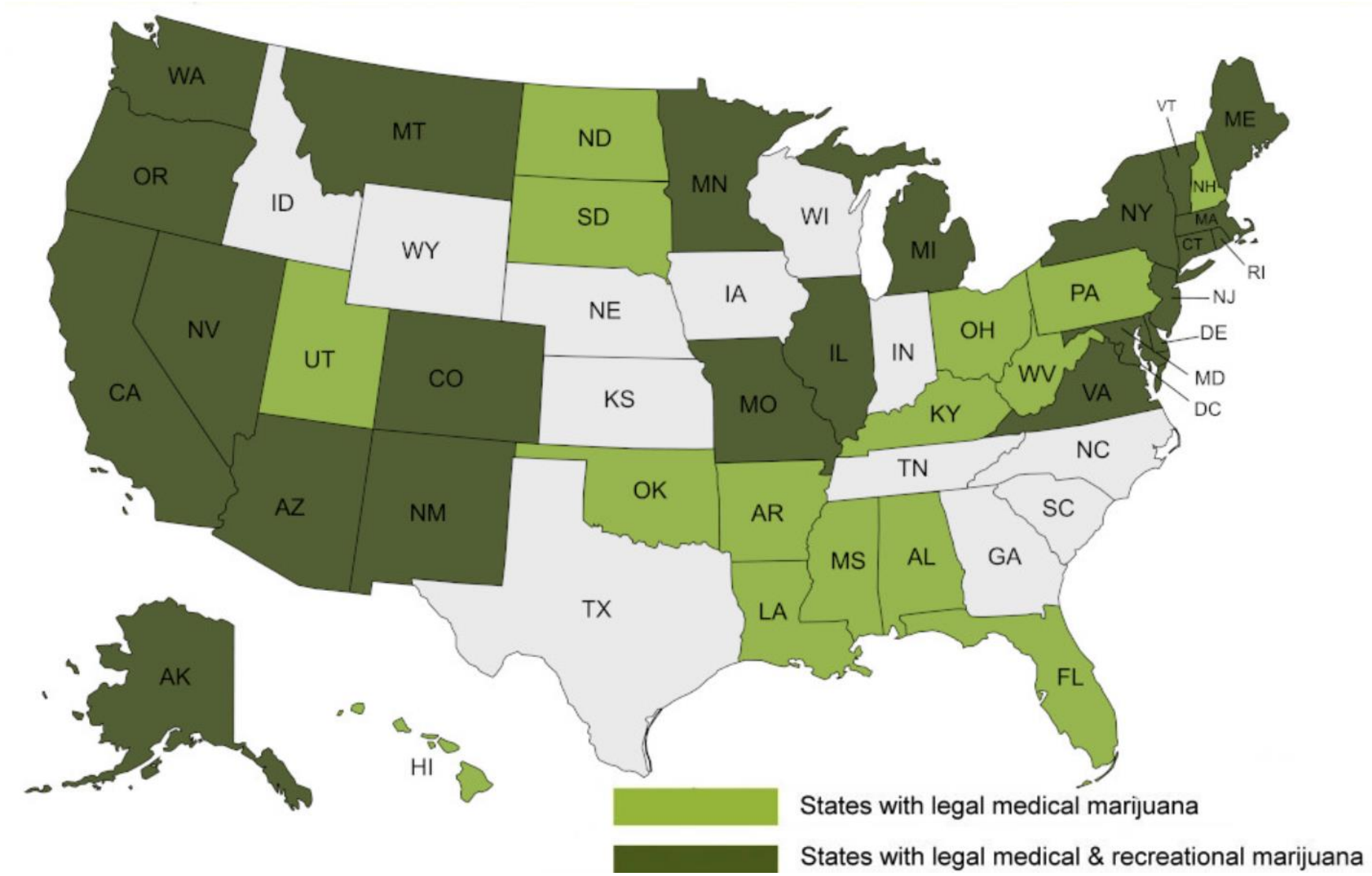
# CANNABIS LEGALIZATION IS SWEEPING THE NATION

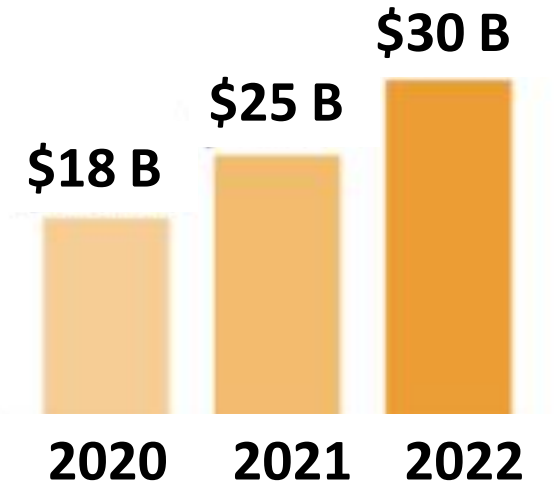
**38** states have legal medical cannabis

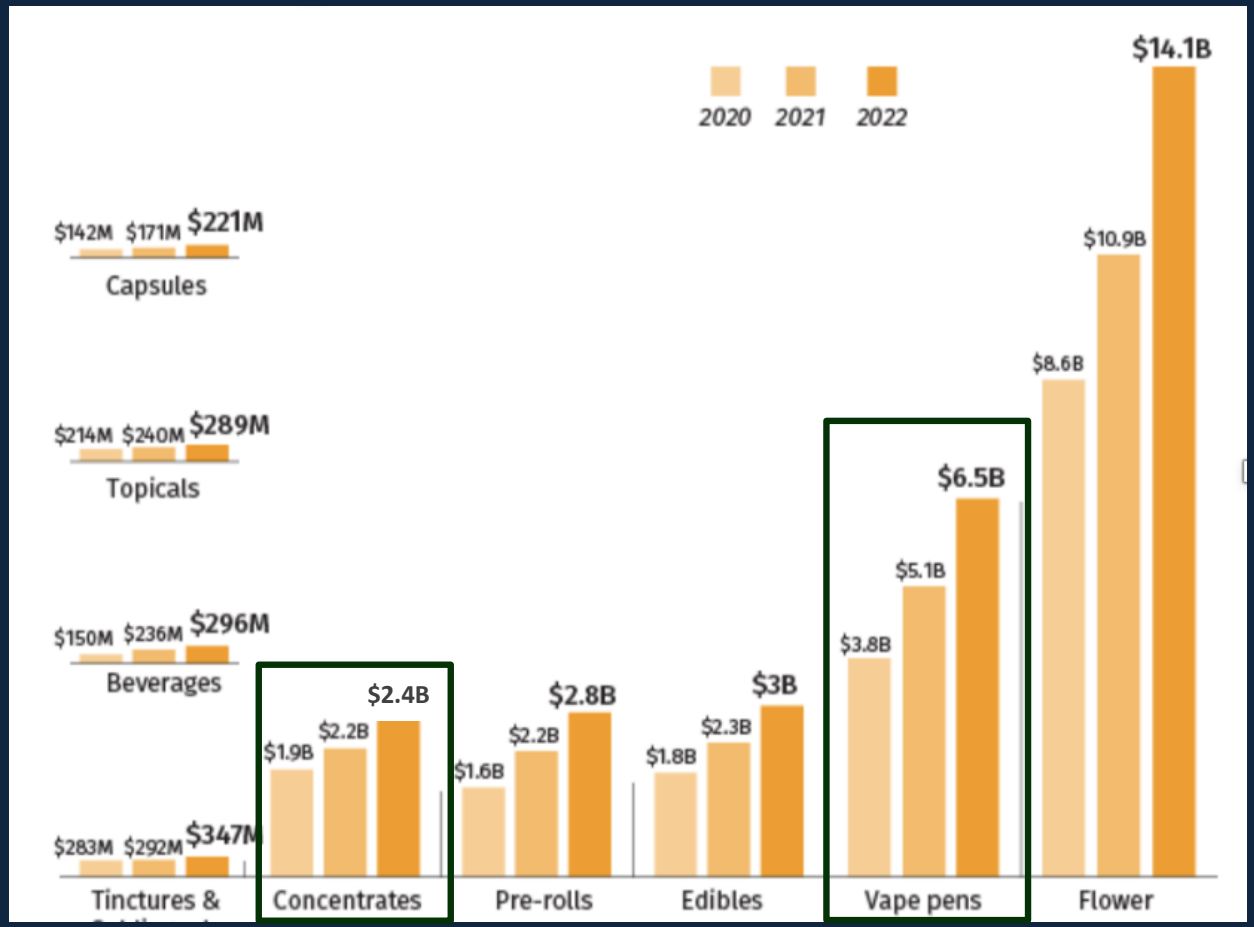
**23** states have legal recreational and medical cannabis



# US SALES

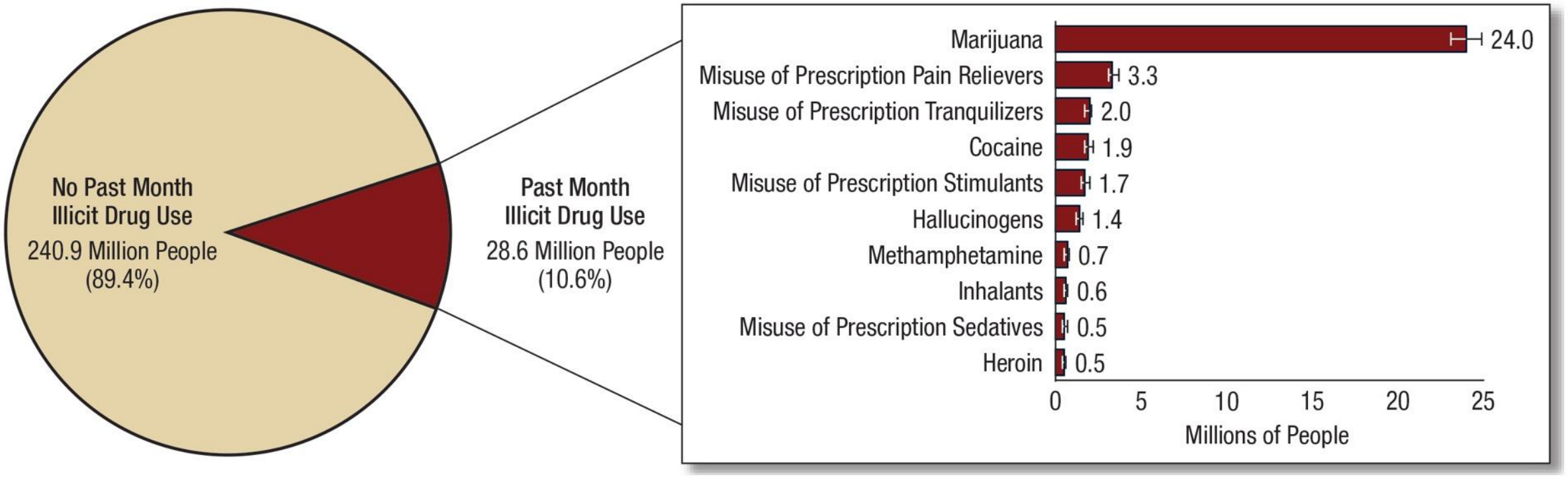
## Cannabis sales are projected to exceed $33 billion in 2023



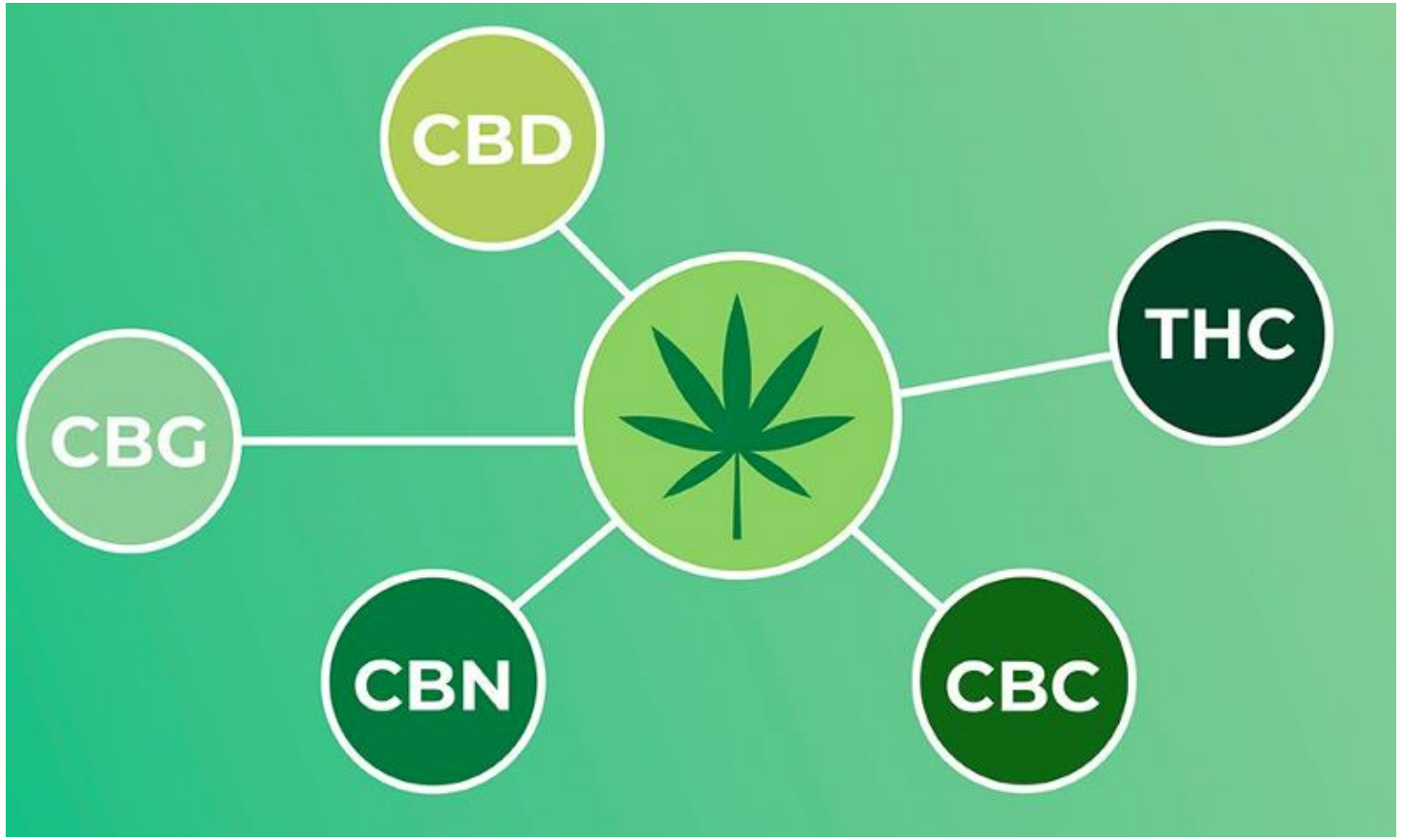

# Explosive Growth in Legal Cannabis Sales

The legal cannabis industry is a multi-billion-dollar industry with sales exceeding **$30 billion** in 2022 and projected to exceed $33 billion in 2023




# Prevalence of Cannabis Use

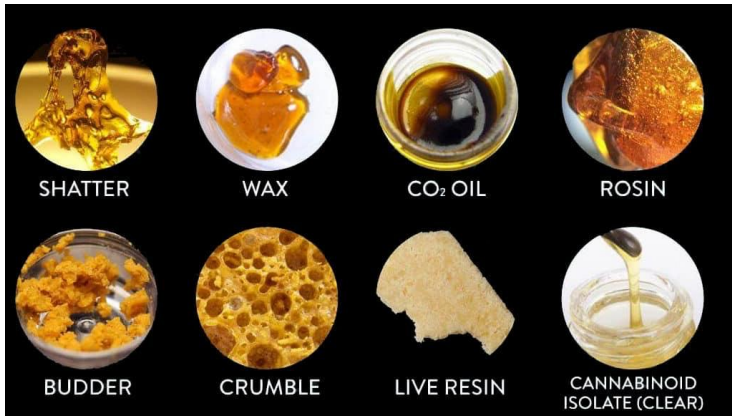
- Most used federally illicit drug in America
- Nearly half of Americans have tried cannabis
- Nearly 20% of Americans report using in past month
  - 35% of 18–25-year-olds report using in past month




# CANNABIS CONSTITUENTS

- Over 100 cannabinoids in the cannabis plant
- **Δ-9-tetrahydrocannabinol (THC):** primary psychoactive (intoxicating) constituent
- **Cannabidiol (CBD):** primary non-intoxicating component
- Minor Cannabinoids include cannabigerol (CBG), cannabinol (CBN), cannabichromene (CBC) (effects largely unknown)

# DIVERSITY OF PRODUCTS IN LEGAL DISPENSARIES



Legal dispensaries carry a wide variety of high-potency products including:

- Flower
- Edibles
- Tinctures
- Lotions
- Suppositories
- Concentrates

- *Past research has focused almost exclusively on flower and edibles*

# CANNABIS CONCENTRATES


**Becoming Increasingly Popular**

- Typically contain >60% THC but can exceed 90% THC (Raber et al., 2015; Smart et al., 2017)
- >50% of cannabis users have used concentrates and about 1/3 use them regularly (Daniulaityte et al., 2017; Sagar et al., 2018)
- Concentrate shares increased by 146% from 2014-2016 in WA state (Smart et al., 2017)
- *People are concerned these extremely high-potency products will magnify harms*

# LEGAL BARRIERS TO CANNABIS RESEARCH

**Market Cannabis**

**NIDA Cannabis**

- U.S. classification of cannabis as Schedule I drug imposes legal restrictions and hurdles that have impeded research on its acute effects
- Researchers must spend years applying to various agencies (IRB, FDA, DOH, DEA) before they can administer cannabis in their labs
- Until very recently only low quality, low-potency (<12% THC) cannabis flower has been available to researchers through the NIDA drug supply

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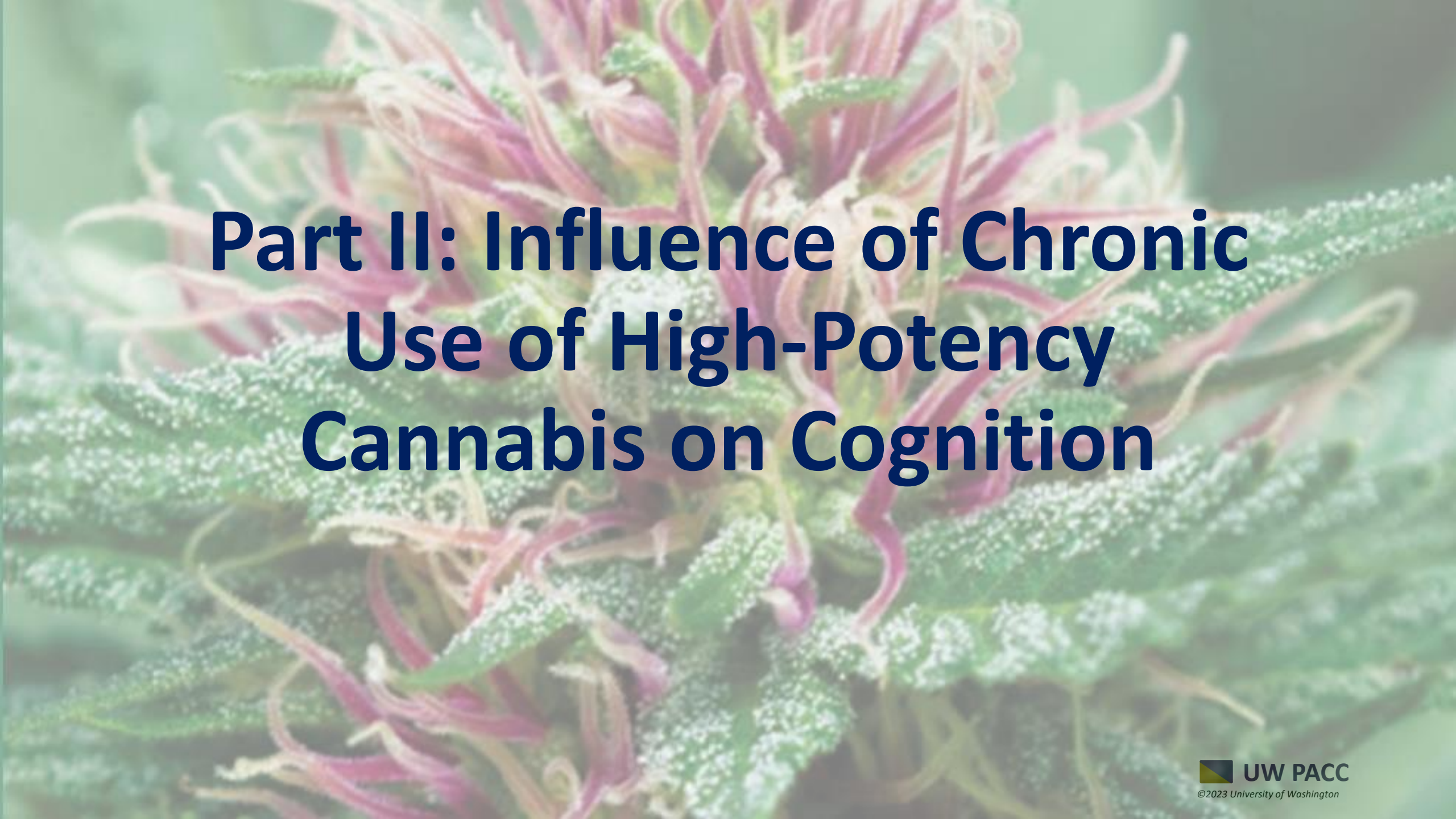

# Part II: Influence of Chronic Use of High-Potency Cannabis on Cognition

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# BACKGROUND – CHRONIC CANNABIS USE & COGNITION

- Recent review of meta-analyses (Dellazizzo et al., 2021) indicates chronic effects of cannabis are most reliably detected on tests of:
  - Memory (verbal, working)
  - Executive functioning
  - Processing speed and attention
- Most are small or small-to-moderate sized effect
- Many aspects of memory have not been examined
- No research has *objectively* examined effects of chronic concentrate use on cognition
- Concentrate users *perceive* greater risk of developing problems with memory, concentration and motivation (Daniulaityte et al., 2017)

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# STUDY 1: GOAL & AIM

- **Goal:** Examine which aspects of cognition are affected by <u>chronic use of high-potency cannabis</u>
  - **Aim:** Examine whether concentrate users have objectively worse cognitive test performance than exclusive flower users under sober conditions

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# INCLUSION CRITERIA

- 18-39 years of age
- Cannabis users – daily/near daily use for ≥ 1 year and urine test positive for THC
- Non-users – no use or use < 10 times in life, no use in past year, and urine test negative for THC

***Cannabis users had to abstain from using cannabis on the day of the testing session***

# EXCLUSION CRITERIA

- Serious medical, neurological, or psychiatric conditions
- Learning disabilities, concussions, head injuries
- Substance use disorders
- Illicit drug use in past 6 months
- Heavy drinking (>4 drinks >4 times/week)
- Heavy smoking (>20 cigarettes/day)

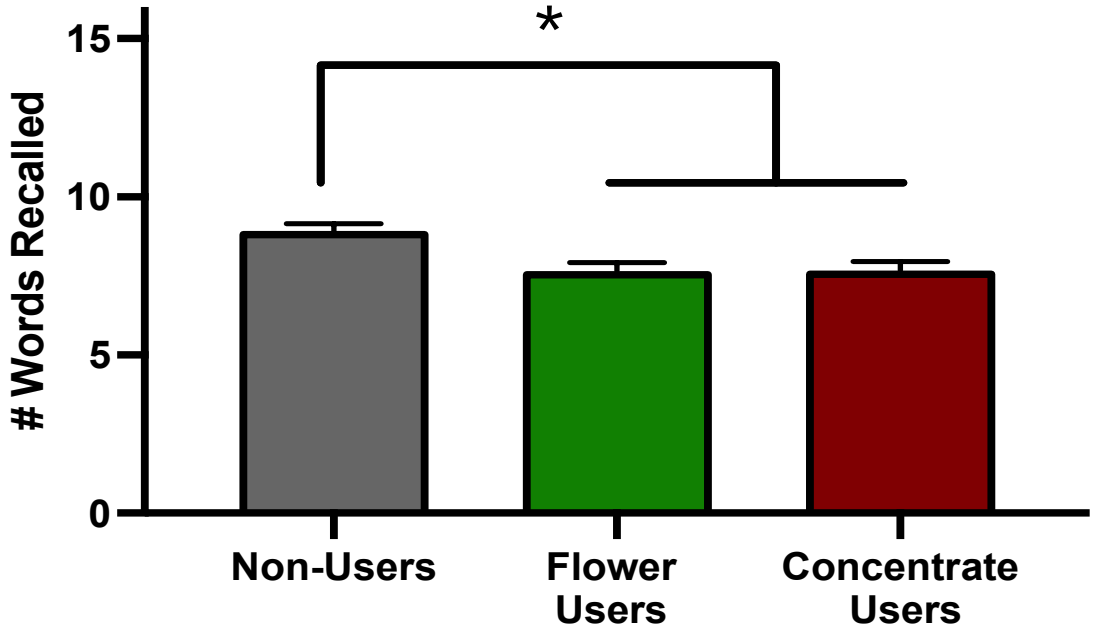
***Experimenters were blind to participants' cannabis use status***

# PARTICIPANTS & METHOD

- 98 Non-Users
  - 54% women, 58% white
  - Age (*M* = 24; *SD* = 4.7)
- 46 Flower Users (exclusive)
  - 48% women, 76% white
  - Age (*M* = 24; *SD* = 4.5)
- 54 Concentrate Users (also used flower)
  - 54% women, 69% white
  - Age (*M* = 22.5; *SD* = 3.2)
- Groups differed in level of education, problematic use of alcohol and anxiety (included as covariates)
- Completed 1.5-hour cognitive test battery in lab while sober

## VERBAL MEMORY

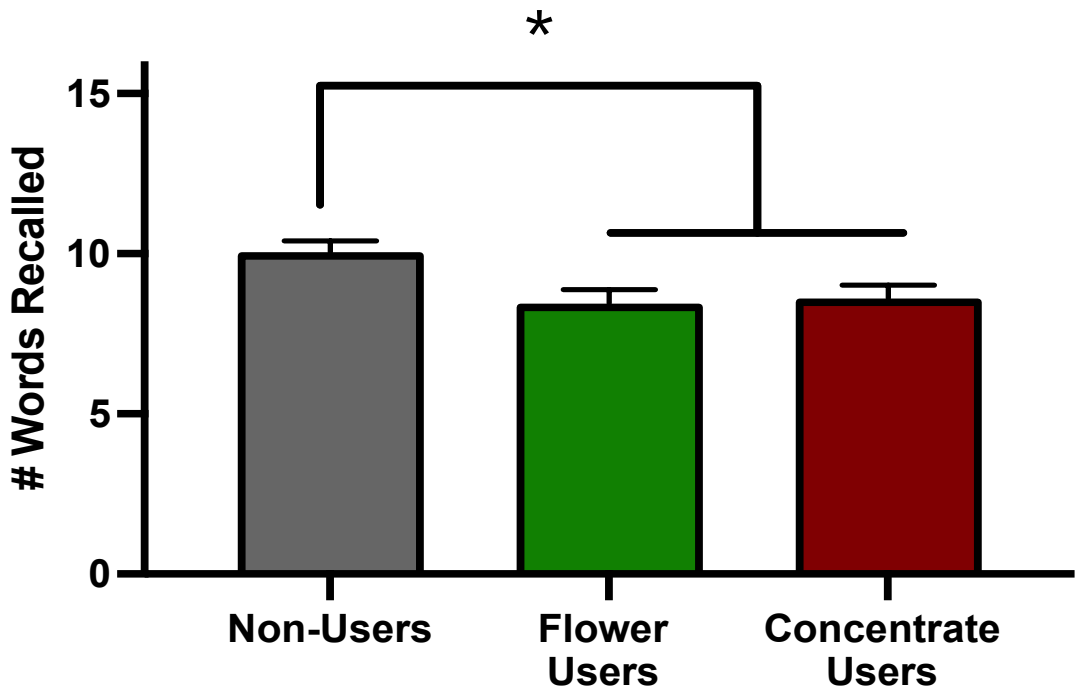
CVLT II Immediate Recall




Flower and concentrate users performed significantly worse than non-users

## VERBAL MEMORY

CVLT II Delayed Recall

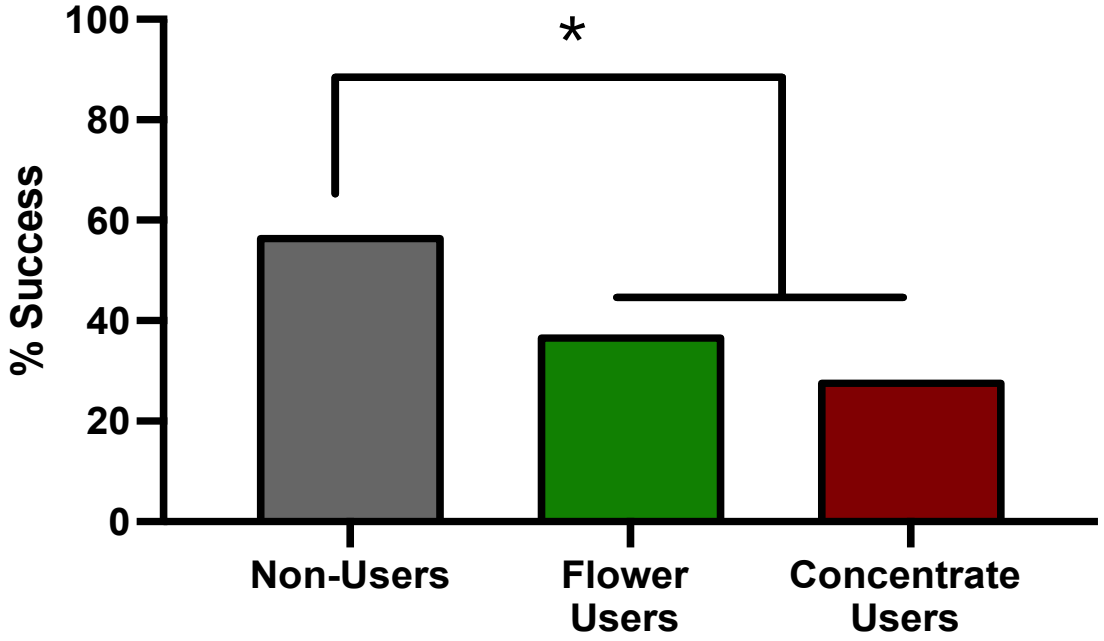



Flower and concentrate users performed significantly worse than non-users

Cuttler, Petrucci, & LaFrance (2023) *Scientific Reports*

## PROSPECTIVE MEMORY

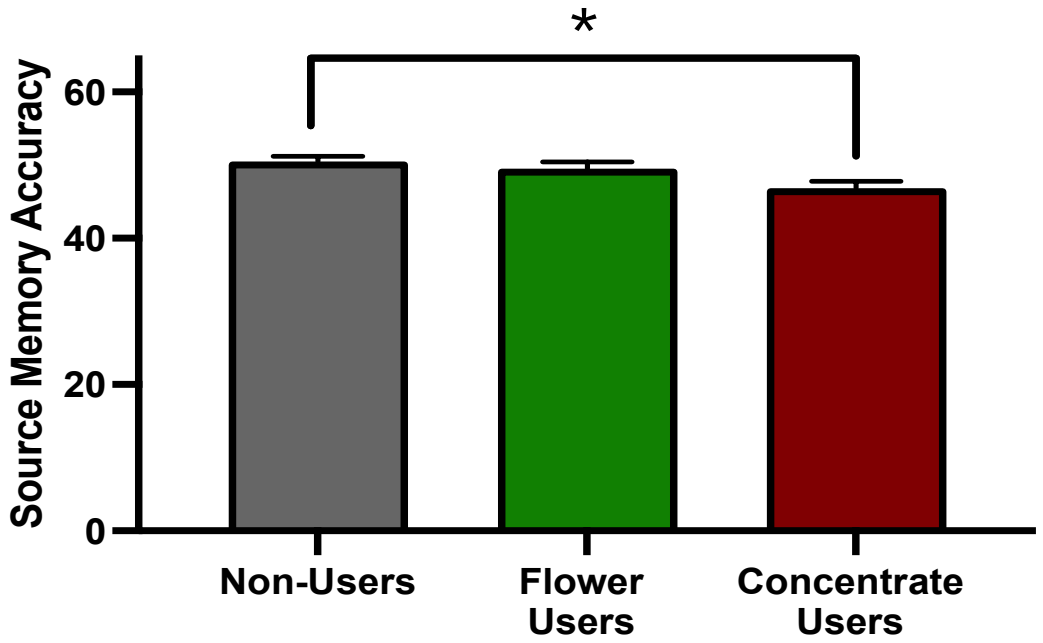
Reminder Task (Episodic)




Flower and concentrate users performed significantly worse than non-users

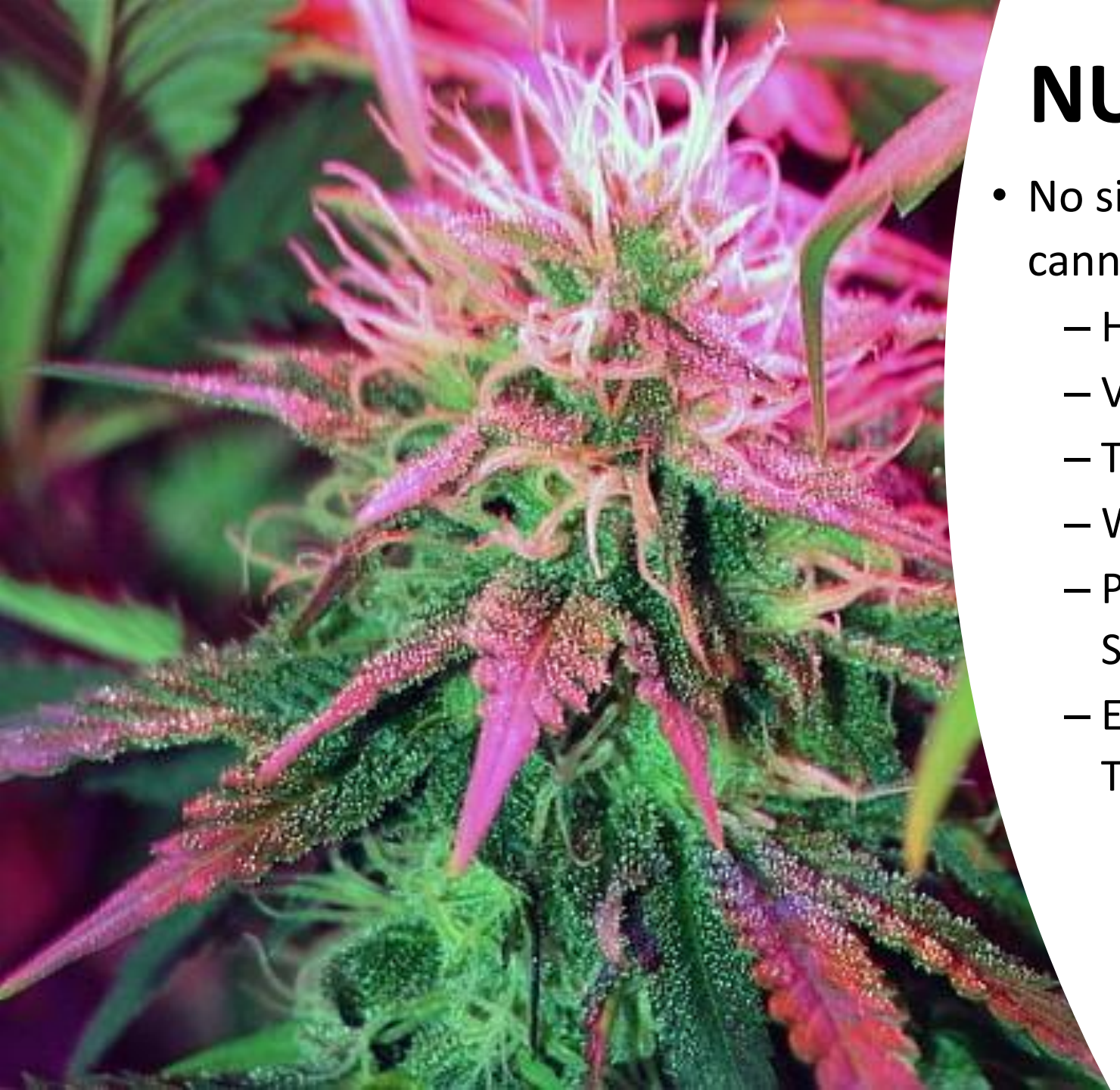
## SOURCE MEMORY

Pictures/Words




Concentrate users performed significantly worse than non-users

Cuttler, Petrucci, & LaFrance (2023) *Scientific Reports*

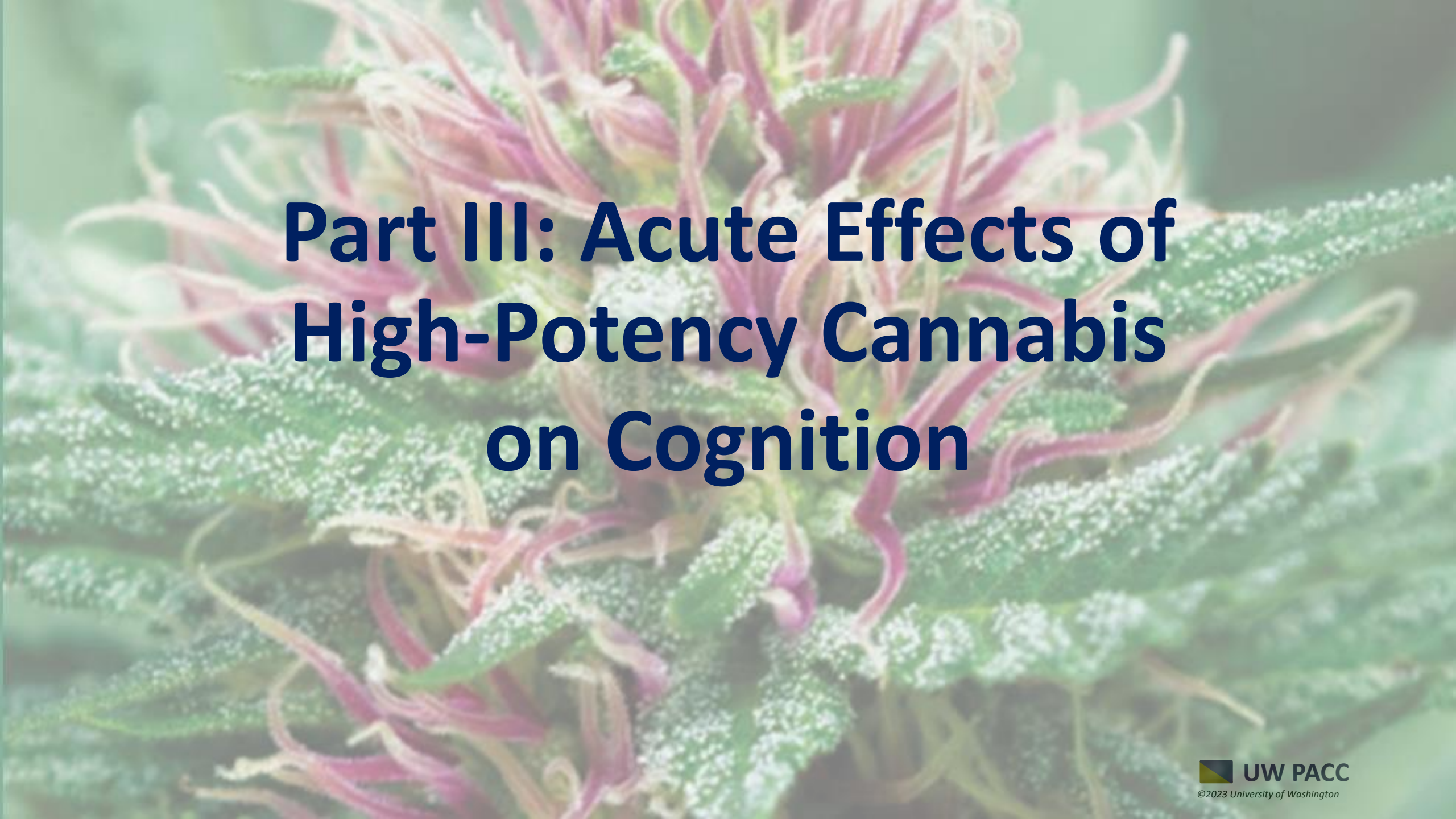


# NULL EFFECTS

- No significant influence of high-potency cannabis flower or concentrates on tests of:
  - Habitual Prospective Memory
  - Visuospatial Memory (BVMT-II)
  - Temporal-Order Memory
  - Working memory (Digit Span Backwards)
  - Psychomotor Speed/Attention (Digit Symbol Substitution Test, Ruff 2 & 7s Test)
  - Executive Function (Stroop, Zoo Map, Tower Test)

***No significant differences in concentrate vs. flower users***

Cuttler, Petrucci, & LaFrance (2023) *Scientific Reports*



# Part III: Acute Effects of High-Potency Cannabis on Cognition

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# BACKGROUND – ACUTE EFFECTS

- Most robust detrimental acute effects of cannabis is on memory, particularly verbal memory
  - Limited evidence that CBD may protect against effects of THC (Englund et al., 2013; Morgan et al., 2010)
- Little known about acute effects of cannabis on naturalistic tests of memory (prospective, temporal-order, source, false memory) or decision-making (non-normative)
- Reliance on low-potency products may driving null results
- Acute concentrate intoxication not associated with worse objective impairment in memory (than flower intoxication) (Bidwell, et al., 2020)
- Cannabis users subjectively report worse memory & attention when using concentrates (Chan et al., 2017)

# STUDY 2: GOAL & AIMS

- **Goal:** Examine <u>acute</u> effects of high-potency cannabis on performance on naturalistic memory (prospective, temporal order, source, false) and decision-making (non-normative) tests
  - **Aim 1:** Examine whether cannabis concentrates produce objectively worse cognitive test performance than flower
  - **Aim 2:** Examine whether cannabis flower with CBD mitigates the cognitively impairing effects of high THC


# ZOOM METHOD


- Bypassed legal restrictions by having participants (aged 21+) purchase and administer their own cannabis in their own environment in WA state while being observed over Zoom
- Eligible participants emailed product lists
- Asked to abstain from cannabis use prior to testing session
- Remained sober or inhaled their cannabis product over Zoom
- Completed cognitive tests over Zoom
- Amazon gift card for compensation of time NOT cannabis purchase

# INCLUSION CRITERIA

- 21+ years of age (able to legally purchase cannabis)
- Reside in Washington state (where recreational cannabis is legal)
- Fluent in English
- Access to computer with stable internet connection in personal/home environment
- Experienced cannabis user
  - Used cannabis ≥ once per week for ≥ one year
  - ≥ 50 lifetime uses
  - Experience with BOTH flower & concentrates

# EXCLUSION CRITERIA

- Serious medical, neurological, or psychiatric conditions
- Learning disabilities, concussions, or head injuries
- Substance use disorders
- Illicit drug use in past 6 months
- Heavy drinking (> 4 drinks > 4 times/week)
- Heavy smoking (> 30 cigarettes/week)
- **Pregnant or breastfeeding**
- **Prior serious adverse reactions to cannabis (e.g., psychosis, panic attack)**

# EXPERIMENTAL CONDITIONS


80 healthy adults (45M, 35W)

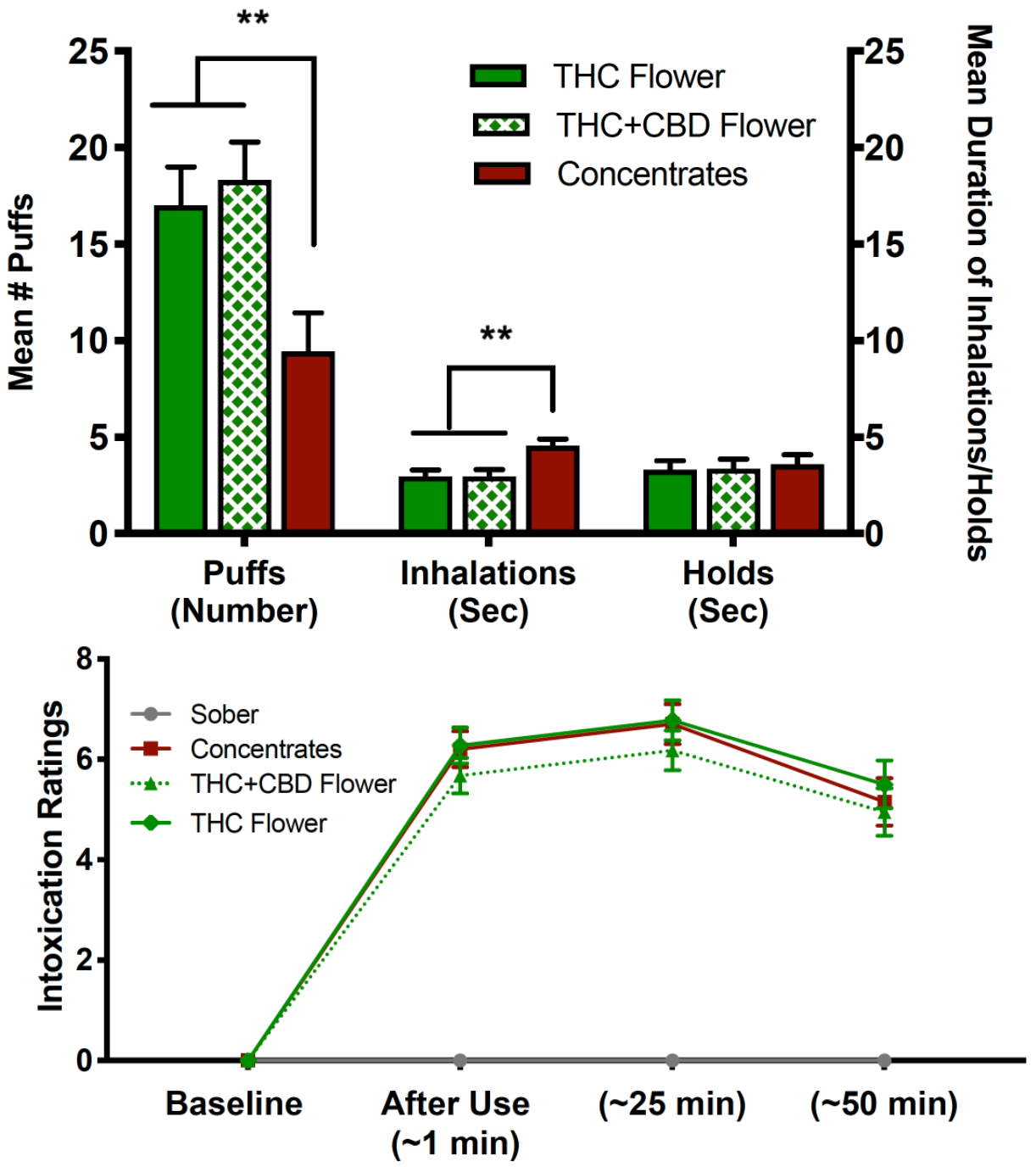
- $M_{age}$ = 24 (*SD* = 5.67)

1. Sober: control (*n* = 20)
2. THC Flower (*n* = 20)*:* High THC (>20%), no CBD (0.00%)
3. THC + CBD Flower (*n* = 20): High THC (>20%) with CBD (≥0.70%)
4. Concentrate (*n* = 20): High THC (>60%) with CBD (≥0.70%)

*Random assignment produced equivalent groups*

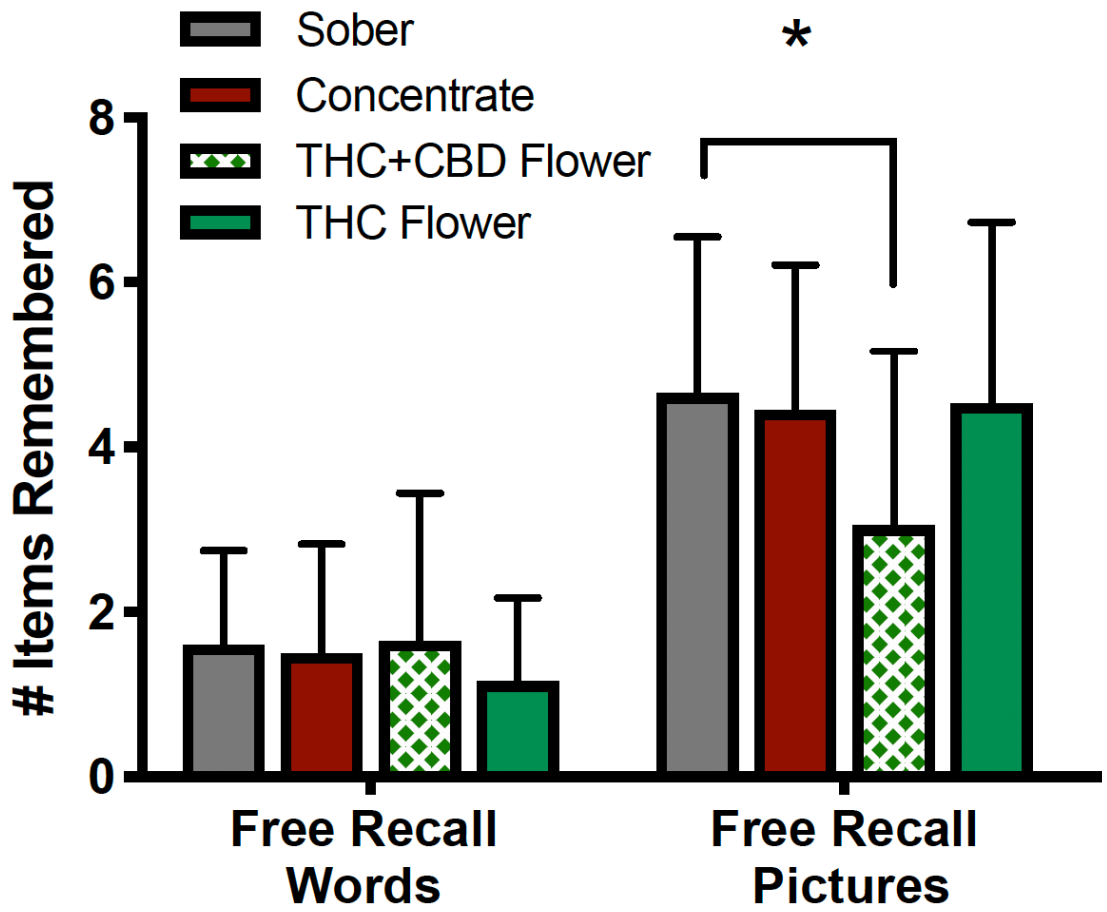
Participants self-titrated their use of extremely high potency cannabis concentrates

As a result, they achieved the same subjective high as those inhaling high potency flower




Cuttler, LaFrance, & Stueber (2021) *Scientific Reports*

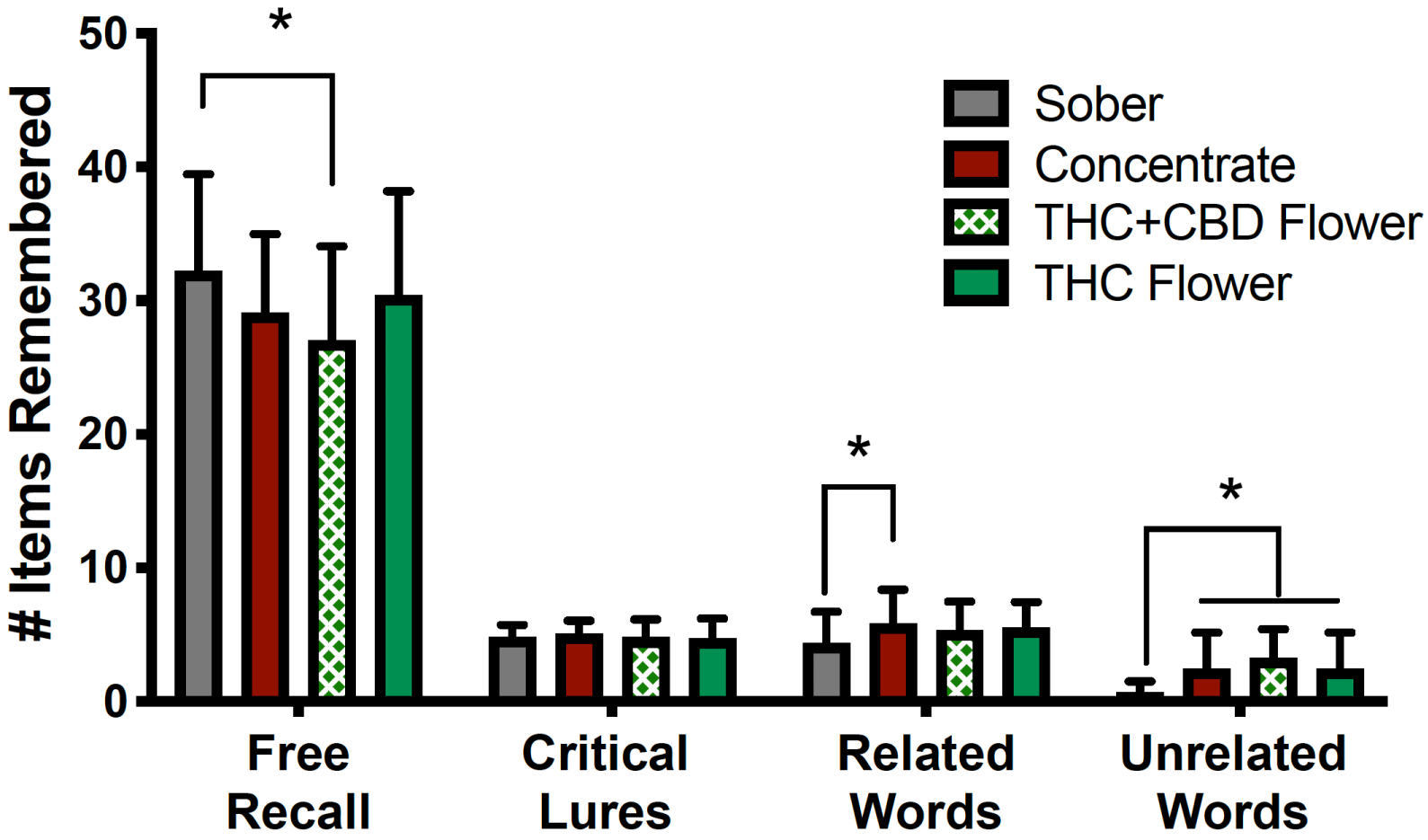
# MEMORY




The THC+CBD flower group recalled fewer pictures than the sober group

Cuttler, LaFrance, & Stueber (2021) *Scientific Reports*

# FALSE MEMORY




The THC+CBD flower group recalled fewer words than the sober group

The concentrate group falsely recalled more related words than the sober group

All three cannabis groups falsely recalled more unrelated words than the sober group

Cuttler, LaFrance, & Stueber (2021) *Scientific Reports*

# Null Effects

- No significant effects of high-potency cannabis flower or concentrates on tests of:
  - Prospective Memory
  - Temporal-Order Memory
  - Non-Normative Decision Making
- ***No significant differences in those who used flower vs. concentrates***

Cuttler, LaFrance, & Stueber (2021) *Scientific Reports*

# INTERIM SUMMARY

- High-potency cannabis impaired free recall and source memory and increased susceptibility to false memory
- No significant effects on decision-making, prospective or temporal-order memory
  - Power may be diminished to detect these effects
- CBD did not offset negative effects of high THC
  - More memory impairments found in the THC+CBD flower group than the no CBD flower group
- No significant differences in performance of participants who inhaled cannabis concentrates vs. flower
  - People use smaller doses of concentrates to achieve comparable effects
- Limitations/Criticisms – no placebo control group, no non-users control group, between-subjects design, unstandardized tests


# STUDY 3: GOAL AND AIM

**Goal:** Examine <u>acute</u> effects of high-potency cannabis on more standardized tests of cognition using a within-subjects design and a control group  of non-users

**Aim:** Examine whether cannabis concentrates produce larger impairments in cognition than flower

# INCLUSION CRITERIA

- 21+ years of age (able to legally purchase cannabis)
- Reside in a state where recreational cannabis is legal
- Access to computer with stable internet connection in personal/home environment
- Experienced cannabis user or non-user
  - Cannabis User: Used cannabis ≥ once per week for ≥ one year
  - **Non-user: no past year use and < 6 lifetime uses**

# EXCLUSION CRITERIA

- Serious medical, neurological, or psychiatric conditions
- Learning disabilities, concussions, or head injuries
- Substance use disorder
- Illicit drug use in past 6 months
- Heavy drinking (> 4 drinks > 4 times/week)
- Heavy smoking (> 30 cigarettes/week)
- **Pregnant or breastfeeding**
- **Prior serious adverse reactions to cannabis (e.g., psychosis, panic attack)**

# STUDY 2: METHODS

- ✓ Control group of non-users
- ✓ Within-subjects design
- ✓ Standardized tests
  - **Inquisit for online tests**

INQUISIT by millisecond

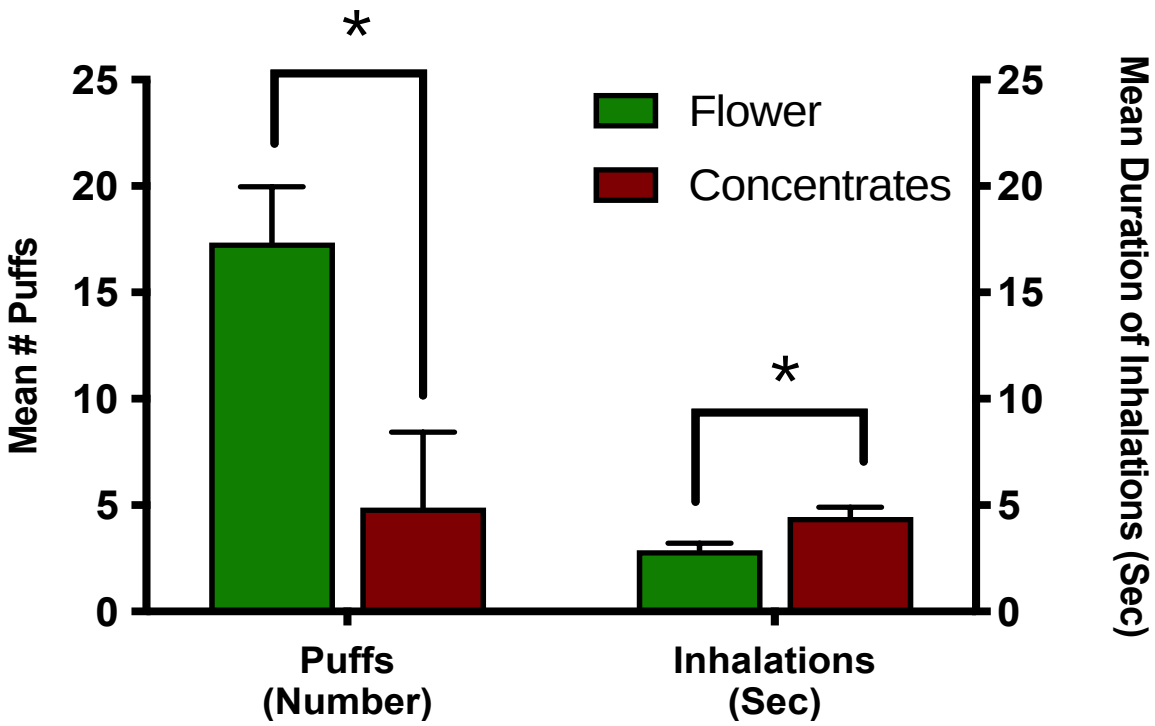
zoom

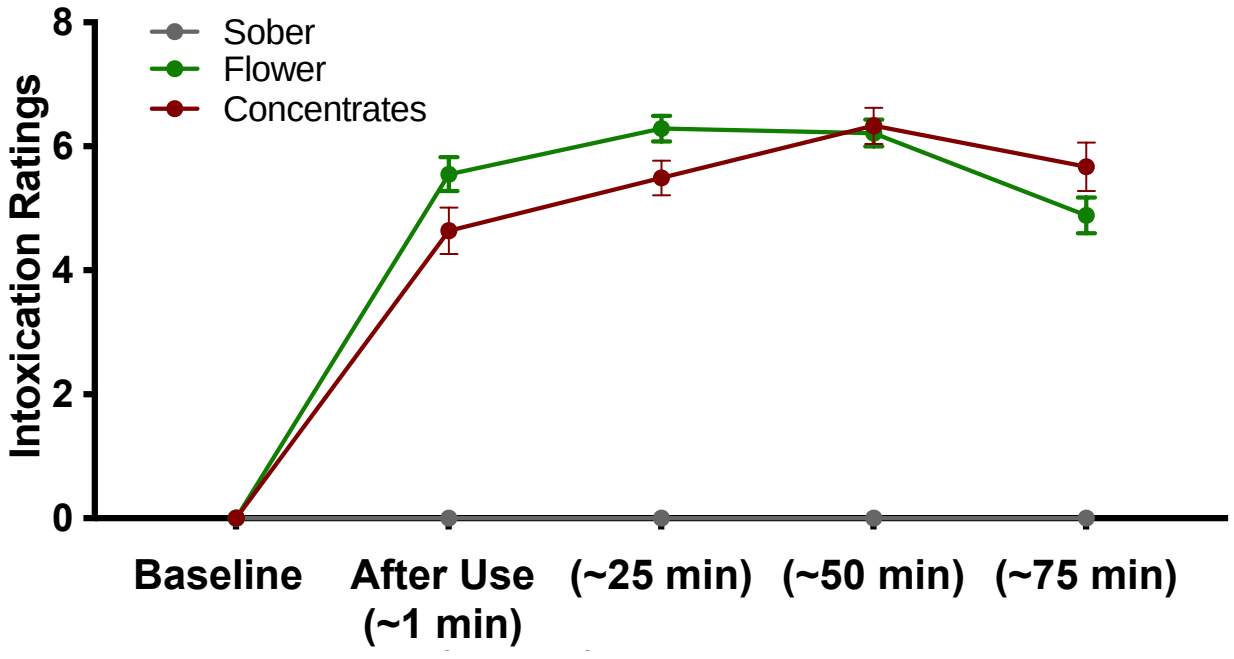
| | Session 1 | Session 2 |
|---|---|---|
| Non-Users (*n* = 51)<br>16M 34W 1 Non-Binary | Sober | Sober |
| Flower Users (*n* = 31)<br>14M 16W 1 Non-Binary<br>$M_{THC}$ = 21.13 (18 – 30%) | Sober | High |
| Concentrate Users (*n* = 17)<br>10M 7W<br>$M_{THC}$ = 68.25 (20 – 91%) | Sober | High |

Compared 3 groups **change scores** (Session 2 – Session 1)

Participants self-titrated their use of extremely high potency cannabis concentrates

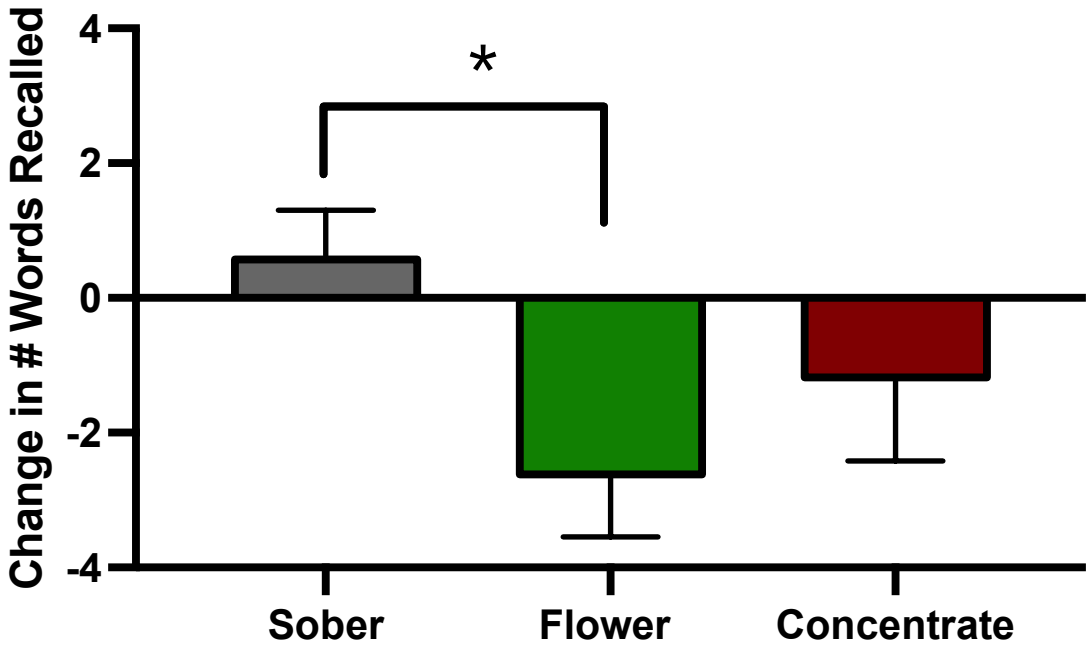
As a result, they achieved the same subjective high as those inhaling high potency flower



## VERBAL MEMORY

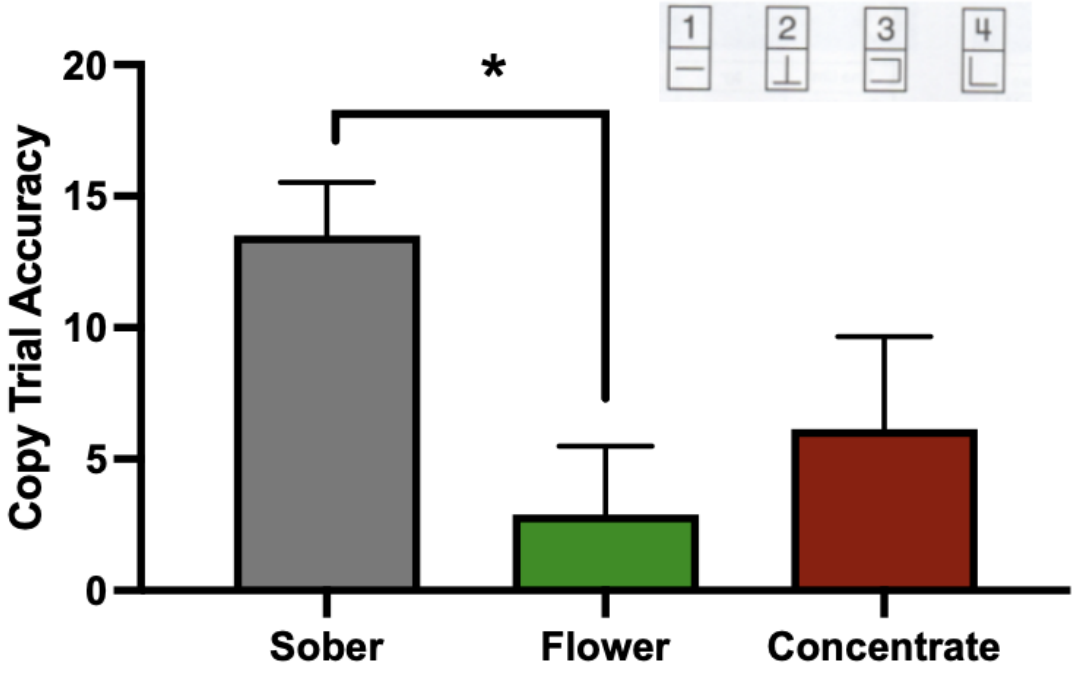
CVLT II Immediate Recall




Participants under the influence of cannabis flower showed a significant decrease in verbal memory test performance compared to sober non-users (whose performance improved)

## PSYCHOMOTOR SPEED/ATTENTION

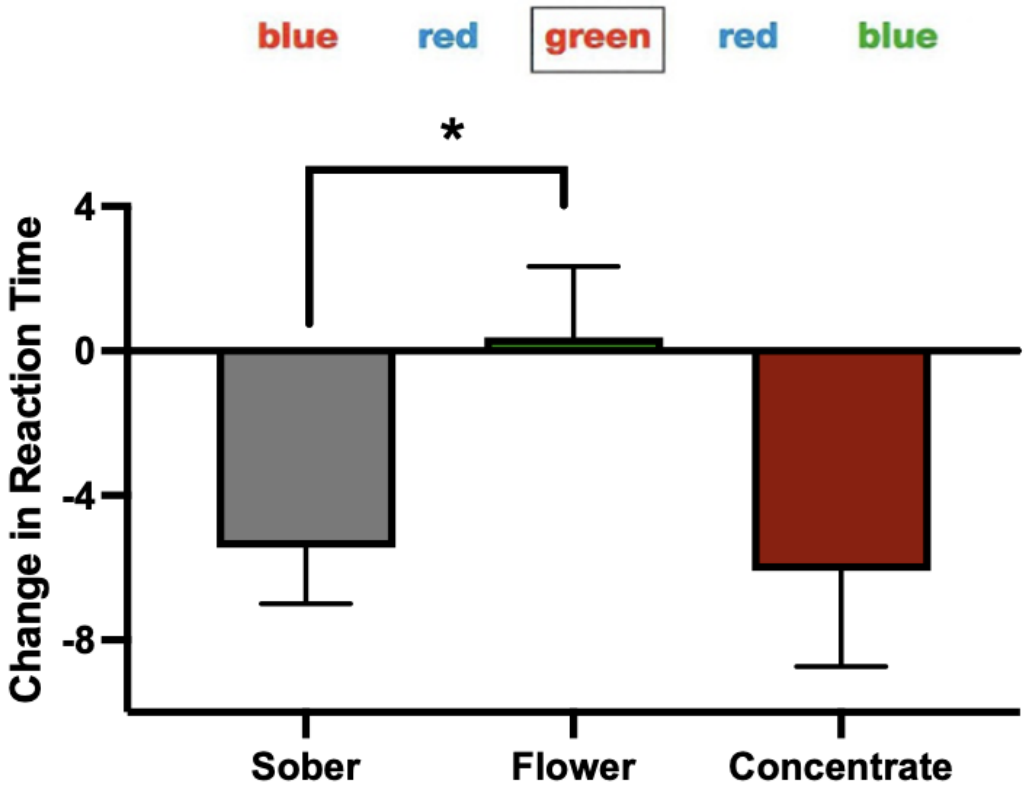
Digit Symbol Substitution Copy




Participants under the influence of cannabis flower showed significantly less improvement in performance relative to sober non-users

## EXECUTIVE FUNCTIONING

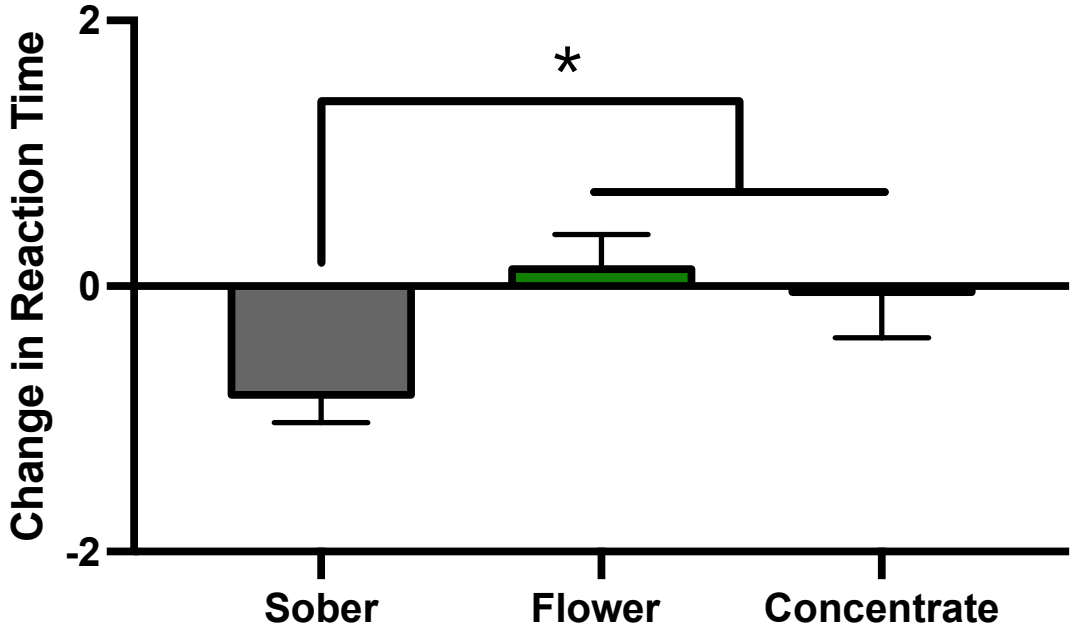
Stroop Switching Trial




Sober non-users showed a significant decrease in response times relative to participants under the influence of cannabis flower

## DECISION MAKING (SPEED)

Delay Discounting Test Reaction Time




Sober non-users showed a significant decrease in response times relative to participants under the influence of cannabis flower or concentrates

# Null Effects

- No significant effects of high potency flower or concentrates on tests of:
  - Short-Term/Working Memory (Digit span forwards and backwards)
  - Attention (TOVA)
  - Executive Functioning (Verbal Fluency Test, Trail Making Test, Cued Go-No/Go Task)
- ***No significant differences in flower vs. concentrates***


## LIMITATIONS

- Lack of placebo control group (expectancy effects)
- Lack of control over puffs, inhalations, holds
- No control over product used (Study 3)
- Samples of experienced users

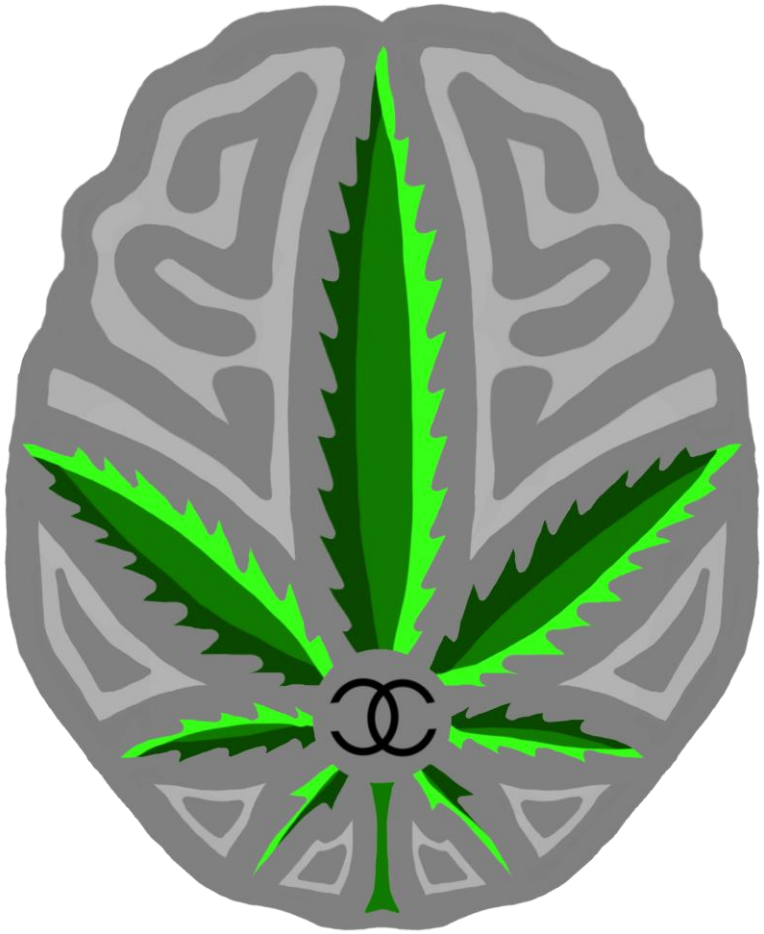
## STRENGTHS

- Bypass US federal restrictions on acute cannabis research
- High ecological validity
  - High-potency dispensary products
  - Self-titrated
  - Own environment
- Cost effective methodology

# SUMMARY & CONCLUSIONS

- Effects of chronic cannabis use on tests of verbal memory, prospective memory, and source memory
- Acute effects of high-potency cannabis on source memory, false memory, verbal memory/free recall, psychomotor speed/attention, and reaction time
- Lack of other effects may pertain to use of highly experienced cannabis users tested in their homes
- No evidence that chronic or acute use of cannabis concentrates is worse for cognition than flower
  - Participants self-titrate concentrates to achieve similar intoxication and impairment as flower

# The Health & Cognition



## THC Lab

ADARP
Alcohol and Drug Abuse Research Program

WSU's Dedicated Marijuana Account


WSU