Relationships of cannabis use to neurocognitive structure and function and risk behavior among adolescents

Angela D. Bryan, PhD

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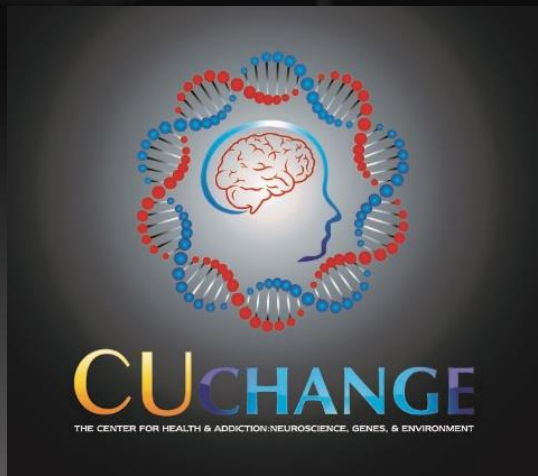
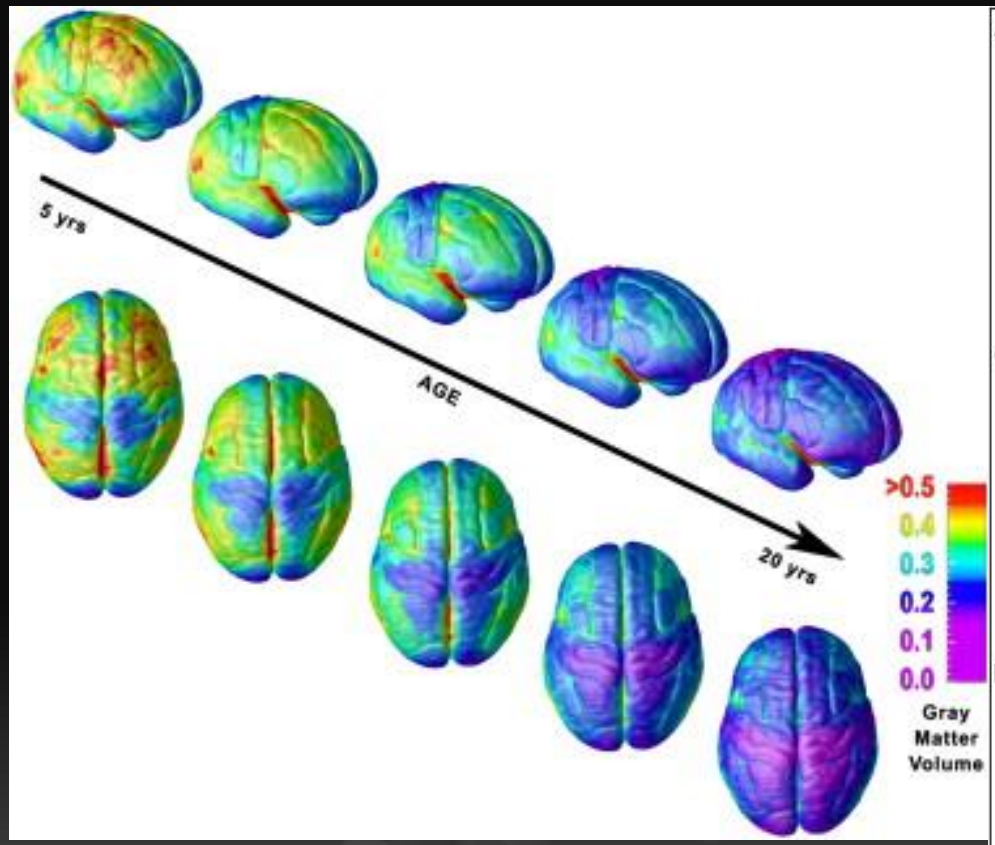


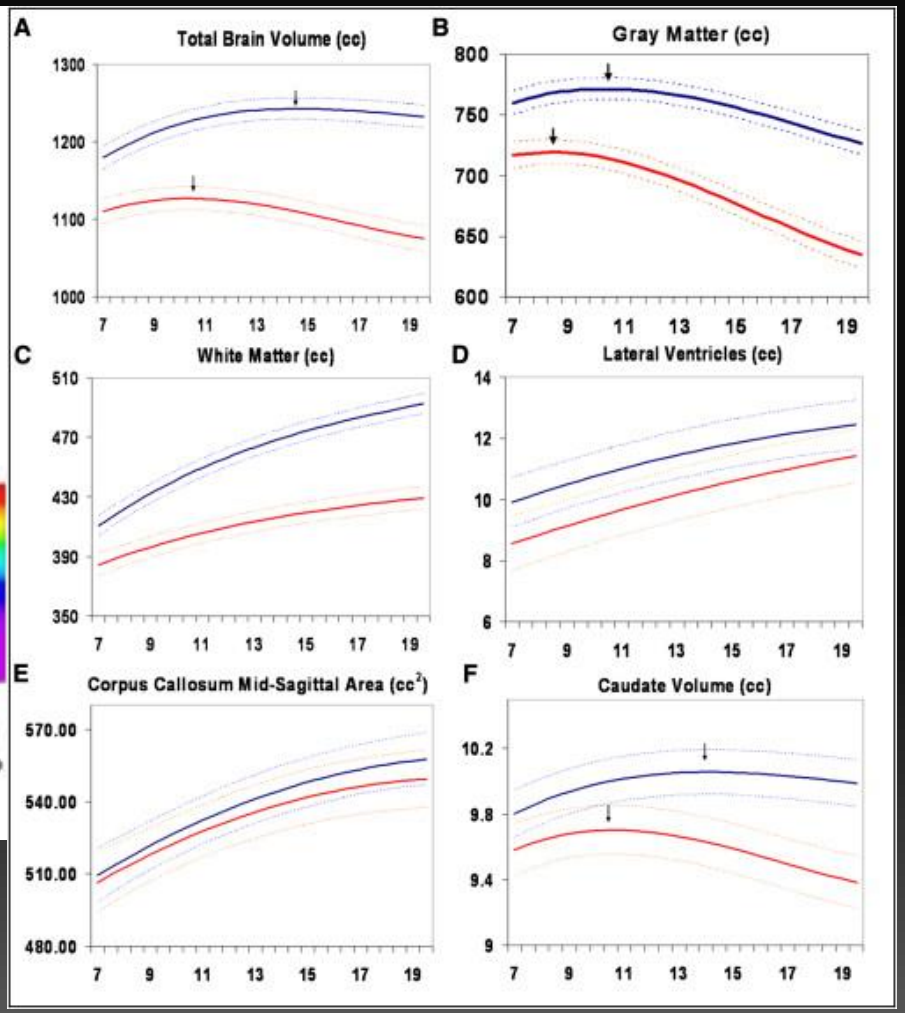
The Adolescent Brain

A PARENT'S GUIDE TO THE
TEEN BRAIN

Giedd & Rappaport, 2010, Neuron

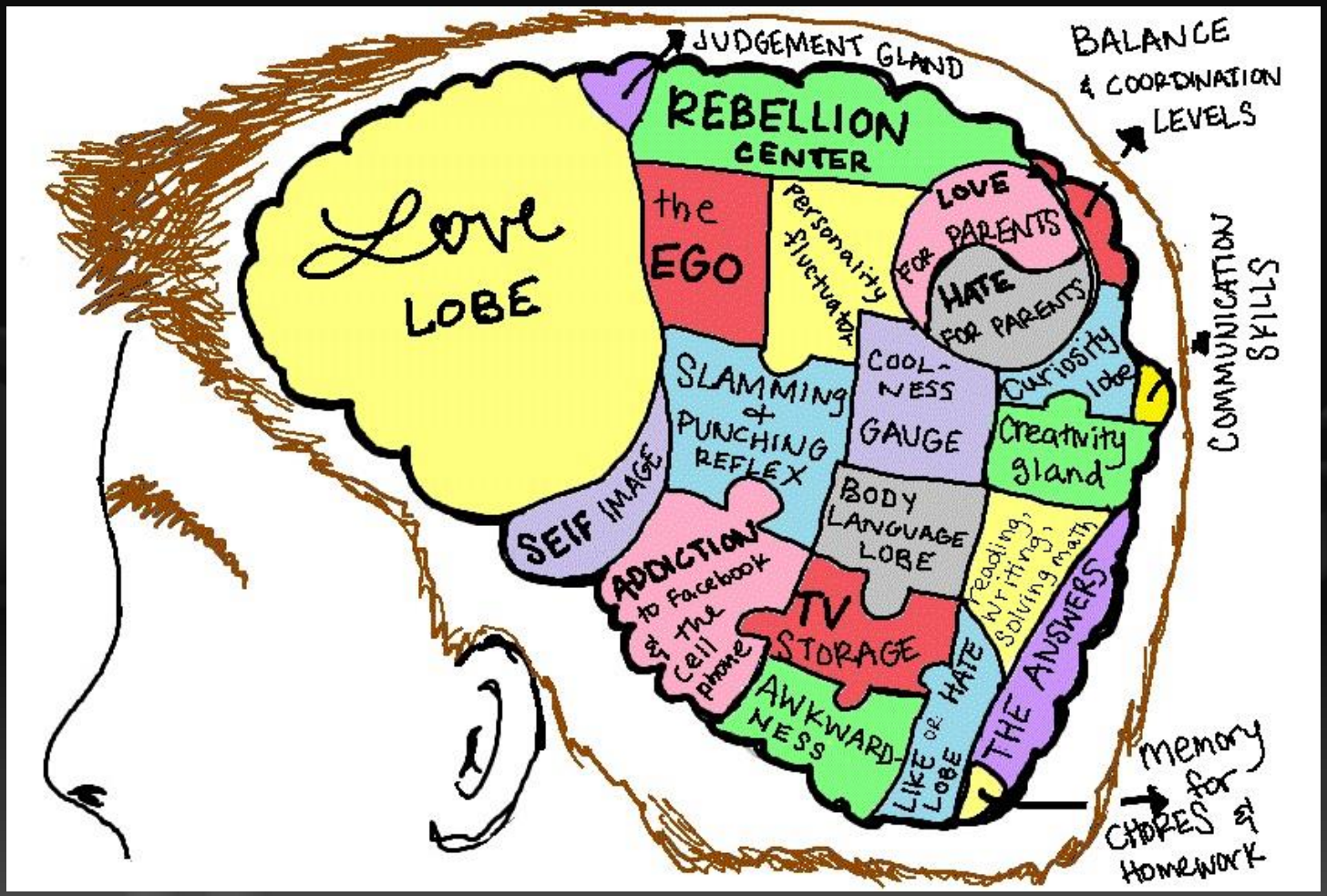
The Adolescent Brain





Giedd & Rappaport, 2010, Neuron

The Adolescent Brain…a work in progress!



Cannabis Use and the Brain

- Inspired us to conduct a study in which:
  - 29 adult non MJ users compared to 29 adult daily users
  - 50 adolescent non MJ users compared to 50 adolescent daily users
  - Very carefully matched on alcohol use and other variables
  - No differences between those who reported cannabis use every day and those who reported no use

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Neurobiology of Disease

Daily Marijuana Use Is Not Associated with Brain Morphometric Measures in Adolescents or Adults

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Cannabis and the Brain: Part 2

- Sample Ascertainment
  - 813 adults (age 18-55), 439 adolescents (age 14-18), participants from substance use and neuroimaging studies in New Mexico

- Analysis
  - Relationship of quantity of substance use and Gray Matter Volume (VBM) and White Matter Integrity (DTI)
    - Analyzed the effect of alcohol while controlling for cannabis
    - Analyzed the effect of cannabis while controlling for alcohol

Thayer et al. (2017). *Addiction*

Cannabis and the Brain: Part 2

Table 1 Sample characteristics.

	Adults		*Adolescents*	
	Whole sample	*Weekly or greater cannabis users*	*Whole sample*	*Weekly or greater cannabis users*
n	853	191	439	201
Ethnicity				
Caucasian	474 (56%)	111 (58%)	66 (15%)	29 (14%)
Latino	136 (16%)	19 (10%)	285 (65%)	133 (66%)
Native American	60 (7%)	13 (7%)	32 (7%)	17 (8%)
African American	25 (3%)	7 (4%)	28 (6%)	11 (5%)
Asian/Pacific Islander	10 (1%)	0 (0%)	6 (1%)	3 (1%)
Mixed	120 (14%)	30 (16%)	21 (5%)	8 (4%)
Unknown/declined	28 (3%)	11 (6%)	1 (<1%)	0 (0%)
Females : males	326 : 527 (62% male)	64 : 131 (69% male)	134 : 305 (69% male)	52 : 149 (74% male)
Age	31.64 (9.64)	28.81 (8.44)	15.97 (1.17)	16.00 (1.08)
AUDIT total score	13.14 (8.47)	14.00 (7.79)	6.39 (6.67)	8.48 (6.65)
TLFB alcohol drinking days	12.78 (8.95)	13.81 (8.89)	2.17 (3.78)	3.39 (4.48)
TLFB cannabis smoking days	4.33 (8.66)	18.19 (9.24)	9.69 (11.94)	20.60 (9.51)

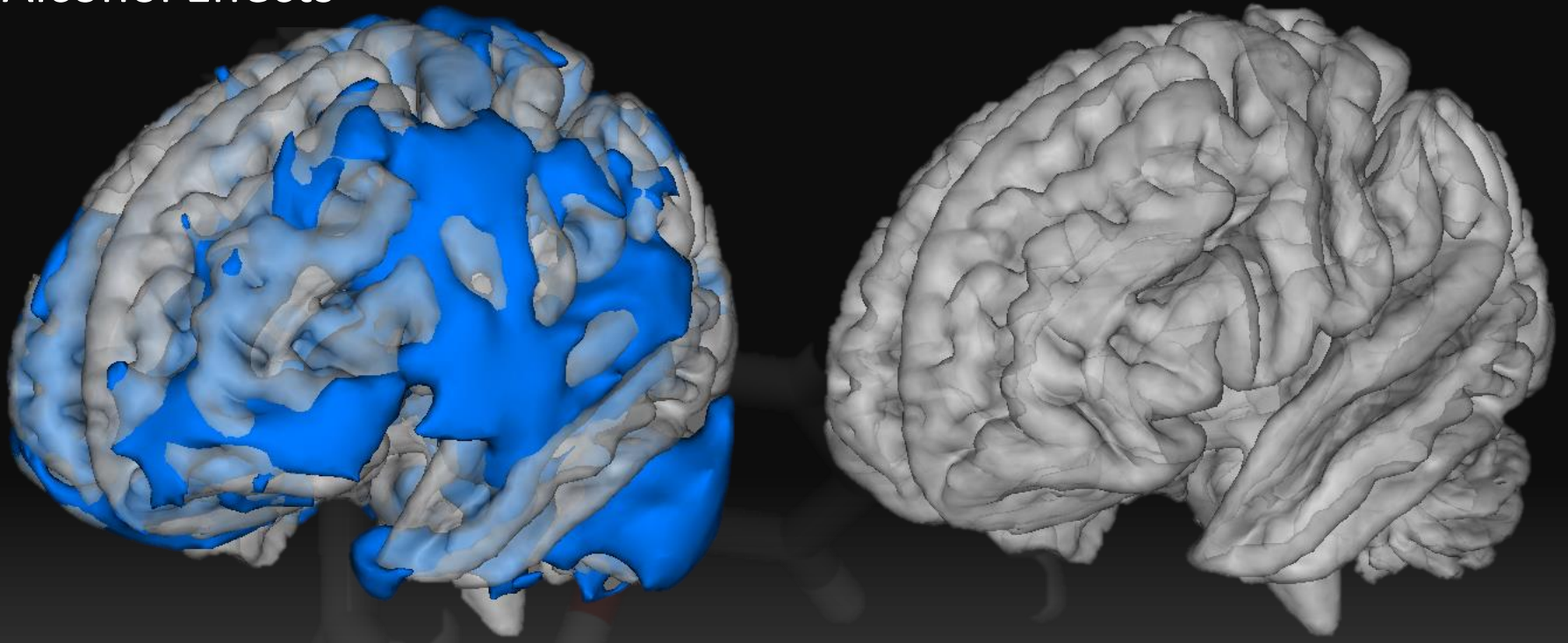
AUDIT = Alcohol Use Disorders Identification Test; TLFB = Time-line Follow-Back (30 days). Percentages approximate due to rounding error.

Thayer et al. (2017). *Addiction*

Adult Sample – Gray Matter Volume

Alcohol Effects

Cannabis Effects

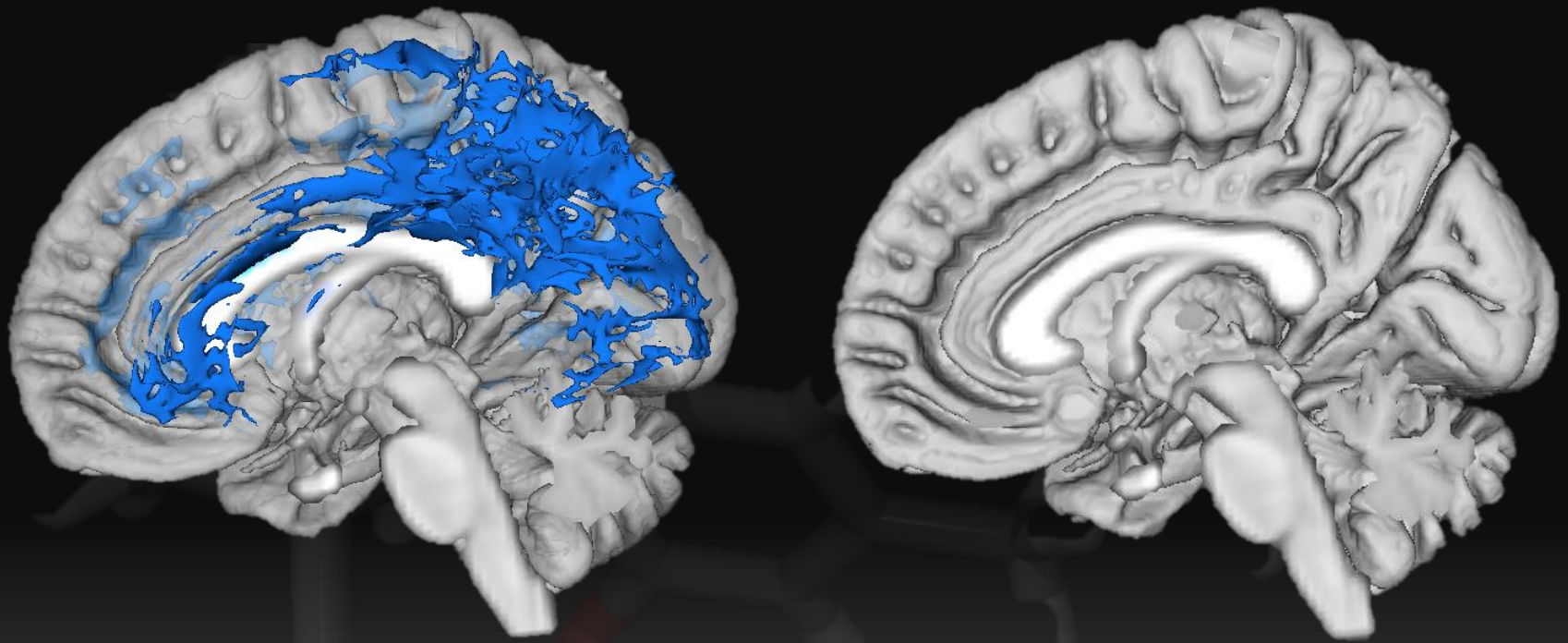


Thayer et al. (2017). Addiction

Adult Sample – White Matter Integrity

Alcohol Effects

Cannabis Effects

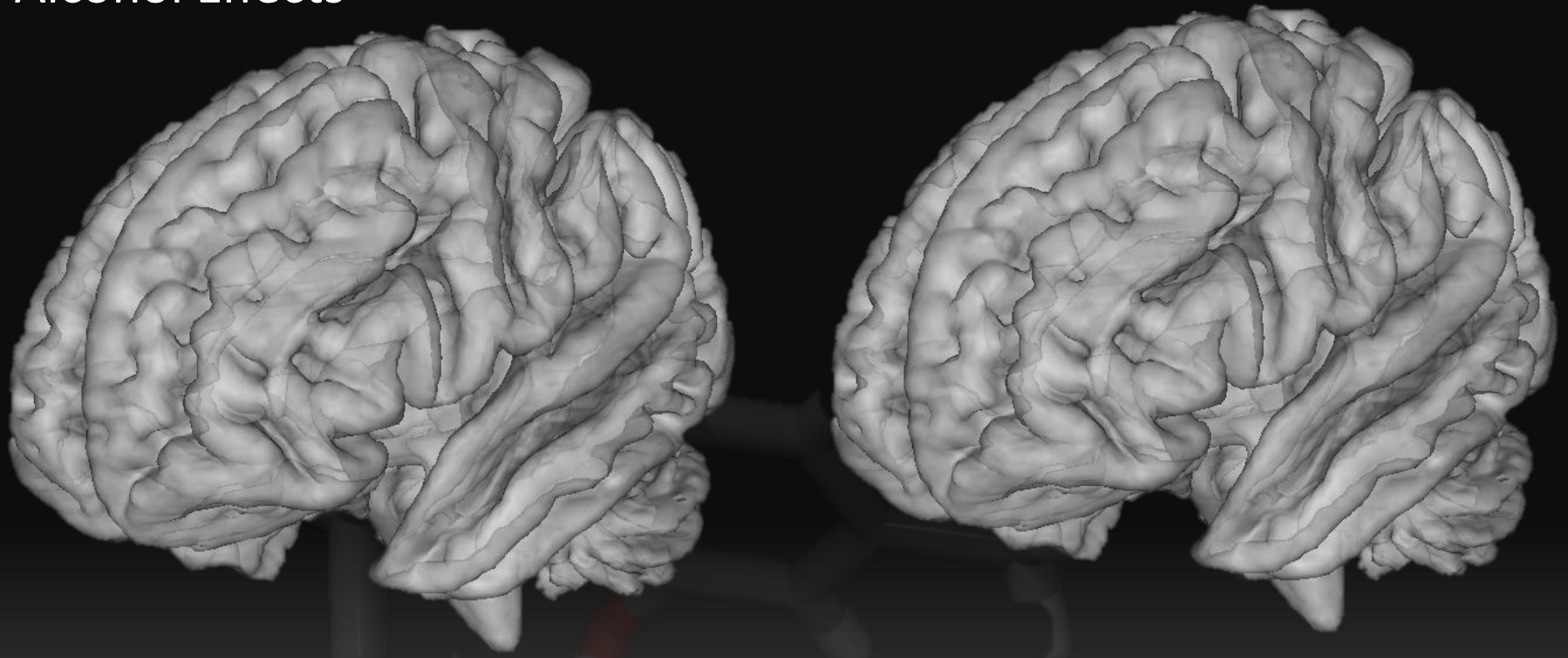


Thayer et al. (2017). Addiction

Adolescent Sample – Gray Matter Volume

Alcohol Effects

Cannabis Effects

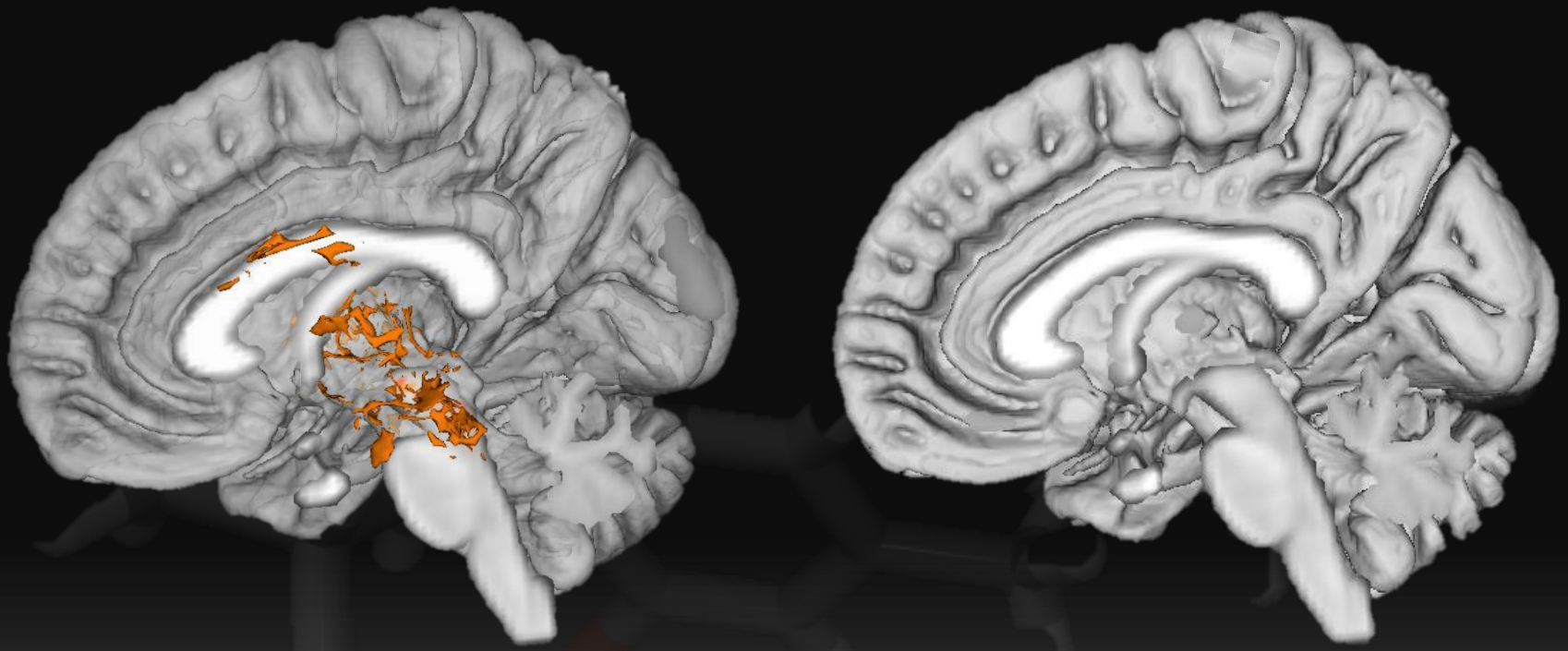


Thayer et al. (2017). Addiction

Adolescent Sample – White Matter Integrity

Alcohol Effects

Cannabis Effects



Thayer et al. (2017). Addiction

Bad for the Brain?

- Right now, there is no consistent evidence that cannabis use causes long-term, pervasive changes in brain morphology
  - Confirmation bias in the literature?

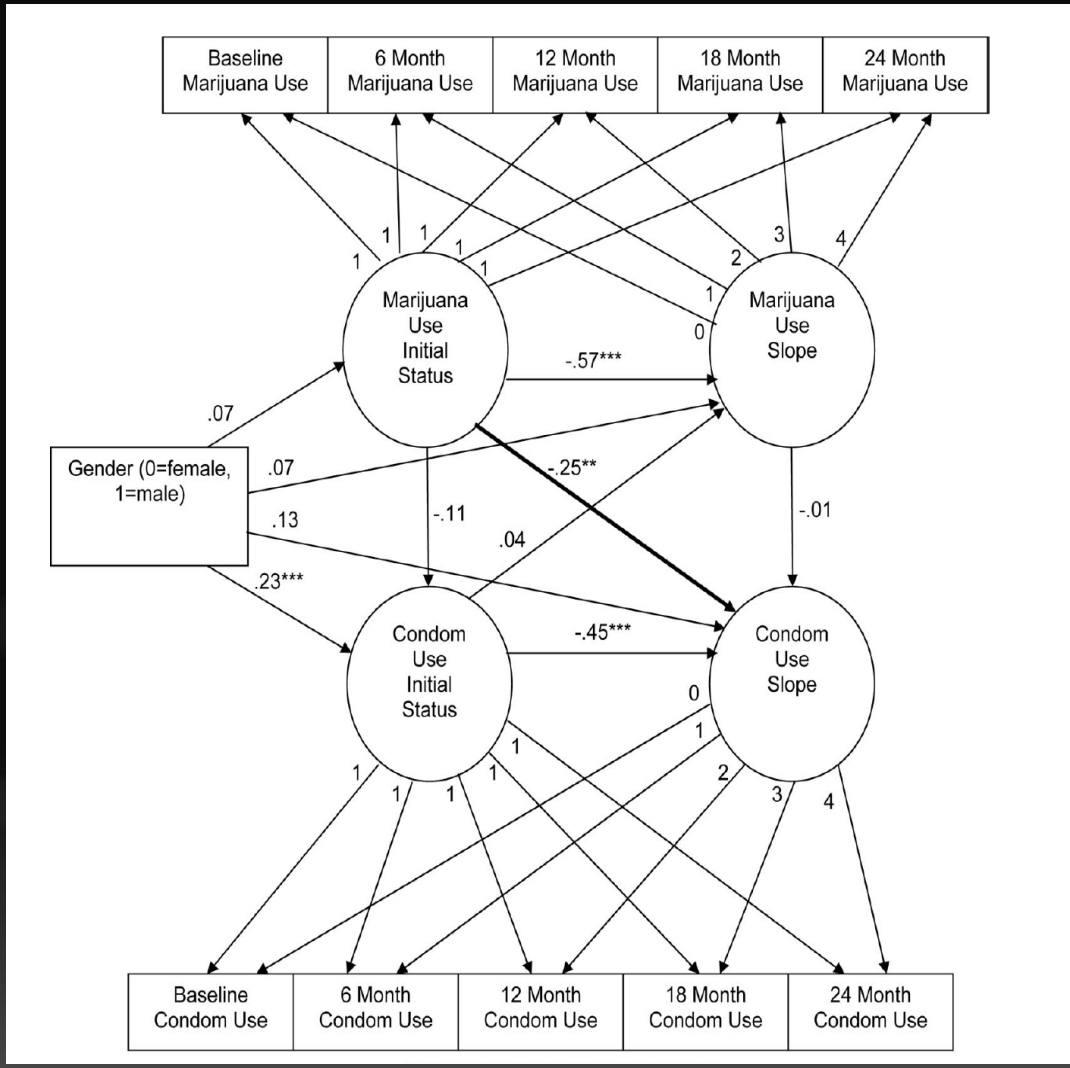
- Absence of evidence not necessarily evidence of absence
  - May eventually find some evidence (ABCD?)

- There may be important individual differences with regard to abuse liability or negative effects

HOWEVER: Even if we don't see "brain" effects, we know that cannabis negatively impacts cognition, learning and memory, particularly in the short term!!!!!

Substance Use and Related Risk Behavior

- Marijuana use is associated with risky sexual behavior both episodic and longitudinal (Bryan et al., 2012, *Dev Psych)*

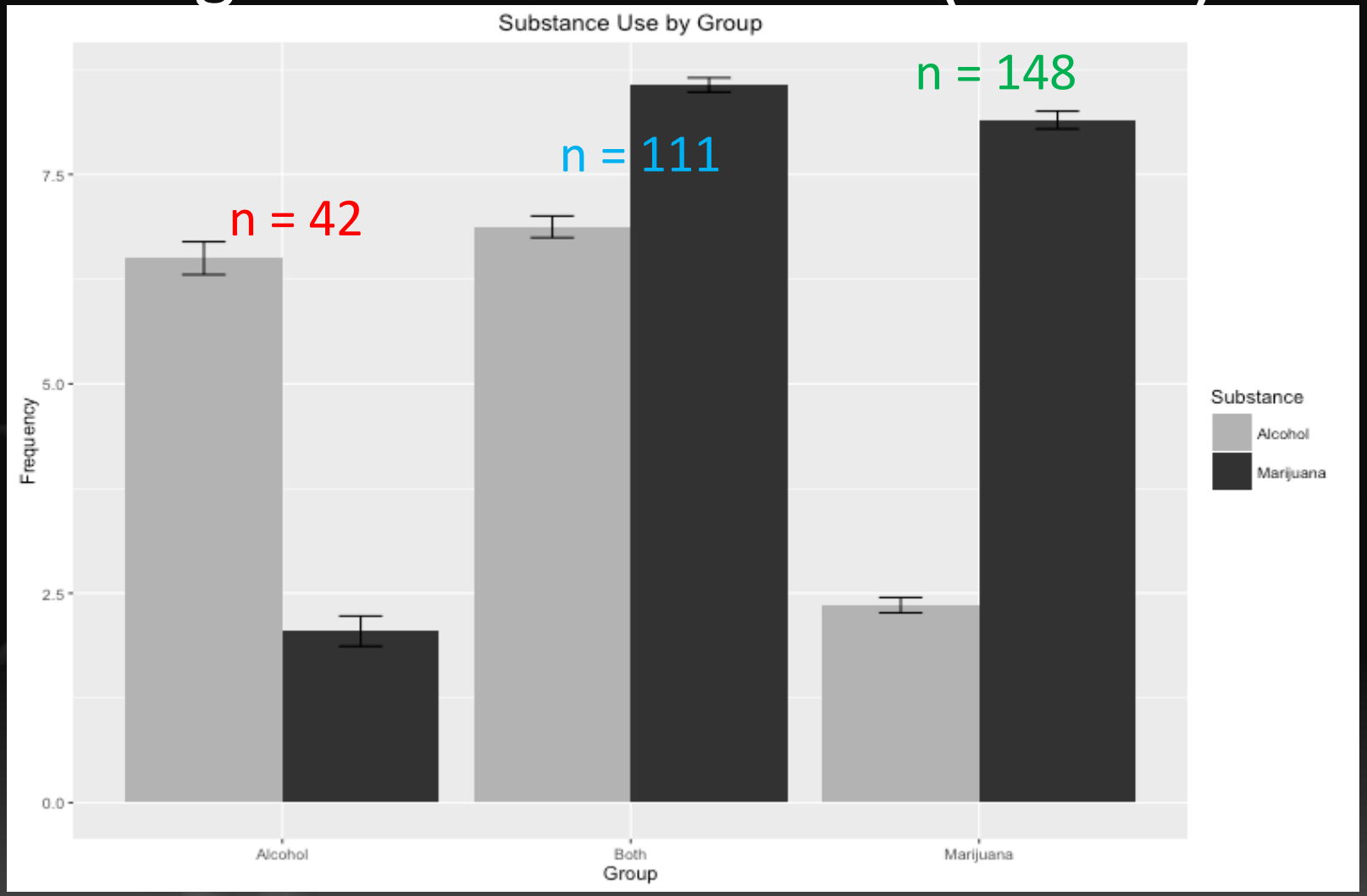


Co-Occurring Alcohol Use

- Simultaneous alcohol and marijuana use is associated with greater negative consequences than alcohol use alone (Subbaraman & Kerr, 2015).

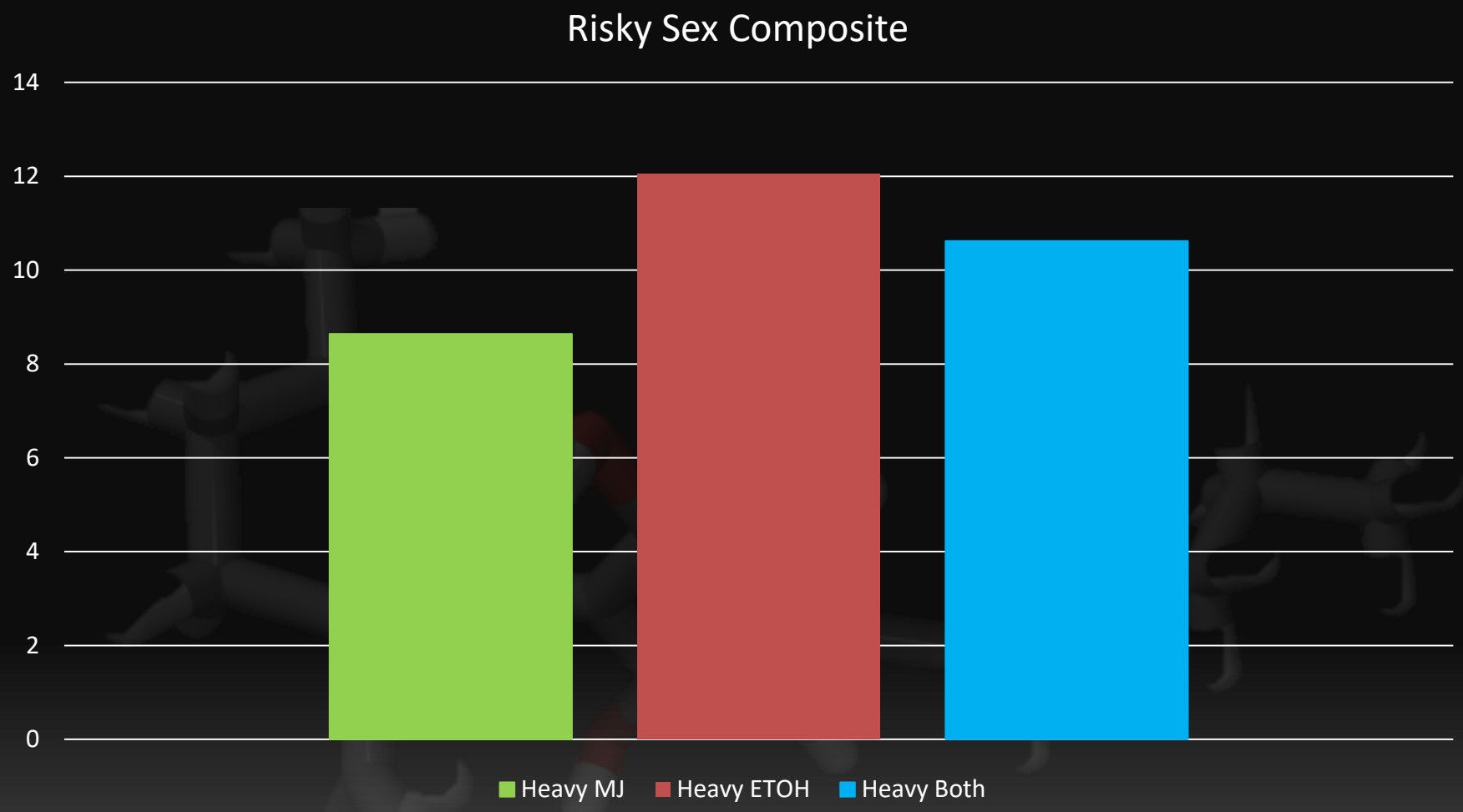
- Alcohol and marijuana are commonly used together by adolescents (Arnett, 2005).

Substance Use Patterns
High Risk Adolescents (*n*=301)



(Gillman et al., 2017, *AIDS & Behavior)*

Sexual Risk Behavior



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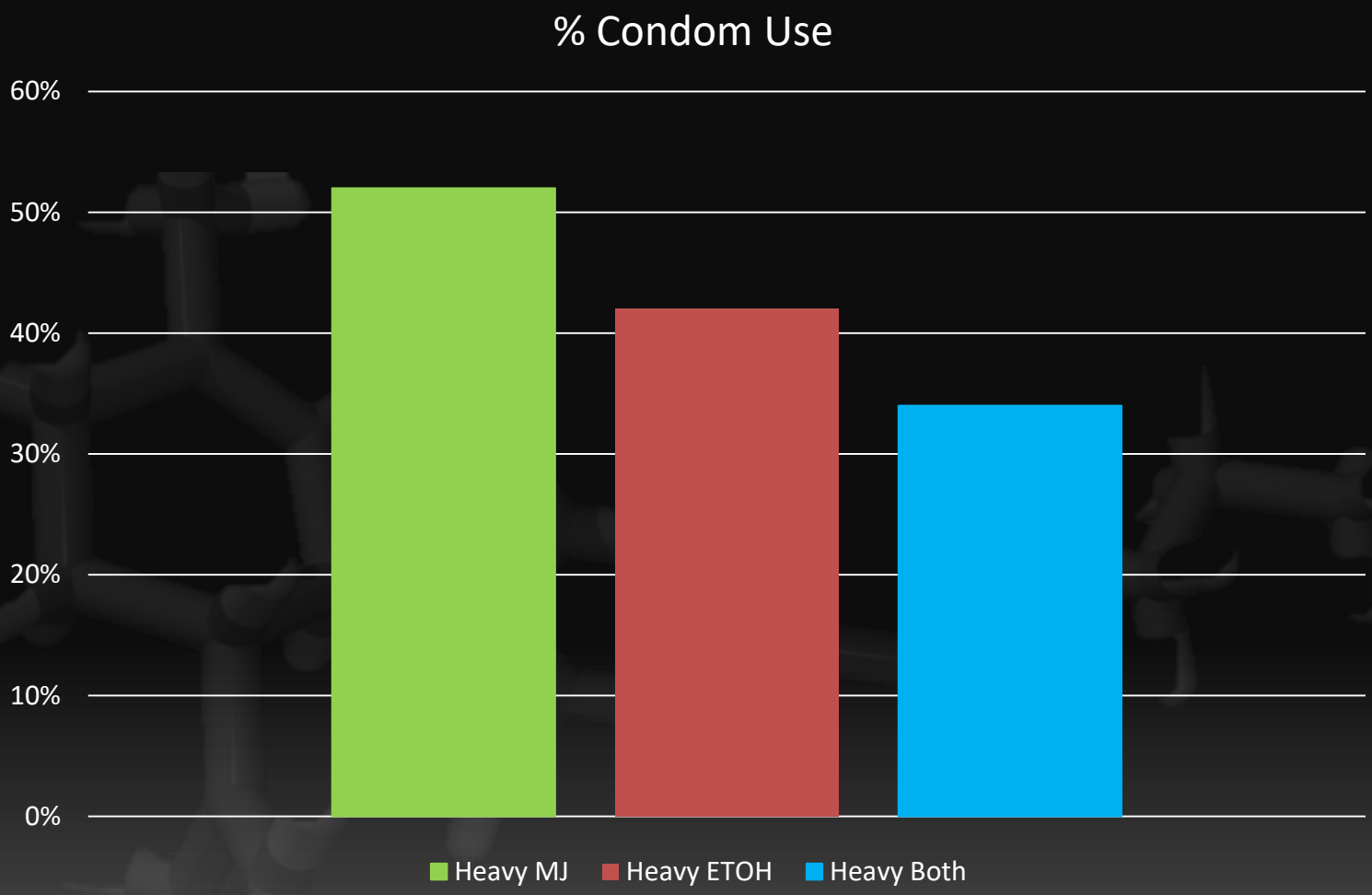
Sexual Risk Behavior



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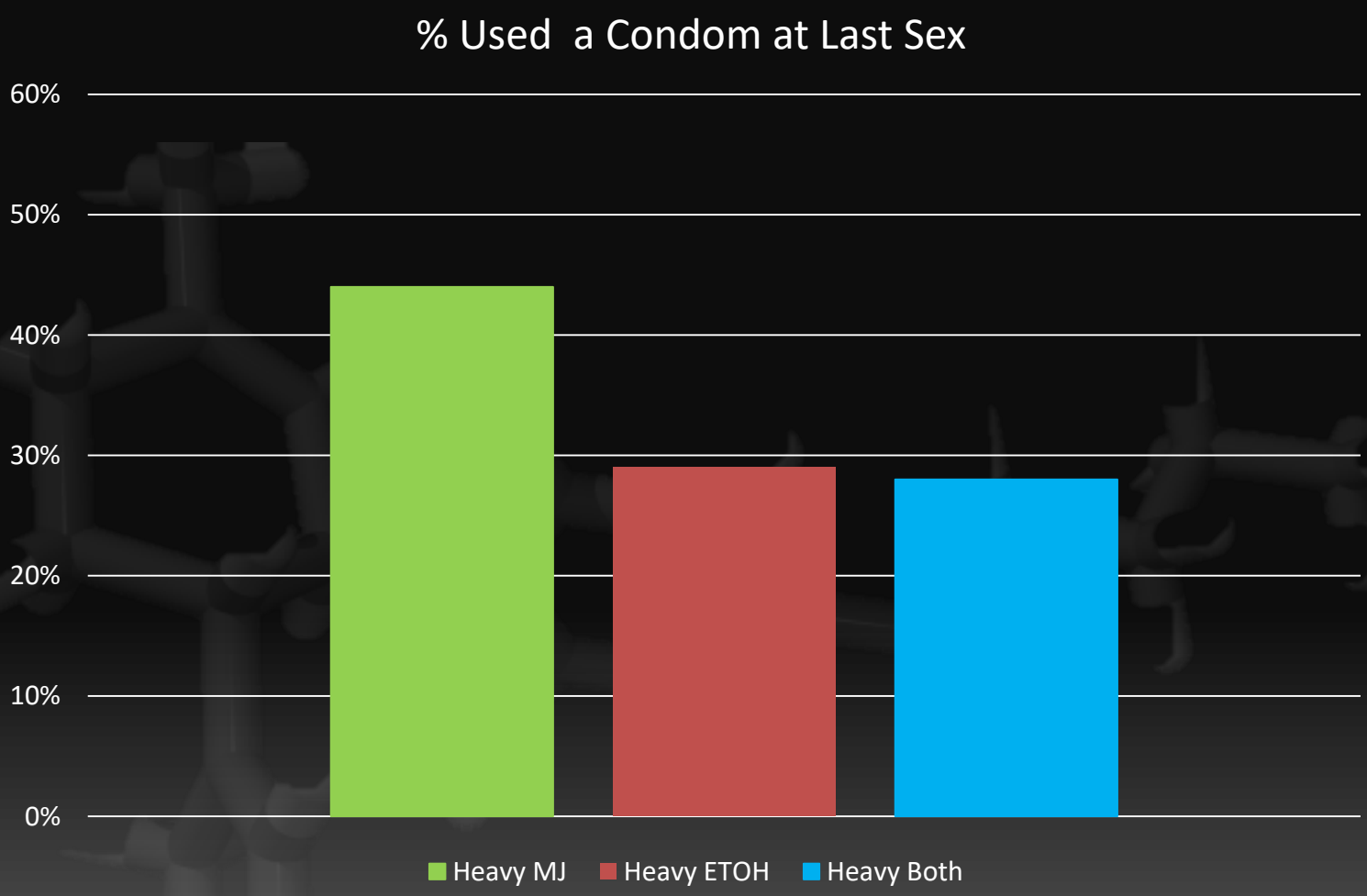
Sexual Risk Behavior



(Gillman et al., 2017, *AIDS & Behavior)*

Bad for Behavior?

- Adolescents engage in developmentally appropriate exploratory behavior
  - Substance Use, Romantic Relationships, Sexual Behavior
- Substance use compromises judgment and potentially disinhibits other risk behavior
- Marijuana use linked to higher levels of sexual risk behavior
- Combination of alcohol and marijuana may be particularly problematic

Research Reboot

- Most previous research has failed to factor in the following:
  - Potency and dose
  - Cannabinoid and terpene profiles
  - Type of product
  - Risks and benefits may differ between medical vs. recreational user

- Need new approaches to study impact of cannabis products available in state-regulated markets

Mobile Cannabis Pharmacology Lab

- We cannot bring people to the lab – but we can bring the lab to the people

Observational Study Design

Time 1

- Regular users
- Baseline Assessment
- Blood Draw
- *Randomly assigned* to product that they purchase themselves

Purchase of Assigned Product (A or B)
Followed by 5 day period of *ad libitum* use

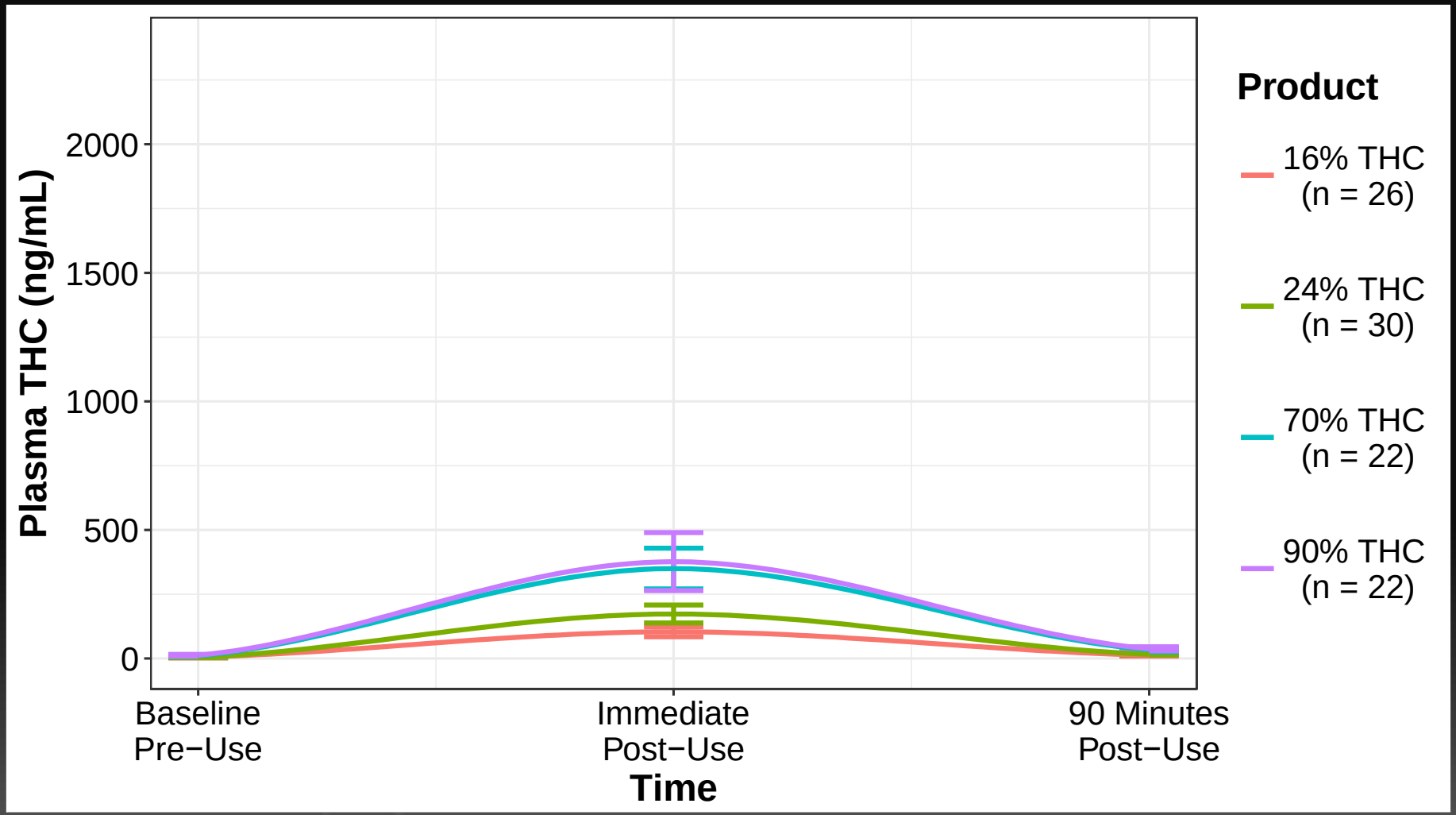
Time 2

- Pre-arranged time
- Assessed in Mobile Pharmacology Lab before and after self-admin
  - Blood Draw
  - Subjective Effects
  - Cognitive Battery
  - Motor Control Battery
  - Driving Ability

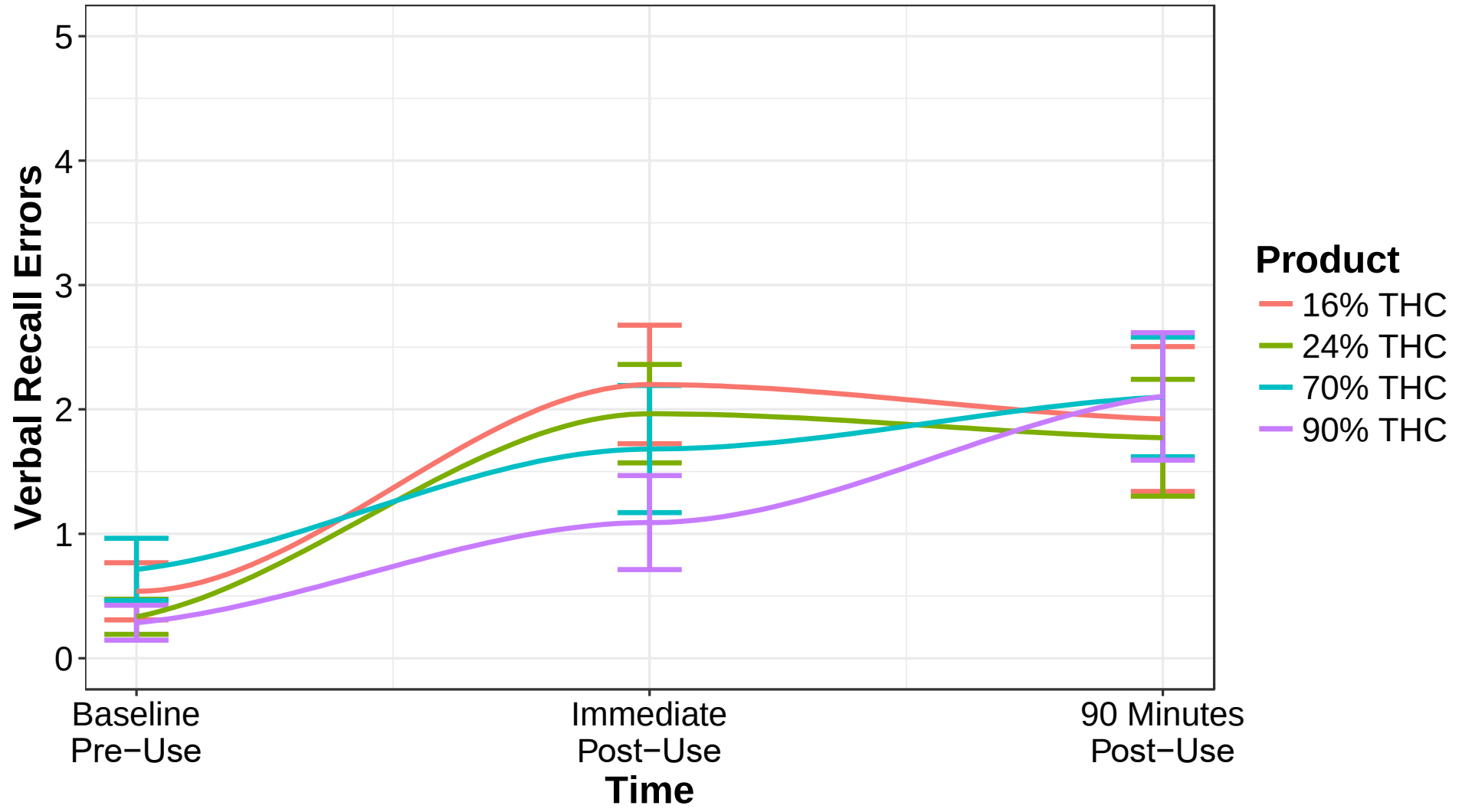
← **Flower/Strains:** 24% vs 16% THC

Dabbing/concentrates: 70% vs 90% THC → concentrated hash oil

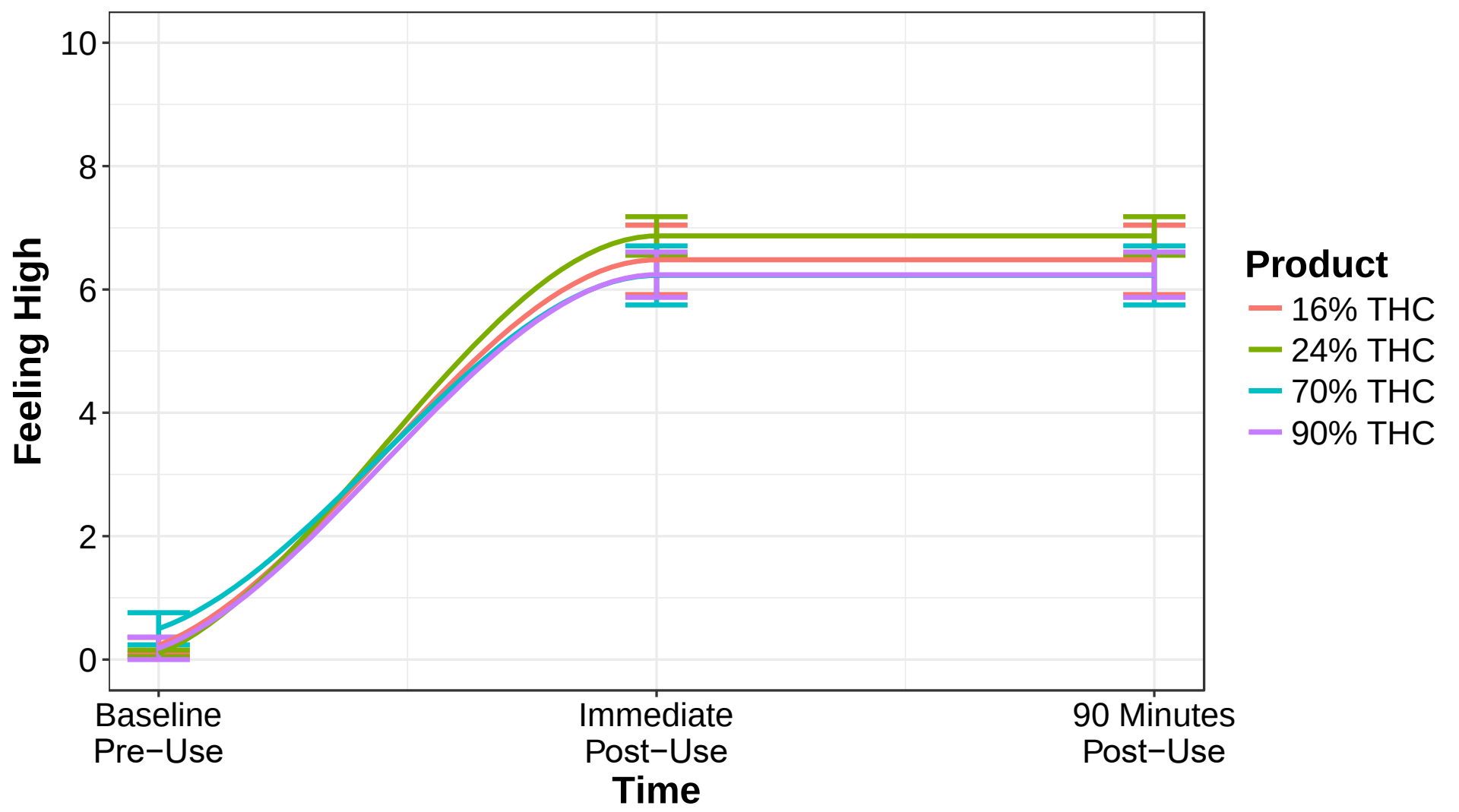
Plasma THC concentrations



Delayed Verbal Recall Errors



Subjective effect - “Feeling High”



Summary

- Blood levels clearly greater for concentrate
- Yet no significant differences in cognitive or intoxication measures
- Individuals probably titrate dose to achieve effect
- Tolerance is likely very important predictor
- Risks associated with high tolerance and high blood levels? If adolescents are using these products, what are the consequences?

Ongoing and Future Studies

- Comparing 3 different groups taking a range of THC:CBD (funded by NIDA)

- NIH grants to understand implications for public health
  - Adolescents with CUD (J. Ellingson, PI, grant under revision)
  - Cannabis and pain (funded by NCCIH)
  - Cannabis and anxiety (funded by NIDA)
  - Cannabis and risk for diabetes (pending funding by NIDDK)
  - Cannabis use for side effects of cancer treatment (Pilot funded by CU Cancer Center)
  - Cannabis and opiate use (pending council review by NIDA)
  - Aging, cognition, and cannabis (submission for NIA)

Thank You!!