



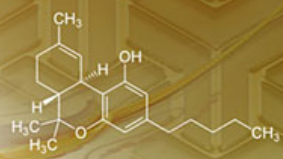
CANNABIS AND PREGNANCY

ASAM
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National Institute on Drug Abuse



National Institute
on Drug Abuse



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T.H.C
TETRAHYDROCANNABINOL

DISCLOSURES: MERCK SHAREHOLDER (SRBW);
NONE (NDV)

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LEARNING OBJECTIVES

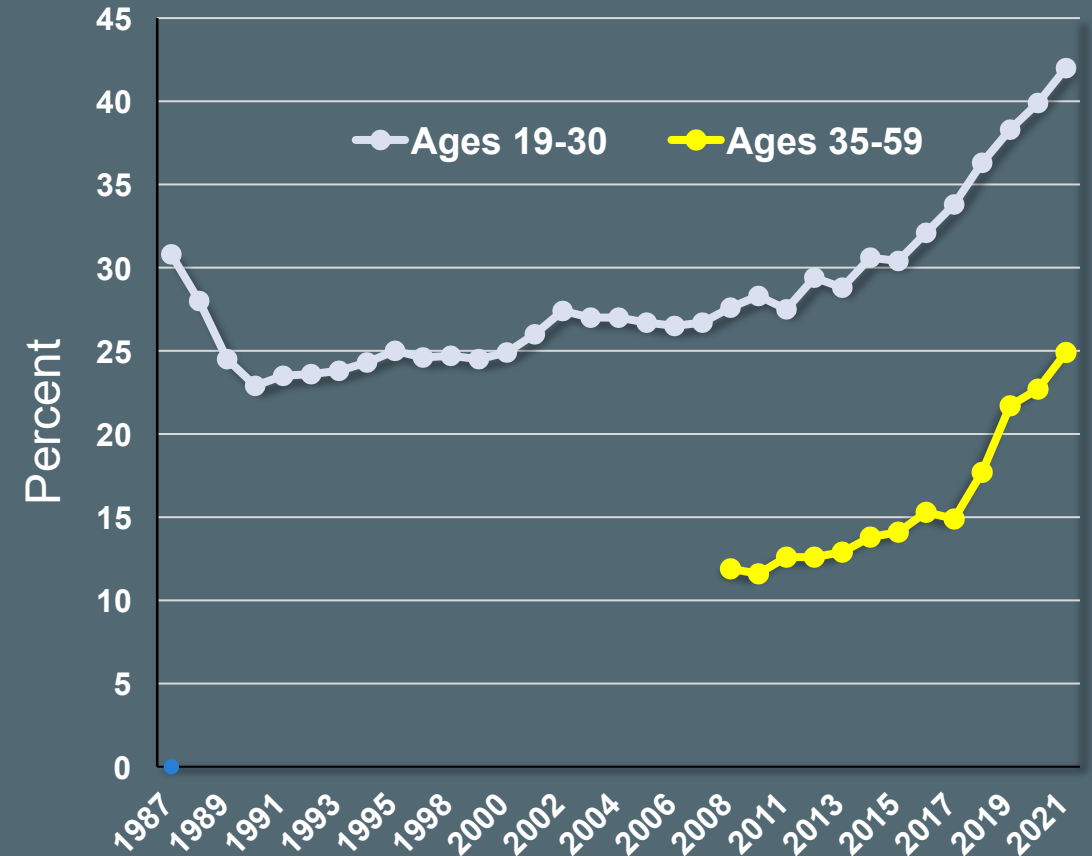
AT THE COMPLETION OF THIS PRESENTATION THE ATTENDEES WILL BE ABLE TO DESCRIBE:

1. Trends and patterns of cannabis use in the U.S.
2. Potential short and long-term consequences of THC exposure during fetal development
3. Information to convey to pregnant women about cannabis use during pregnancy

CANNABIS: MOST COMMONLY USED FEDERALLY ILLICIT DRUG

- NEARLY **40 MILLION** AMERICANS 12 AND OLDER REPORT PAST MONTH CANNABIS USE.
- APPROXIMATELY **16.3 MILLION*** AMERICANS MET CRITERIA FOR CANNABIS USE DISORDERS IN 2021.
- AN ESTIMATED **2.6 MILLION** AMERICANS USED CANNABIS FOR THE FIRST TIME; **869 THOUSAND** WERE BETWEEN THE AGES OF 12 AND 17.

Trends in 12 Month Prevalence
Among Respondents Modal Ages 19
through 59

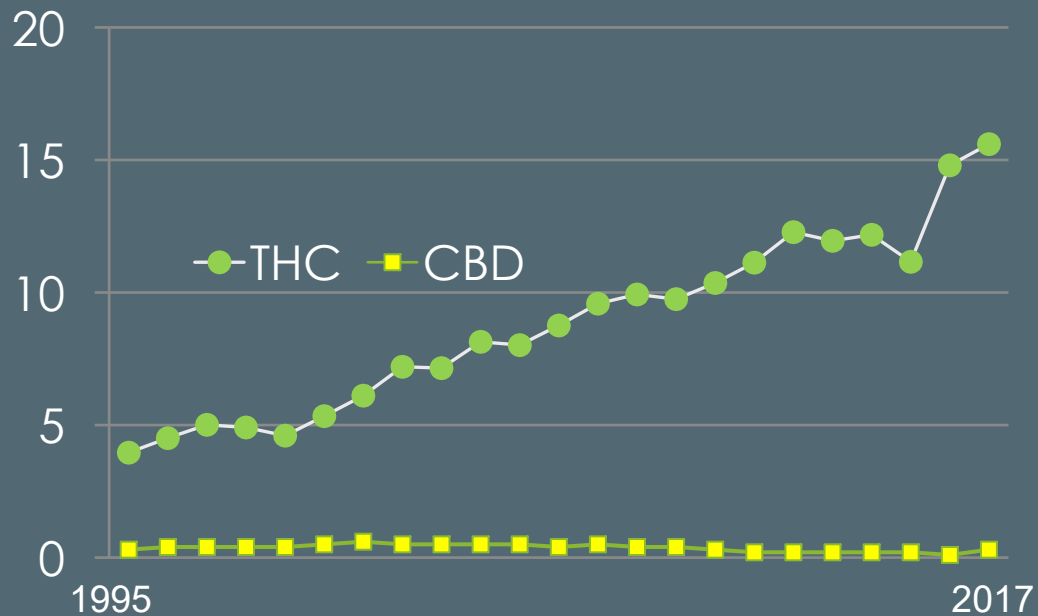


*Change in measure from DSM IV to DSM V in 2020; data not comparable to prior years Source: 2021 National Survey on Drug Use and Health, SAMHSA

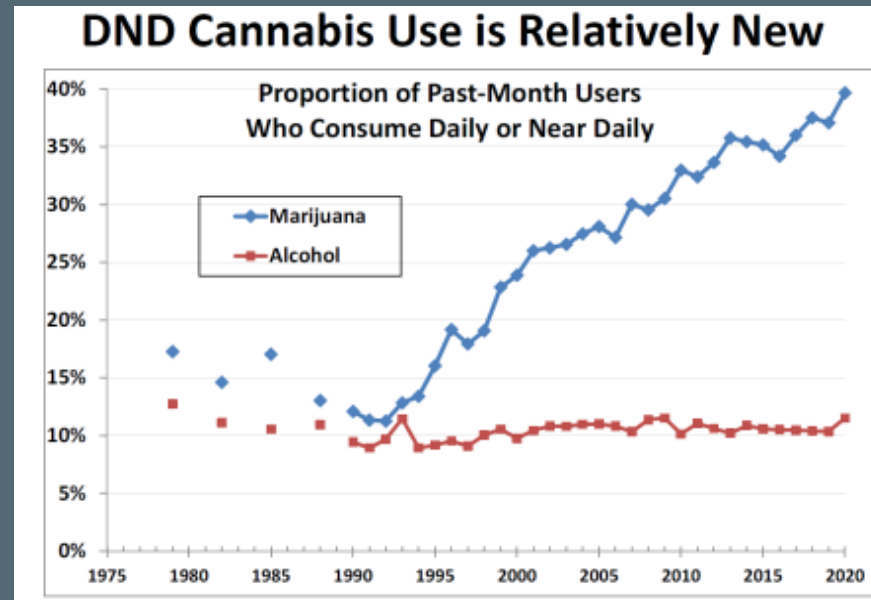
CHANGING LANDSCAPE: PRODUCTS AND PATTERNS OF USE



- PRODUCTS ARE CHANGING: POTENCY IS INCREASING DRAMATICALLY; NEW ROUTES OF ADMINISTRATION (EDIBLES, CONCENTRATES, VAPES, TINCTURES...)
- PATTERNS OF USE ARE CHANGING: MORE DAILY/NEAR DAILY USERS
- MARKETING: PRODUCTS ARE NOT LABELED CONSISTENTLY OR IN WAYS THAT CONSUMERS UNDERSTAND



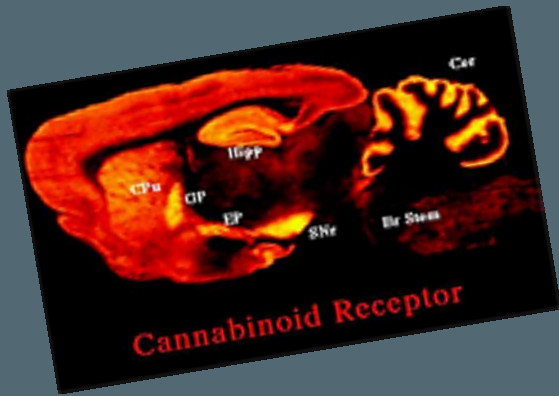
Source: U Miss, Potency Monitoring Project



Slide Courtesy of Jonathan Caulkins

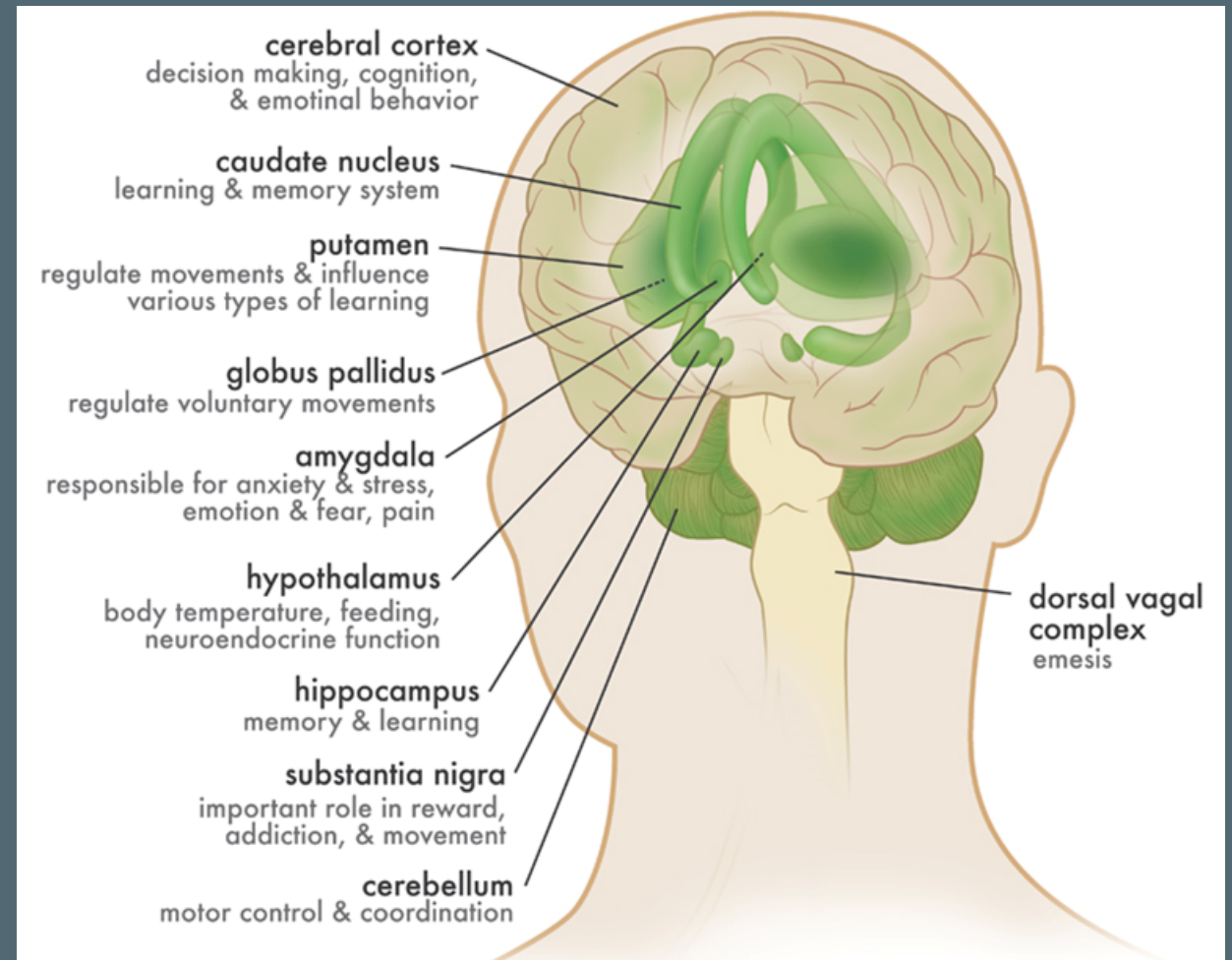


CANNABINOID RECEPTORS ARE LOCATED THROUGHOUT THE BRAIN



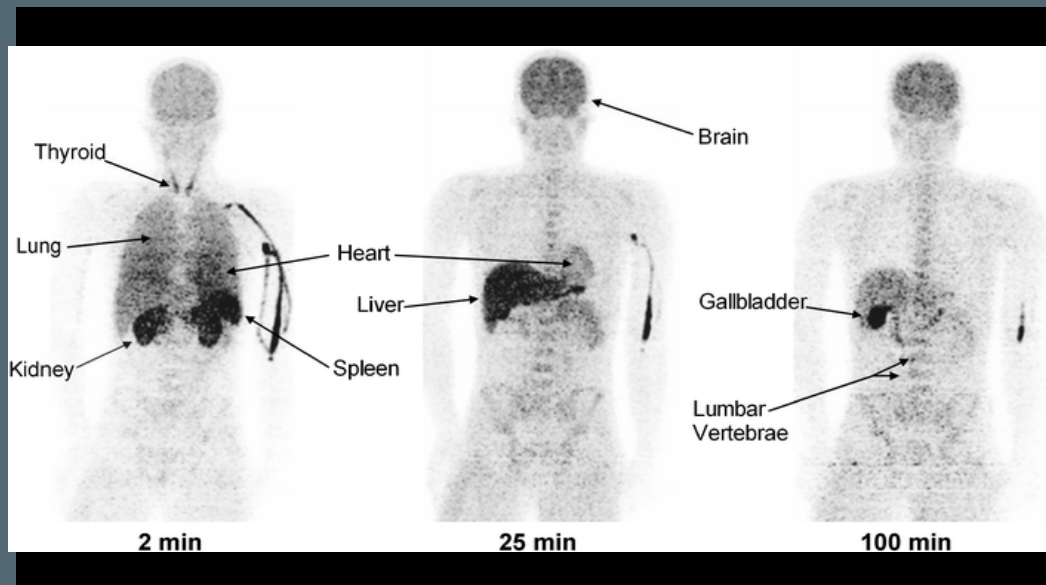
REGULATION OF:

- BRAIN DEVELOPMENT
- MEMORY & COGNITION
- MOVEMENT COORDINATION
- PAIN REGULATION & ANALGESIA
- IMMUNE FUNCTION
- APPETITE
- MOTIVATIONAL SYSTEMS & REWARD



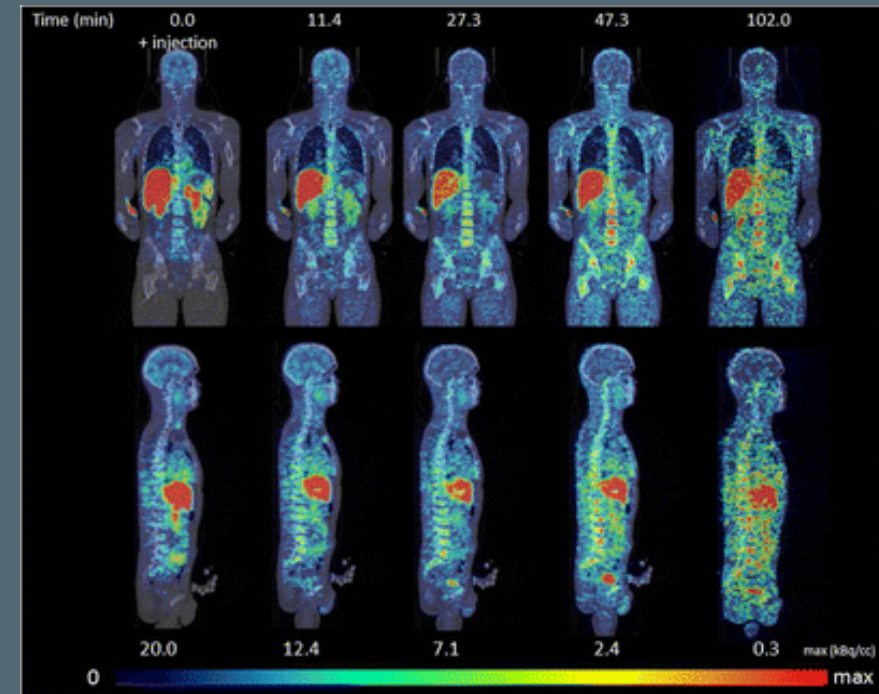
CANNABINOID RECEPTORS ARE ALSO LOCATED THROUGHOUT THE BODY

Whole Body Distribution of CB1 Receptors (2, 25, and 100 min after injection of ^{11}C -MePPEP)



Source: Terry et al., Eur J Nucl Med Mol Imaging. 2010

PET images of ^{11}C -NE40 (CB2R radioligand)



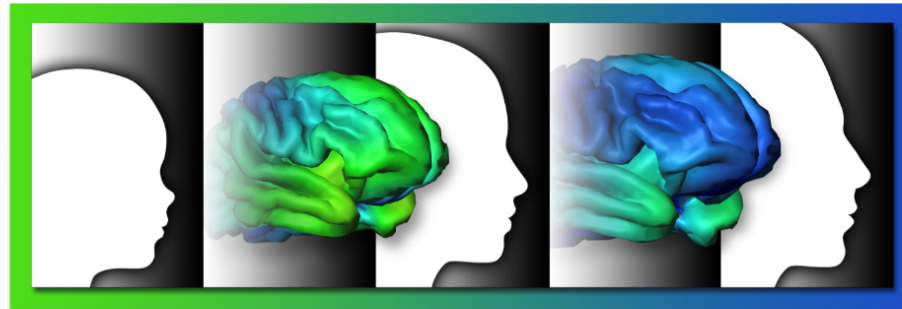
Source: Ahmad et al., Mol Imaging Biol. 2013 A

ADVERSE HEALTH CONSEQUENCES: WHO IS AT GREATEST RISK?

Mothers/Newborns



Children and Adolescents



Adolescent Brain Cognitive Development[®]
Teen Brains. Today's Science. Brighter Future.

Older Adults?



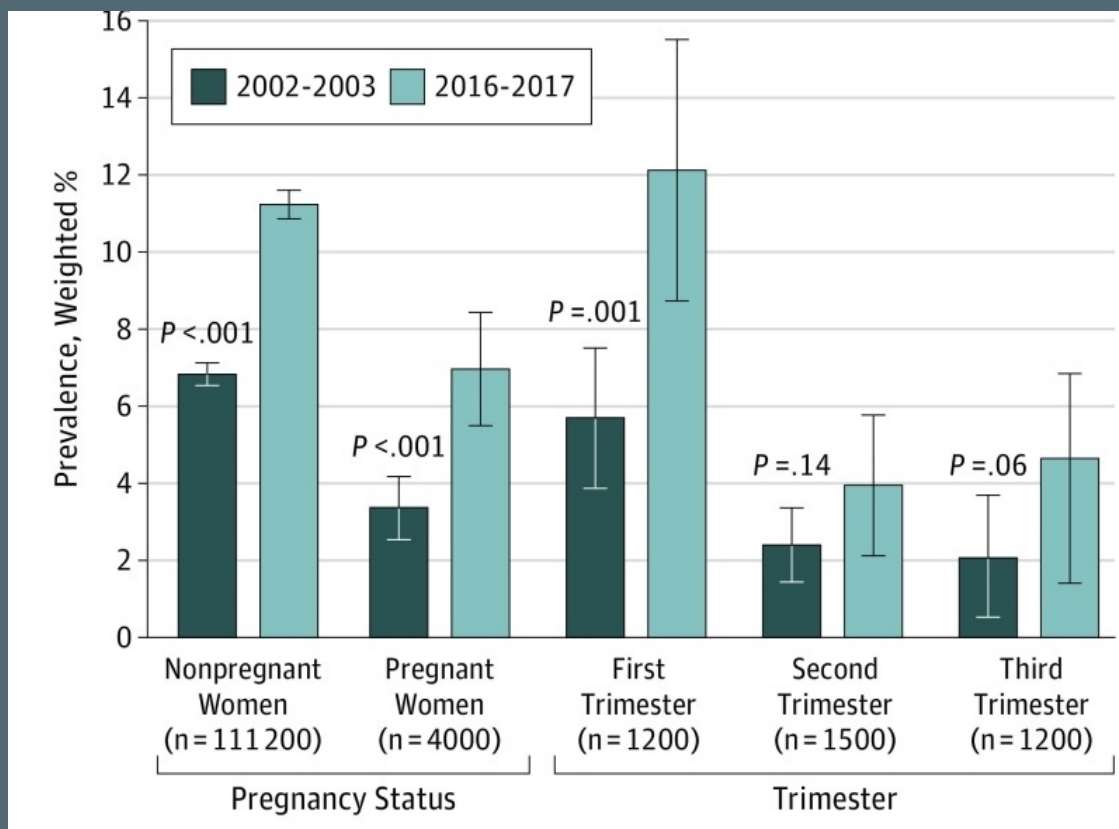
**Persons With
Mental Illness**



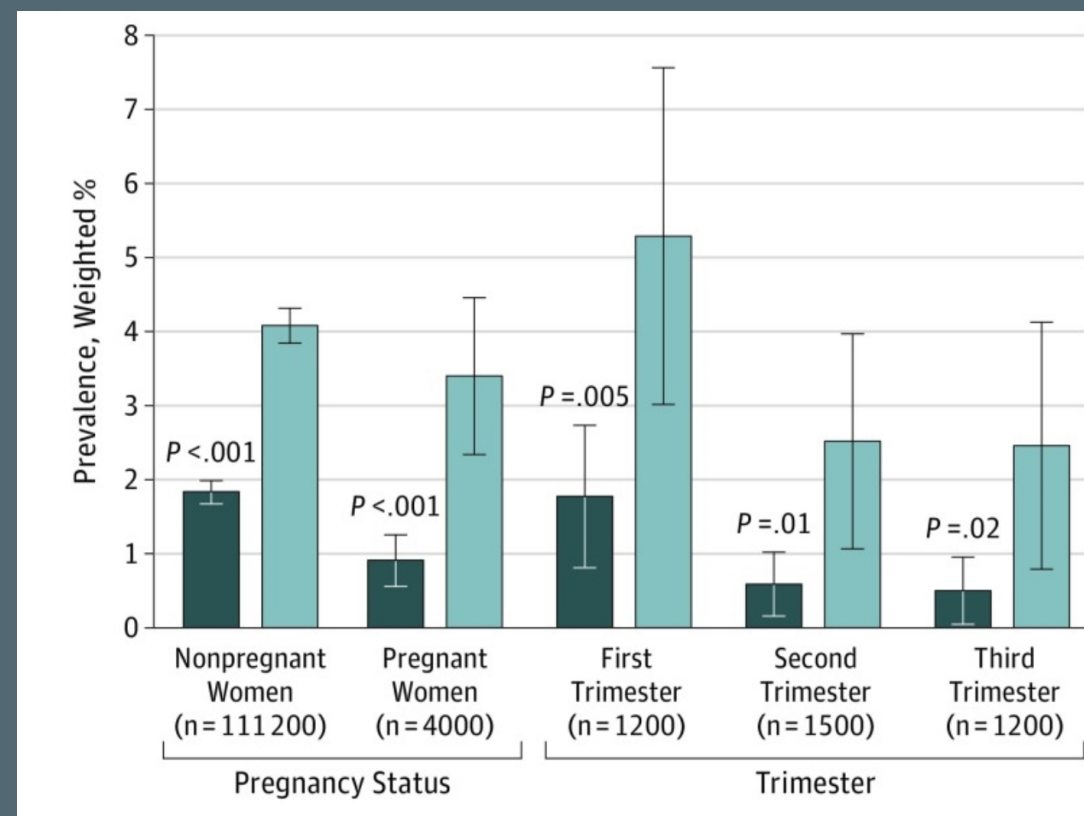
**Tobacco
Smokers**

CANNABIS IS THE MOST WIDELY USED ILLEGAL DRUG DURING PREGNANCY IN THE U.S: USE HAS BEEN RISING

Adjusted Prevalence of Past Month Cannabis Use



Adjusted Prevalence of Daily/Near Daily Cannabis Use



MARIJUANA USE INCREASED IN PREGNANT FEMALES IN CALIFORNIA (2009-2016)

Figure 1. Adjusted Prevalence of Marijuana Use Among 279 457 Pregnant Females in KPNC by Screening Type, 2009-2016

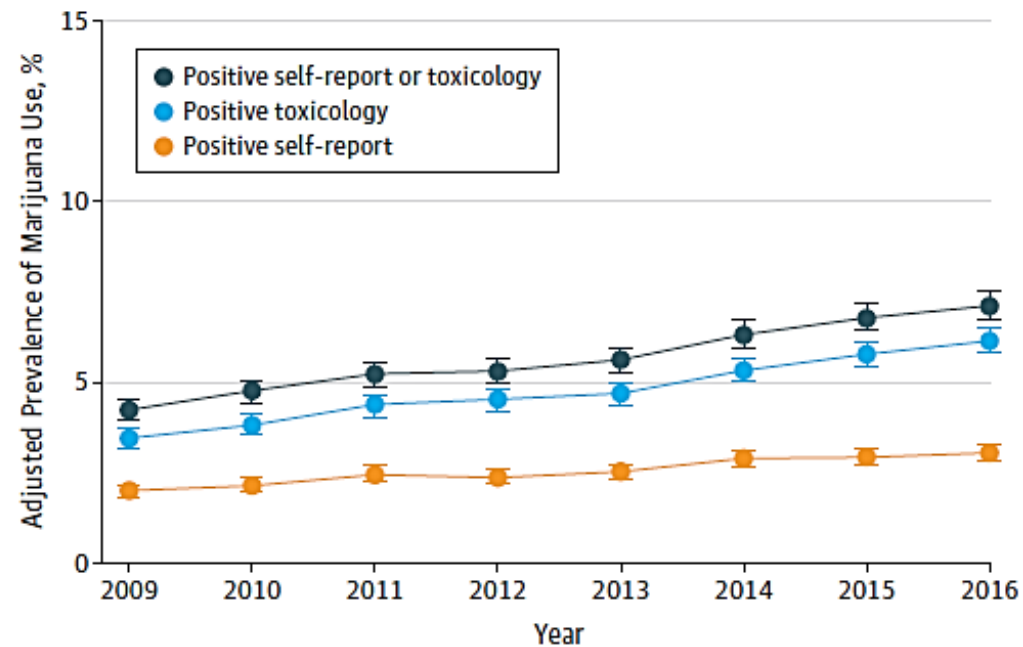
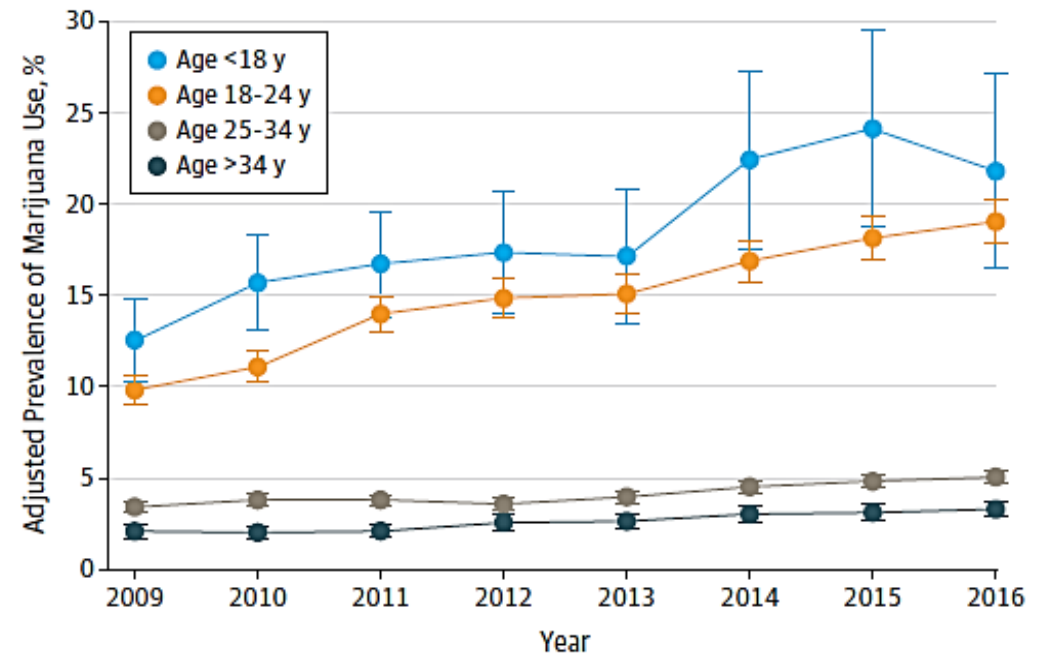


Figure 2. Adjusted Prevalence of Marijuana Use Among 279 457 Pregnant Females in KPNC by Age, 2009-2016



PRENATAL CANNABIS EXPOSURE: OVERVIEW OF EFFECTS*

Lower birth weight; smaller head circumference; hyperarousal; increased risk of NICU

Lower scores in verbal and memory domains

Externalizing behaviors (attention, impulsivity); ADHD; depressive symptoms; delinquency; psychosis proneness



Attention Problems

Lower IQ; decreased verbal/quantitative reasoning; hyperactivity; increased frontal cortical thickness

Problems with executive function; early onset substance use

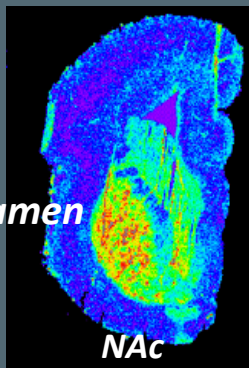
PRENATAL CANNABIS EXPOSURE DECREASES DOPAMINE D2 RECEPTOR BINDING IN THE STRIATUM AND AMYGDALA



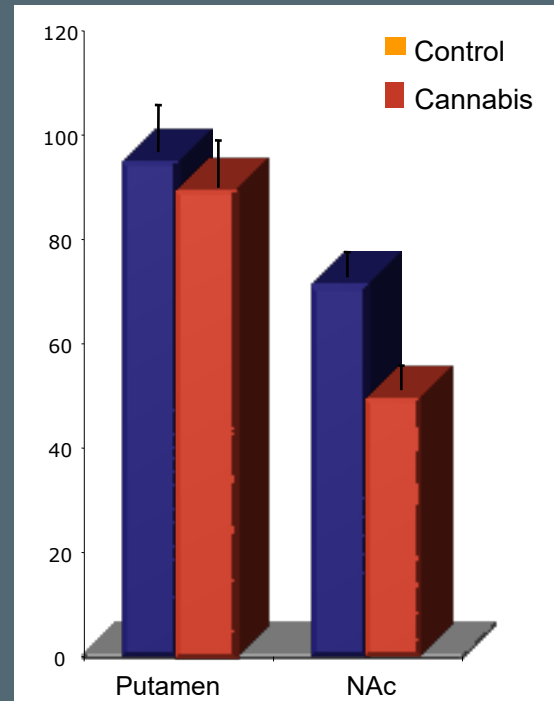
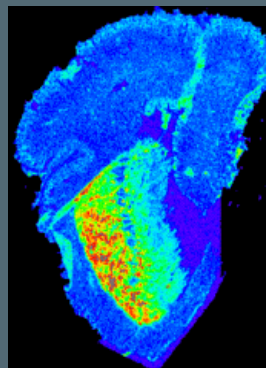
Dopamine D2 receptor

Striatum

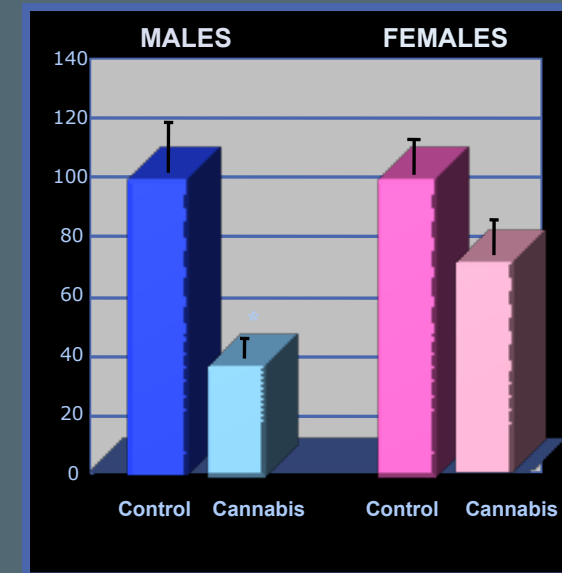
Normal



Cannabis



Amygdala



Source: DiNieri et al *Biol Psychiatry*, 2011; Wang et al. *Biological Psychiatry*, 2004
Slide courtesy of Yasmin Hurd

PRENATAL CANNABIS EXPOSURE (PCE)



- Endocannabinoid system (ECS) is involved in implantation; placentation; fetal organ development; and neural development, including cell differentiation, axon migration, myelination.
- Exogenous cannabinoids cross the placenta and accumulate in fetal tissues, especially brain. Also found in breast milk.
- Human fetal imaging studies find alterations in dopamine D2 receptors; may be sex-dependent.
- PCE is linked to fetal growth restriction and low birth weight.
- Longitudinal studies report subtle to modest impact on cognition and neuropsychiatric outcomes in children, adolescents, and young adults (with multiple caveats).
- Preclinical studies show multiple changes in synapse formation and function; and lasting effects of THC exposure on adult drug seeking, stress responses, and brain reward systems.



PRENATAL CANNABIS: RESEARCH GAPS

FINDINGS ARE OFTEN MODEST, RESULTS ARE INCONSISTENT,
AND MAY BE CONFOUNDED BY OTHER VARIABLES



- Better measures of cannabis exposure (biological vs. self report)
 - Frequency of use
 - Timing of exposure (1st, 2nd, 3rd trimester; post natal; pre-conception)
 - Quantification of exposure (THC or other components)
- Data from recent cohorts: high potency products; varying THC/CBD ratios; CBD alone
- Consideration of sex dependent outcomes
- Measures of polysubstance use/other adverse or protective factors (prenatal care, food/housing insecurity, stress, support)
- Paternal exposure
- Post-natal parenting behaviors
- Pre-clinical and clinical research, including longitudinal studies

HEALTHY BRAIN AND CHILD DEVELOPMENT (HBCD) STUDY

NIDA, NIMH, NINDS, NIAAA, NICHD, NIBIB, NIEHS, NIMHD, OBSSR, ORWH, NEI, NIH HEAL Initiative

Multi-site longitudinal study (n=7500) examining individual brain development trajectories and behavior from birth through childhood (ages 9-10) including *in utero* substance exposure and effects of adverse social environments.

Pregnancy History



EEG



Biospecimens

Risk and Protective Factors



MRI



Behavioral,
neurocognitive
assessments



Wearables



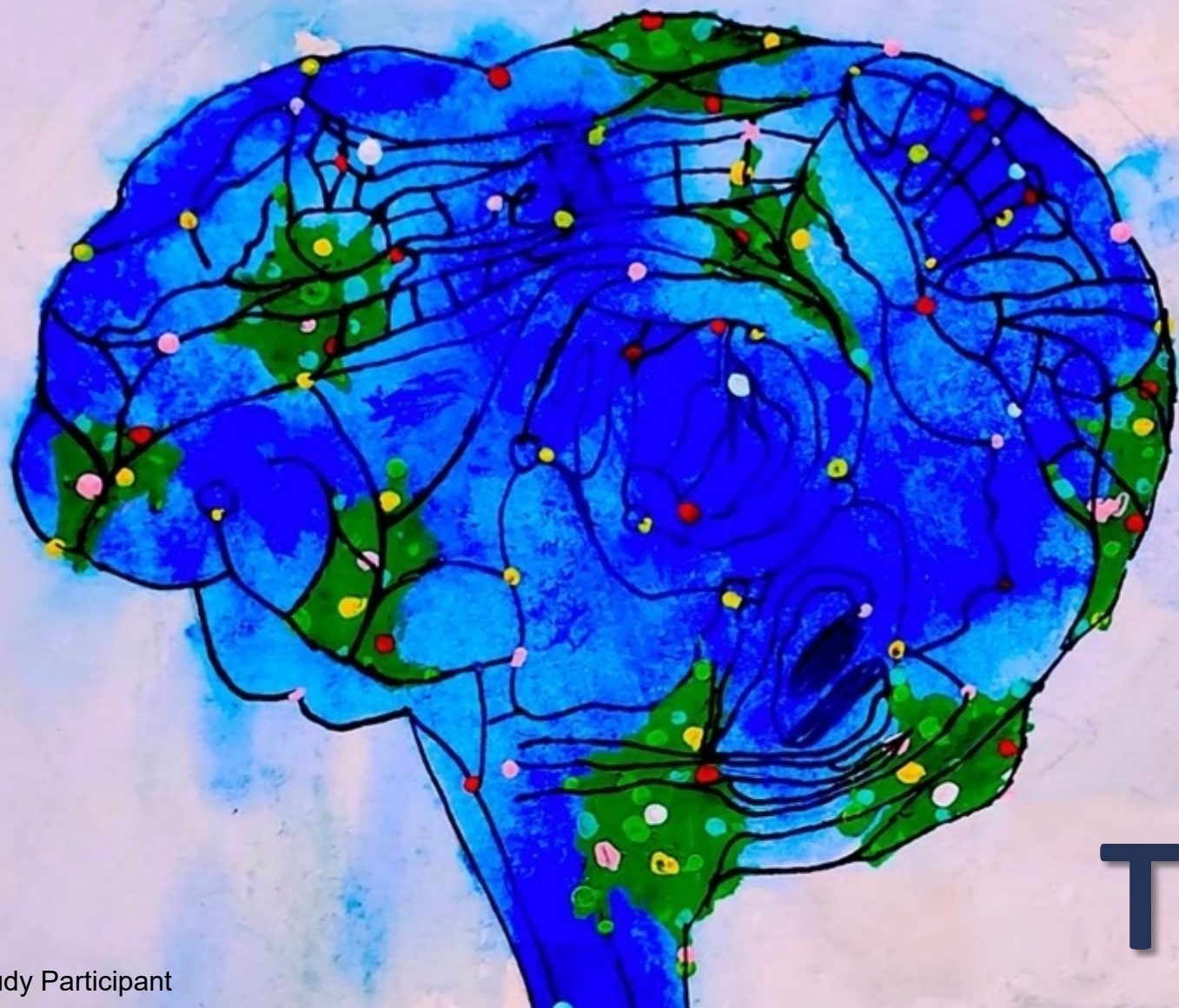
PRENATAL CANNABIS EXPOSURE: CLINICAL IMPLICATIONS *AND OBLIGATIONS*

- Current landscape: many pregnant women do not believe cannabis use during pregnancy is harmful.
- They consider its beneficial effects on nausea (first trimester has the highest rate of use), anxiety, sleep, stress management (also preferable to psychiatric and other medications).
- Highest rates of cannabis use in young pregnant women (18-25); and those from low SES environments.
- Most health care providers are not asking about cannabis use or providing recommendations to their patients.
- Can be interpreted as cannabis not being risky (unlike alcohol and tobacco).
- Pregnant women are getting information through internet, dispensaries, not health care providers
- While the data are not yet conclusive, they are sufficiently robust to warrant concern about the newborn (low birth weight, increased NICU risk), possibly continuing into childhood or young adulthood.

PRENATAL CANNABIS EXPOSURE: CLINICAL SUGGESTIONS



- Universal, non-judgmental screening of all pregnant persons
 - *Caveat: State laws may have reporting requirements that could have serious consequences for the mother and the infant*
- Recommendation to abstain during pregnancy and while breast feeding (per professional organizations ACOG and AAP, Surgeon General)
- Explain the known risks (low birthweight, risk of NICU stay)
- Currently, no safe level of use has been determined
- Ask why person is using cannabis—are there alternatives that are less risky; is there an underlying mental disorder that requires treatment?
- Refer to treatment for SUD or other mental illness



THANK YOU!