

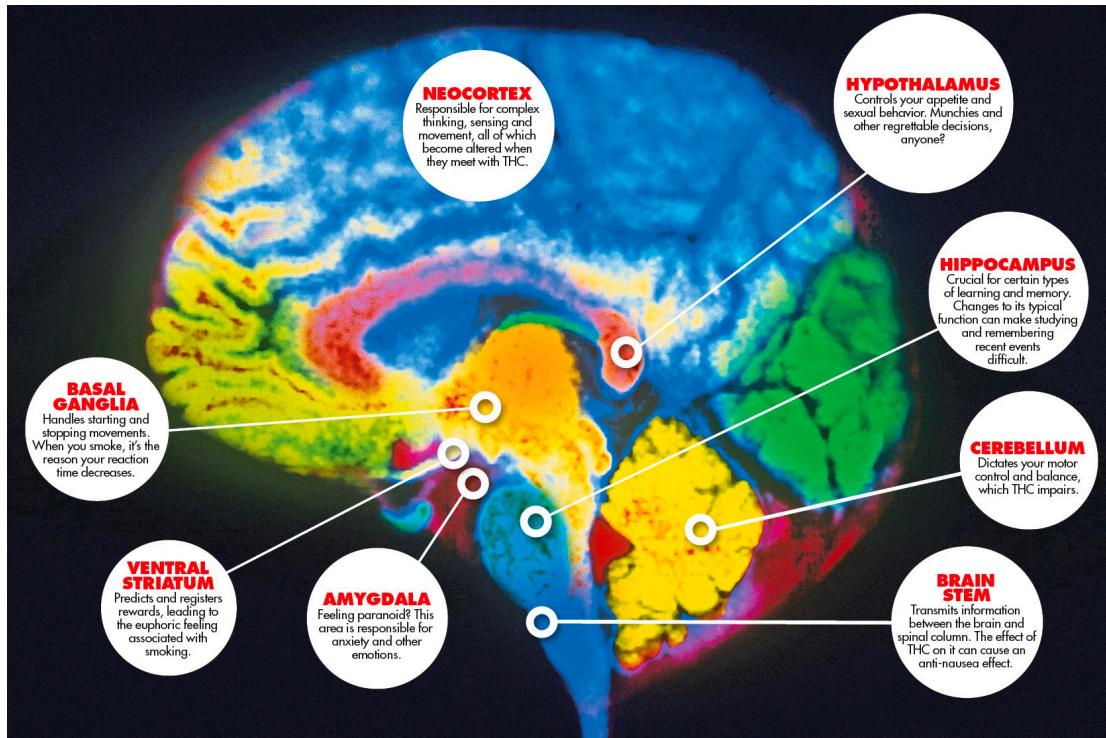
Cannabis and Health

Module 4

Lecture 1: Cannabis and Brain Morphology

Cannabis and the Brain

- Understanding the short and long-term effects of cannabis exposure on the brain has been a research priority for a long time
- NIDA has sponsored studies in animals and in humans



Morphological Effects

- Reviews of mostly smaller studies have found cannabis use to be associated with changes in gray matter density (see Lorenzetti et al., 2016 for review)
- Yet, large studies have tended to show no association with gray matter density (Gillespie et al., 2018; Orr et al., 2016)
- And, a large sibpair/twin study suggests any association is due to shared vulnerability (Pagliaccio et al., 2015)
- And while additional large datasets exist, no reports of a positive association in those datasets

Why the discrepancies across studies?

- Our 2014 study:
 - 29 adult non MJ users compared to 29 adult daily users
 - 50 adolescent non MJ users compared to 50 adult daily users
 - Very carefully matched on alcohol use and other variables
 - No differences between those who reported marijuana use every day and those who reported no use

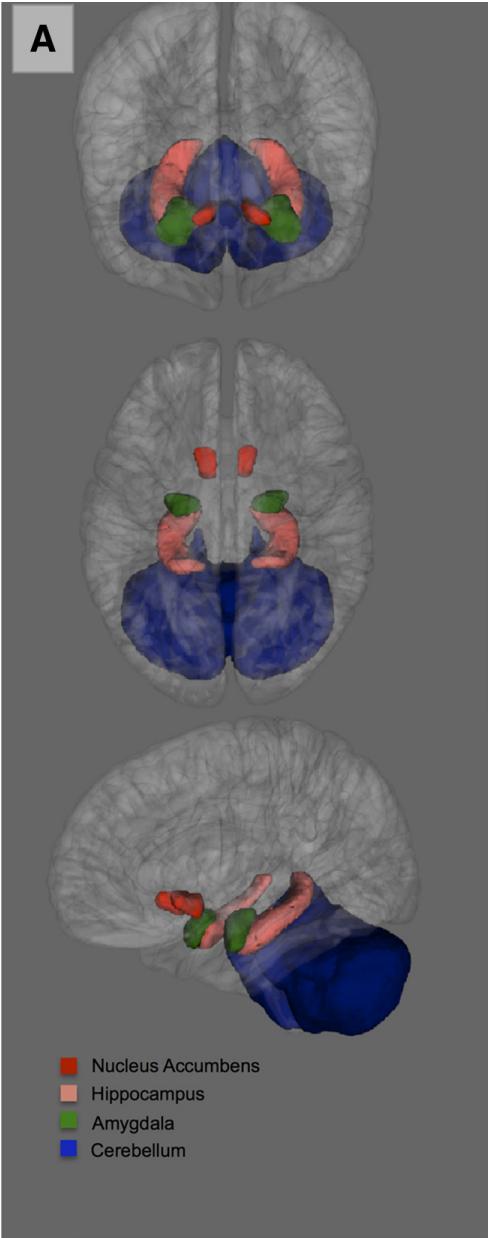
The Journal of Neuroscience, January 28, 2015 • 35(4):1505–1512 • 150

Neurobiology of Disease

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

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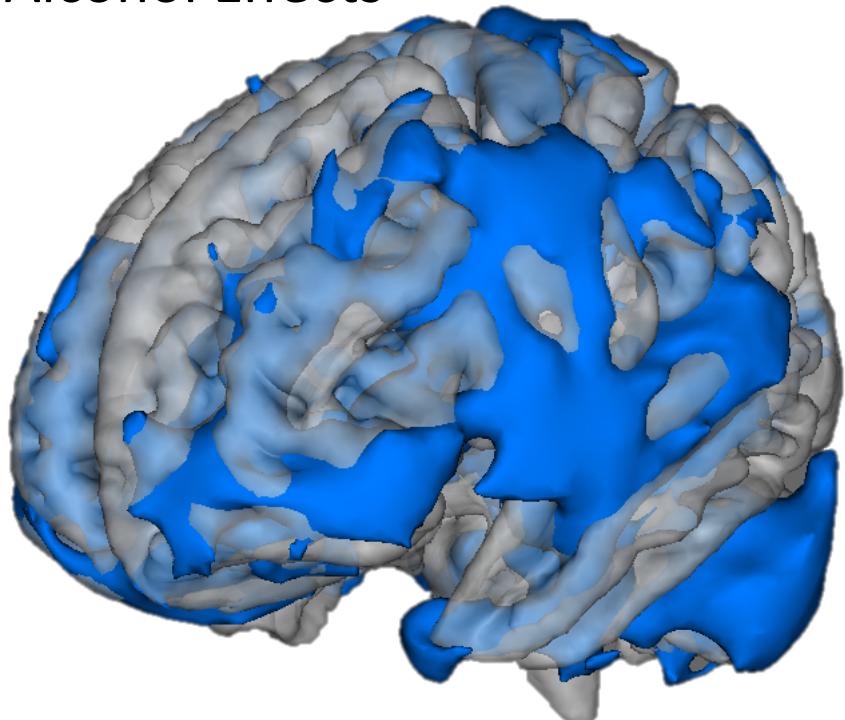


Cannabis, Alcohol, and the Brain

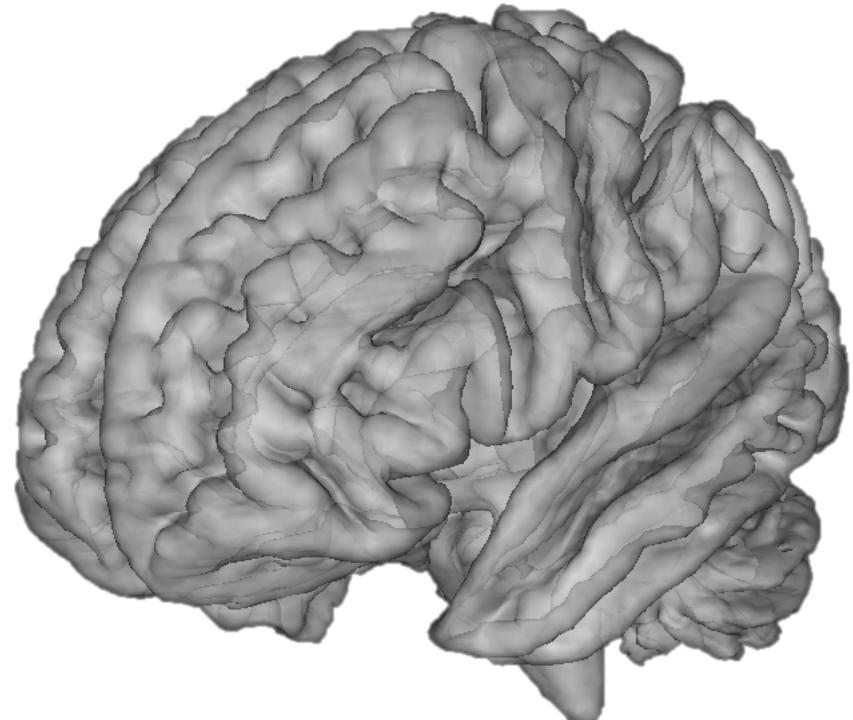
- Sample Ascertainment
 - Total n = 1336, recruited in NM
 - 882 adults (age 18-55), 454 adolescents (age 13-18)
- Adults
 - 345 users; 190 > 1x/week
- Adolescents
 - 275 users; 198 > 1x/week
- Analysis
 - Analyzed the effect of alcohol while controlling for cannabis
 - Analyzed the effect of cannabis while controlling for alcohol

Adult Sample – Gray Matter

Alcohol Effects

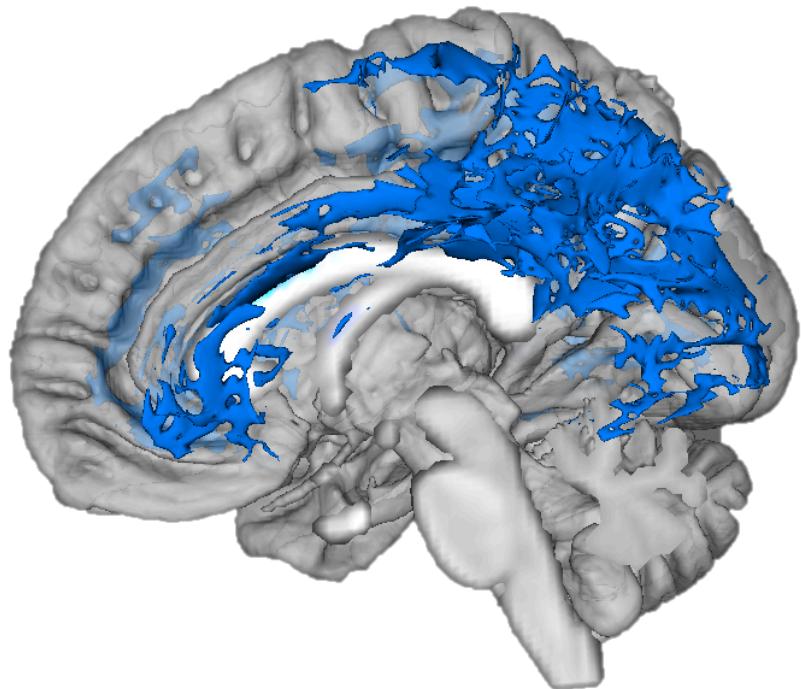


Cannabis Effects



Adult Sample – White Matter

Alcohol Effects

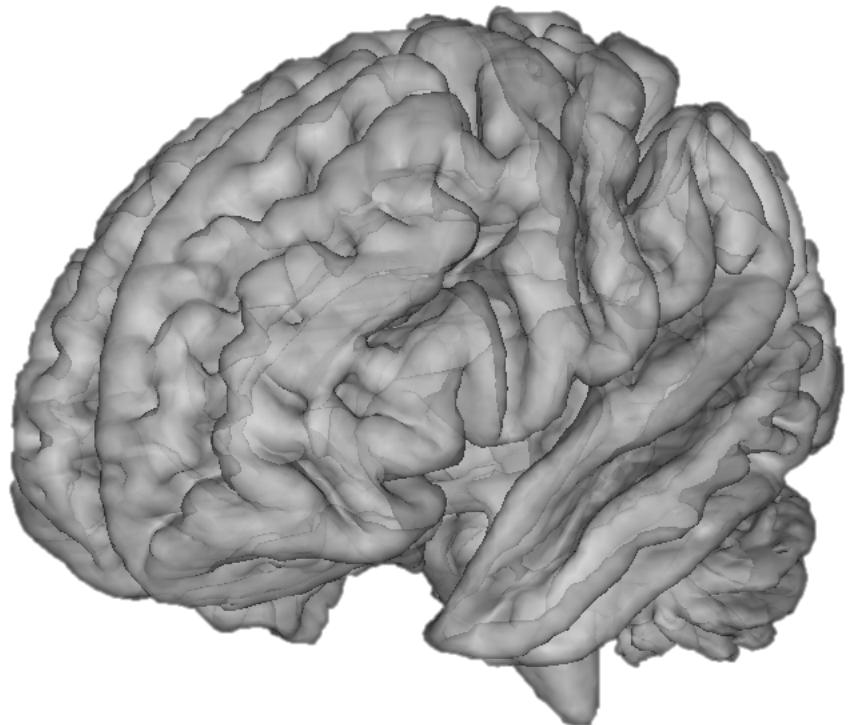


Cannabis Effects

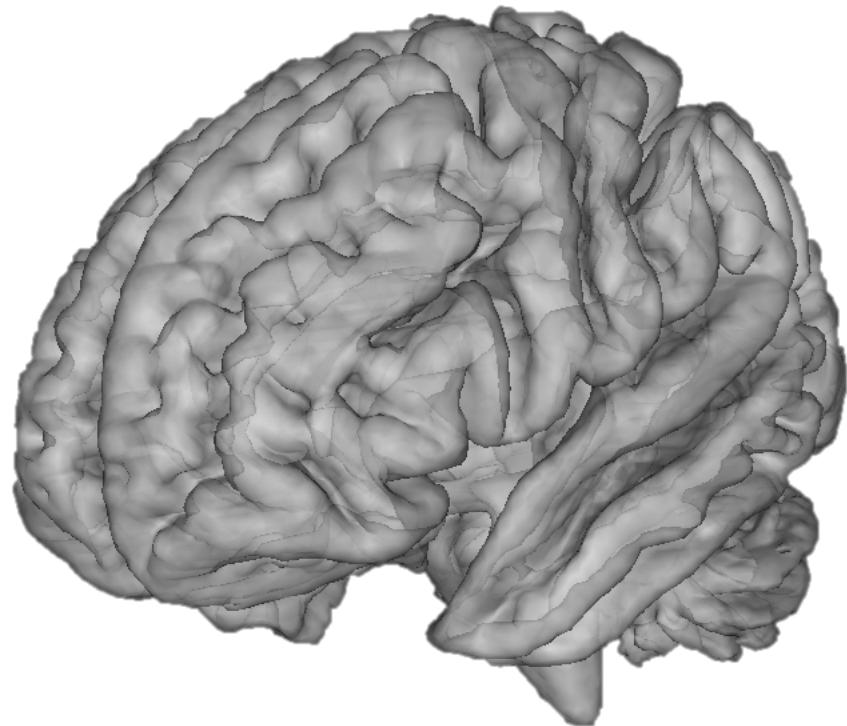


Adolescent Sample – Gray Matter

Alcohol Effects

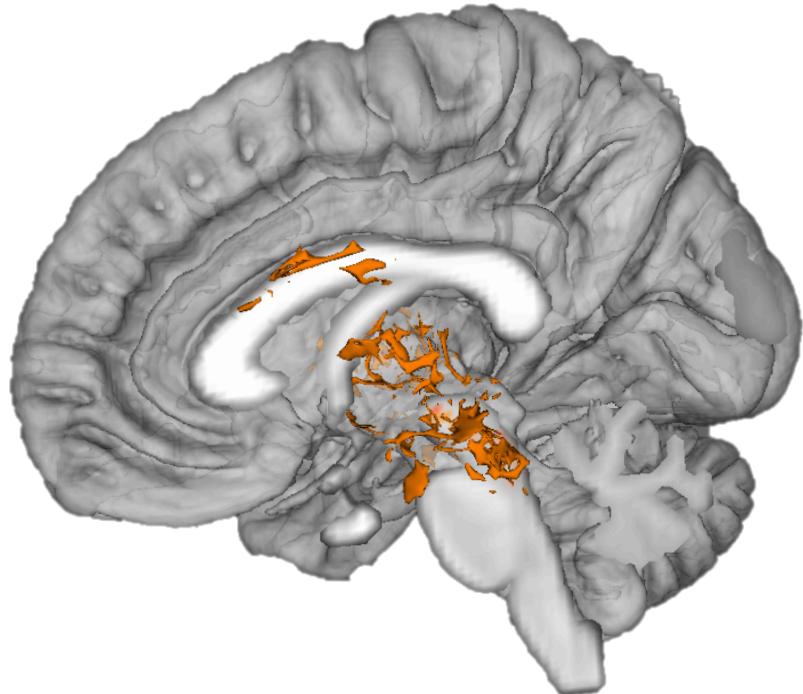


Cannabis Effects



Adolescent Sample – White Matter

Alcohol Effects



Cannabis Effects



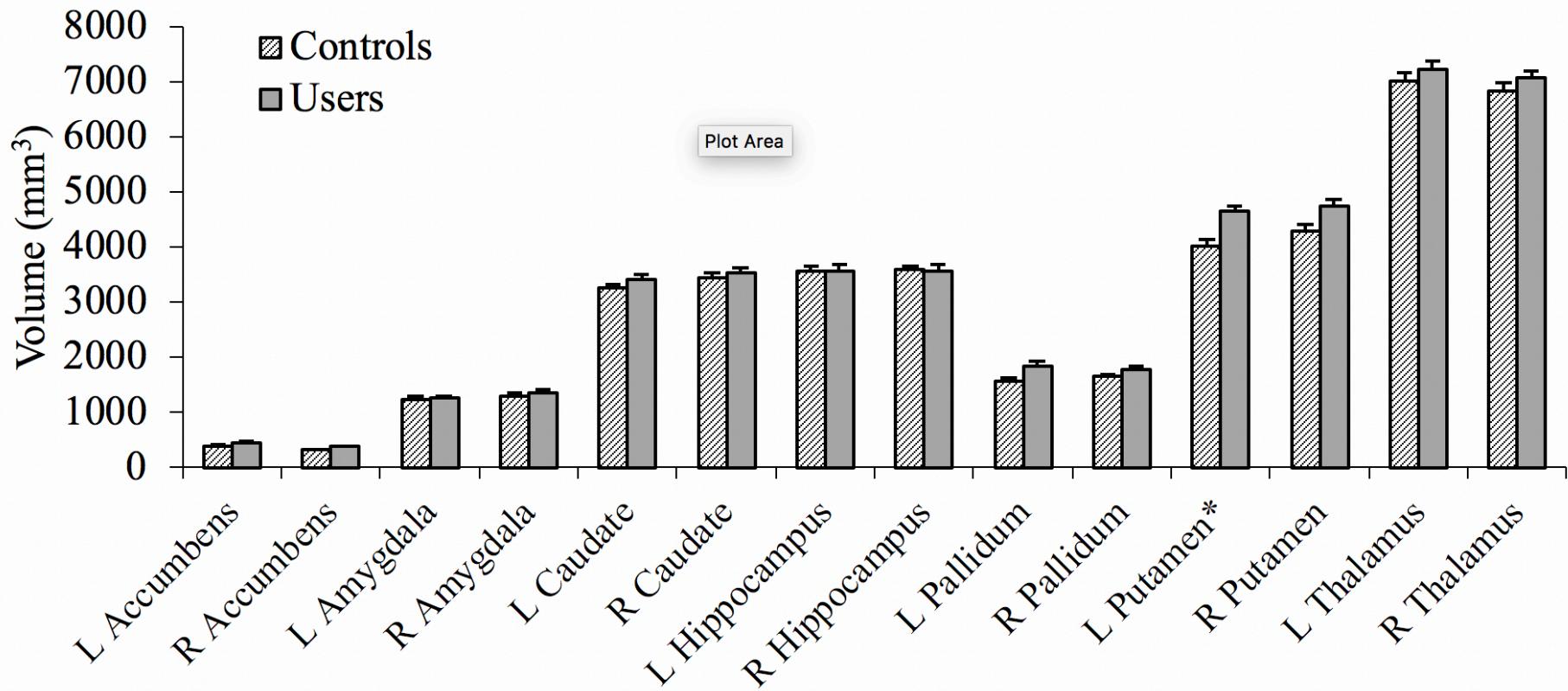
Why conflicting findings?

- Findings can be confounded with alcohol and tobacco use in small studies
- Findings may be an artifact of neuroimaging – easy to find an effect SOMEWHERE in the brain and studies do not highlight fact that they do not replicate previous findings in terms of location
- There likely is a shared vulnerability – people with structural irregularities more likely to use cannabis – this is misinterpreted as causal due to confirmation bias
- Confirmation bias and need to publish lead to stretching – e.g., no positive finding for gray matter volume, but finding of change in “shape” of structure

Older Adults: Regular Users vs. Controls

- Study recruited adults over the age of 60
- 28 regular users (mean of 20 years)
- 28 controls (no history of cannabis use)
- Compared on brain morphology and NIH neurocognitive battery

No significant differences found except for putamen



	Marijuana Users <i>Mean (SD; Range)</i>	Short-term Users <i>Mean (SD; Range)</i>	Lifetime Users <i>Mean (SD; Range)</i>
<i>N</i>	28	13	15
<i>Race/Ethnicity</i>			
Caucasian	26	13	14
Latino	1	0	1
Females:Males	10:18	6:7	4:11
Age	66.79 (5.28; 60-80)	67.38 (4.65; 61-80)	66.27 (5.89; 60-80)
Years Education	16.46 (2.33; 13-22)	16.69 (2.50; 13-20)	16.27 (2.25; 14-22)
AUDIT Total Score	4.14 (3.66; 0-18)	3.23 (2.28; 0-7)	4.93 (4.46; 0-18)
BDI-II Total Score	3.75 (4.71; 0-18)	3.69 (4.99; 0-18)	3.80 (4.63; 0-18)
BAI Total Score	2.39 (2.83; 0-12)	2.23 (3.35; 0-12)	2.53 (2.42; 0-7)
Age at First Use	20.04 (8.11; 14-58)	22.31 (11.41; 14-58)	18.07 (2.49; 14-22)
Years of Regular Use*	23.55 (19.89; 1.5-50.0)	4.19 (1.55; 1.5-7.0)	40.33 (10.56; 19.0-50.0)
MDS	0.79 (1.17; 0-4)	0.85 (1.21; 0-4)	0.73 (1.16; 0-3)
TLFB Alcohol Use Days	33.89 (29.59; 0-88)	34.92 (29.56; 0-88)	33.00 (30.62; 0-88)
TLFB Total Drinks	68.08 (72.68; 0.00-264.00)	56.28 (54.57; 0.00-163.68)	78.31 (85.99; 0-264.00)
TLFB Drinks/Drinking Day	1.50 (1.02; 0-4)	1.21 (0.86; 0-3)	1.74 (1.11; 0-4)
TLFB Marijuana Use Days	63.46 (24.87; 12-90)	53.92 (27.52; 12-90)	71.71 (19.63; 32-90)
TLFB Total mg THC	1033.27 (923.20; 99.82-3502.63)	840.74 (806.81; 99.82-3150.00)	1200.13 (1010.69; 168.13-3502.63)

AUDIT: Alcohol Use Disorders Identification Test; BDI-II: Beck Depression Inventory-Second Edition; BAI: Beck Anxiety Inventory; MDS: Marijuana Dependence Scale; TLFB: Timeline Follow-back

*Group difference $p < .001$

Conclusions

- Right now, there is no consistent evidence that cannabis use causes long-term, pervasive changes in brain morphology (gray matter density or white matter fiber integrity)
 - Confirmation bias in the literature?
- Absence of evidence not necessarily evidence of absence
 - May eventually find some evidence
- Products available today are not represented in the literature
- Does not mean that cannabis is harmless