



# “MARIJUANA AND THE DEVELOPING BRAIN”

BY:

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# DISCLOSURES

Consultant to BMS/ Otsuka

Pharma Research with

Lundbeck on adolescent depression



**UNIVERSITY OF CALGARY**  
CUMMING SCHOOL OF MEDICINE



**Alberta Health**  
**Services**

# LEARNING OBJECTIVES

1. We live in two worlds, the external is planning to legalize marijuana in April 2017. The internal world needs to be ready to better regulate with this increased opportunity for a quick fix, sensation seeking with relief from despair, if we are to avoid addiction.
2. Marijuana is risky for the developing brain, pregnant mom and for those with severe and persistent mental illness.
3. Legalization will happen and regulation should be part of this strategy.
4. Drinking and smoking pot before drinking is a bad idea!

# SOCIAL DETERMINANTS OF HEALTH

|                       |     |
|-----------------------|-----|
| 1. Health care system | 25% |
| 2. Genetics           | 15% |
| 3. Environment        | 10% |
| 4. Socio Economic     | 50% |

## Three Levels of Stress Response

### Positive

Brief increases in heart rate,  
mild elevations in stress hormone levels.

### Tolerable

Serious, temporary stress responses,  
buffered by supportive relationships.

### Toxic

Prolonged activation of stress response systems  
in the absence of protective relationships.

## TOXIC STRESS IN CHILDREN AND ADOLESCENTS

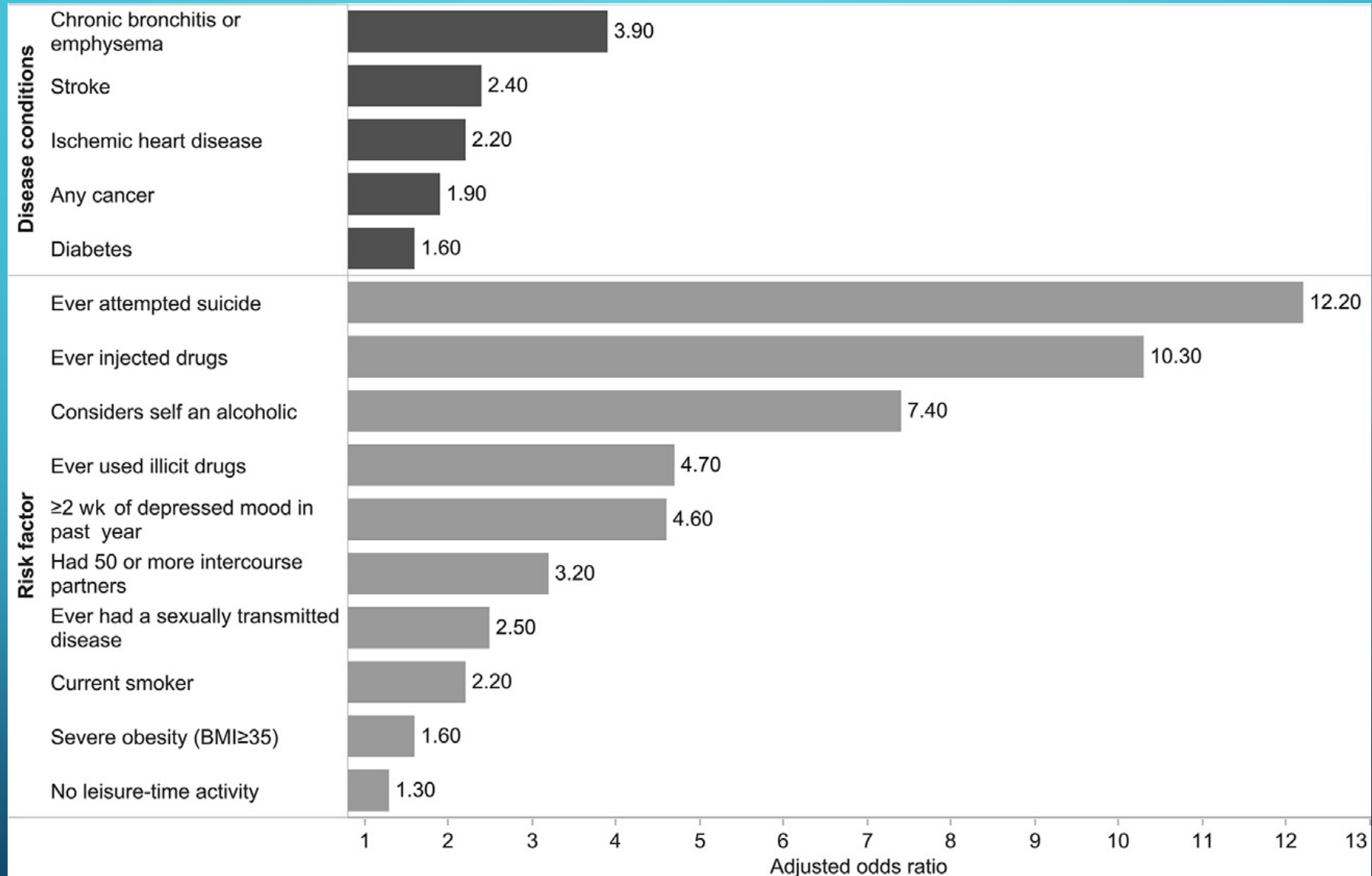


Fig. 1. Odds of outcomes among individuals experiencing 4 or more ACEs. ACEs, adverse childhood experiences; BMI, body mass index. Adjusted for age, gender, race and educational attainment. Referent group 0 ACEs. Data from [9]



## TOXIC STRESS IN CHILDREN AND ADOLESCENTS

**Table 1**  
A adverse childhood experiences, by category

| ACE category          | Definition   |
|-----------------------|--|
| Abuse                 | <ul style="list-style-type: none"> <li>• Psychological<br/><i>Did a parent or other adult in the household –</i> <ul style="list-style-type: none"> <li>○ Often or very often swear at, insult, or put you down?</li> <li>○ Often or very often act in a way that made you afraid that you would be physically hurt?</li> </ul> </li> <li>• Physical<br/><i>Did a parent or other adult in the household –</i> <ul style="list-style-type: none"> <li>○ Often or very often push, grab, shove, or slap you?</li> <li>○ Often or very often hit you so hard that you had marks or were injured?</li> </ul> </li> <li>• Sexual<br/><i>Did an adult or person at least 5 years older ever –</i> <ul style="list-style-type: none"> <li>○ Touch or fondle you in a sexual way?</li> <li>○ Have you touch their body in a sexual way?</li> <li>○ Attempt oral, anal, or vaginal intercourse with you?</li> <li>○ Actually have oral, anal, or vaginal intercourse with you?</li> </ul> </li> </ul>  |
| Neglect               | <ul style="list-style-type: none"> <li>• Emotional<br/><i>Did you often or very often feel that –</i> <ul style="list-style-type: none"> <li>○ No one in your family loved you or thought you were important or special?</li> <li>○ Your family didn't look out for each other, feel close to each other, or support each other?</li> </ul> </li> <li>• Physical<br/><i>Did you often or very often feel that –</i> <ul style="list-style-type: none"> <li>○ You didn't have enough to eat, had to wear dirty clothes, and had no one to protect you?</li> <li>○ Your parents were too drunk or high to take care of you or take you to the doctor if you needed it?</li> </ul> </li> </ul>  |
| Household dysfunction | <ul style="list-style-type: none"> <li>• Divorce or separation           <ul style="list-style-type: none"> <li>○ Were your parents ever separated or divorced?</li> </ul> </li> <li>• Mother treated violently<br/><i>Was your mother (or stepmother) –</i> <ul style="list-style-type: none"> <li>○ Often or very often pushed, grabbed, slapped, or had something thrown at her?</li> <li>○ Sometimes, often, or very often kicked, bitten, hit with a fist, or hit with something hard?</li> <li>○ Ever repeatedly hit over at least a few minutes or threatened with, or hurt by, a gun or knife?</li> </ul> </li> <li>• Substance abuse           <ul style="list-style-type: none"> <li>○ Did you live with anyone who was a problem drinker or alcoholic or anyone who used street drugs?</li> </ul> </li> <li>• Mental illness           <ul style="list-style-type: none"> <li>○ Was a household member depressed or mentally ill or attempt suicide?</li> </ul> </li> <li>• Criminal behavior in household           <ul style="list-style-type: none"> <li>○ Did a household member go to prison?</li> </ul> </li> </ul> |

Adapted from Adverse Childhood Experiences Study. Finding your ACE score. Available at: [http://www.acestudy.org/yahoo\\_site\\_admin/assets/docs/ACE\\_Calculator-English.127143712.pdf](http://www.acestudy.org/yahoo_site_admin/assets/docs/ACE_Calculator-English.127143712.pdf). Accessed May 2, 2016.

Abuse

- Psychological

*Did a parent or other adult in the household \_*

- o Often or very often swear at, insult, or put you down?
- o Often or very often act in a way that made you afraid that you would be physically hurt?

- Physical

*Did a parent or other adult in the household \_*

- o Often or very often push, grab, shove, or slap you?
- o Often or very often hit you so hard that you had marks or were injured?

- Sexual

*Did an adult or person at least 5 years older ever \_*

- o Touch or fondle you in a sexual way?
- o Have you touch their body in a sexual way?
- o Attempt oral, anal, or vaginal intercourse with you?
- o Actually have oral, anal, or vaginal intercourse with you?



Neglect

- Emotional

*Did you often or very often feel that -*

- o No one in your family loved you or thought you were important or special?
- o Your family didn't look out for each other, feel close to each other, or support each other?

- Physical

*Did you often or very often feel that -*

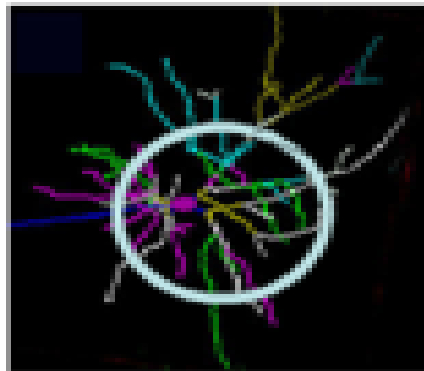
- o You didn't have enough to eat, had to wear dirty clothes, and had no one to protect you?
- o Your parents were too drunk or high to take care of you or take you to the doctor if you needed it?

Household  
dysfunction

- Divorce or separation
  - Were your parents ever separated or divorced?
- Mother treated violently
  - Was your mother (or stepmother) -*
  - Often or very often pushed, grabbed, slapped, or had something thrown at her?
  - Sometimes, often, or very often kicked, bitten, hit with a fist, or hit with something hard?
  - Ever repeatedly hit over at least a few minutes or threatened with, or hurt by, a gun or knife?
- Substance abuse
  - Did you live with anyone who was a problem drinker or alcoholic or anyone who used street drugs?
- Mental illness
  - Was a household member depressed or mentally ill or attempt suicide?
- Criminal behavior in household
  - Did a household member go to prison?

## Toxic Stress Changes Brain Architecture

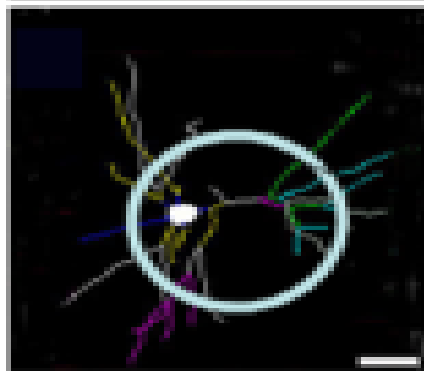
Normal



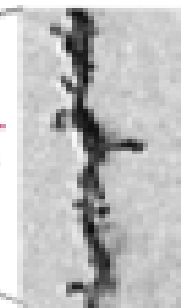
Typical neuron—  
many connections



Toxic  
stress



Damaged neuron—  
fewer connections



Prefrontal Cortex and  
Hippocampus

Sources: Radley et al. (2004)  
Bock et al. (2005)

# Amygdala and Hippocampus





Toxic Stress

Attachment

Reward







## Sativa

Equatorial climates

More stimulating (higher CBD than THC)



## Indica

Colder areas like the Hindu Kush mountains

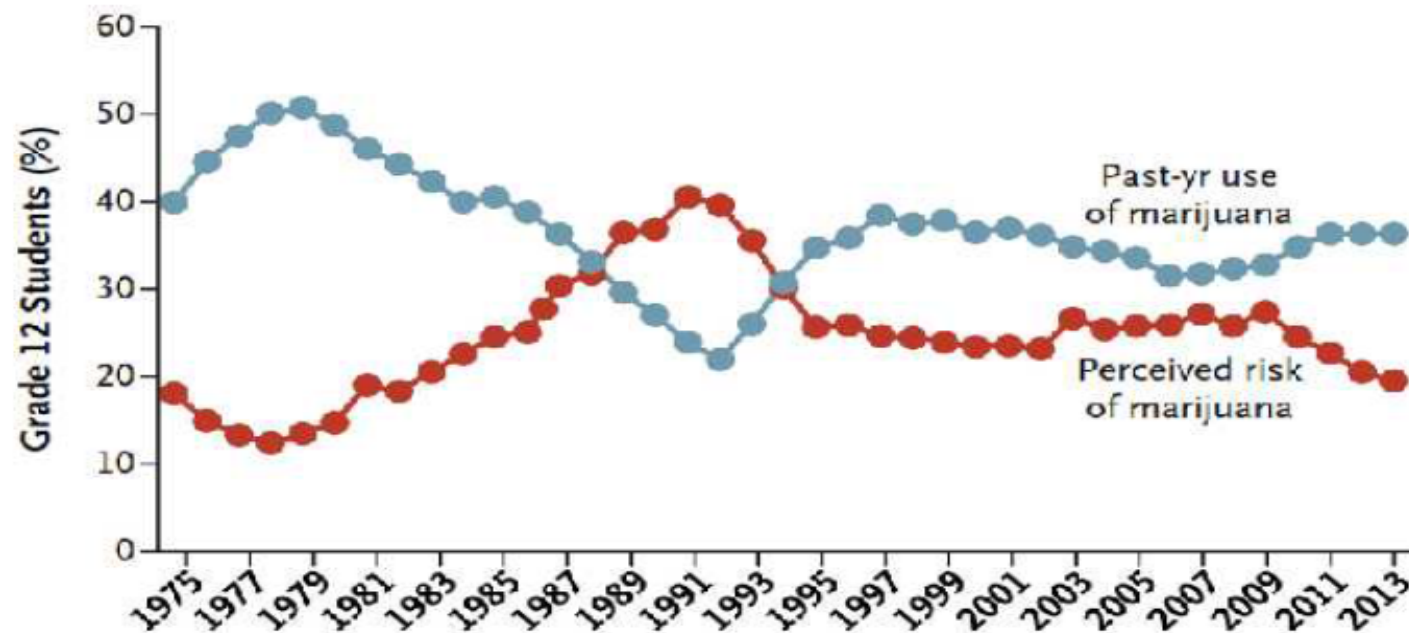
Sleep aid (higher THC than CBD)

Opioid death rates in the United States dropped 24% where marijuana use is legal for medicinal purposes.

# PREVALENCE OF MARIJUANA USE

- 2013 UNICEF
- 29 wealthy nations
- Canadian youth rank first
- 10% of 15 year olds are using
- 22% of 17-18 year olds are high school students
- 9% of users develop addiction
- If using daily as an adolescent, addiction increases 25 to 50%
- No other illegal drug is used by more than 1% of Canadians

# CORRELATION B/W PERCEIVED RISK AND USE IN G12 STUDENT IN US



Lloyd D. Johnston et al 2013 modified by Volkow 2014

# AT RISK

3 populations at risk for THC are:

- Pregnant women
- Adolescents and youth under 25 years
- Those people at risk for psychosis



# MARIJUANA AND PREGNANCY

- (1) Ottawa Prenatal Prospective Study. 1978 middle class, Caucasian families
- (2) Maternal Health Practice and Child Development. 1982 Pittsburgh – lower socio economic African American women
- (3) Generation R Study, Netherlands. Multi ethnic cohort of higher socio economic class



# MARIJUANA AND PREGNANCY

Compared to those who didn't use marijuana, the 3 studies indicate that with heavy marijuana prenatal exposure:

- Adverse effects by 18 months of age with increased aggression and impulsiveness
- At 6 years evidence of cognitive dysfunction, ADHD, requiring educational remediation
- By 10-14 years, increased rates of anxiety and depression
- By 14 years of age increased rates of smoking and substance abuse



# MARIJUANA AND PREGNANCY

This is a public health issue if 10-30%  
of pregnant mothers use marijuana



Marijuana perceived to be low risk

But THC in 1980 = 4%

In 2008 THC increased to 10%

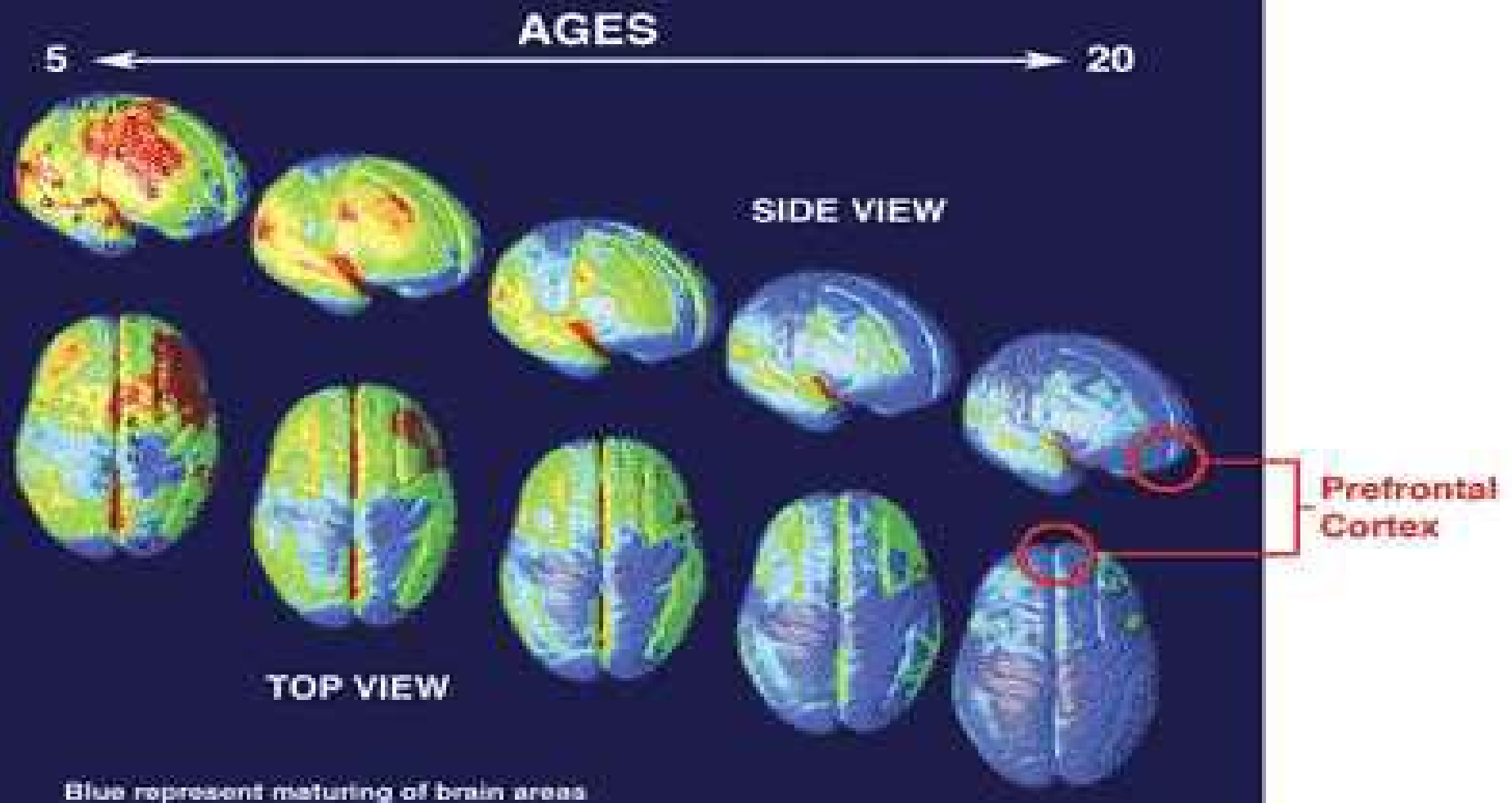
In 2016 THC increased to 28%

# MARIJUANA & ADOLESCENTS

Research in adolescent brain development shows this is a vulnerable period especially for the prefrontal cortex:

- Problem solving
  - Flexibility
- Adaptability and
- Frustration tolerance

# IMAGES OF BRAIN DEVELOPMENT IN HEALTHY CHILDREN AND TEENS (AGES 5-20)



# MARIJUANA & ADOLESCENTS

- Marijuana exposure to rats impact hippocampus development.
- MRI studies in adults who have used heavily have fewer nerve fibers in prefrontal cortex, hippocampus and sensory integrative areas
- Marijuana users have 40% higher risk of developing psychosis
- Frequent users have a 50 to 200% increased risk of psychosis than non-users
- Increase rate of anxiety and depression in adolescents who are using especially if there is a family history of those conditions

# EFFECTS OF MARIJUANA ON MENTAL HEALTH PATIENTS

Patients with severe and persistent mental illness like paranoid schizophrenia, severe bipolar disorder experience a worsening of symptoms and develop poor compliance with medications especially high potency THC because it:

- Increases euphoria, time distortion and perceptual changes
  - Decreases motivation and psycho motor performance
- Negatively impacts parts of the brain that regulate emotions, stress response, verbal memory and learning

# DRIVING AND DRUG TESTING

- Legalization of marijuana in Colorado resulted in an increase in marijuana related traffic deaths and an increase of health care visits due to intoxication, burns from smoking/ vaping as well as overdose of children due to marijuana edibles
- Neither Colorado or Washington adopted a statewide health focused regulatory mechanism, no marketing regulations or limits on availability, potency or formulation



# DRIVING AND DRUG TESTING

## National Highway Traffic Safety Study

- This is a large controlled study. 2015 showed marijuana minimally high risk of being involved in traffic accidents than sober drivers
- Similarly large population study in 9 E.U. countries in 2010 did not find significant impairment with traffic accidents

# CMA REPORT

- Odds Ratio of Risk of driving accidents
- 2012 meta analytic study of 42 studies revealed:
  - Fatal accidents due to marijuana only 1.25
  - Opiate risk (eg. Codeine) 1.4
  - Benzodiazepine (e.g.. Valium) 2.3
  - Anti Depressants (SSRIs) 1.32
  - Cocaine 2.96
  - Amphetamine 4.46
  - Zopiclone (eg. Ambien) 2.6
  - Odds ration for alcohol depending on blood level 2 to 6

**DON'T DRINK AND SMOKE MARIJUANA!!!!!!!!!!!!!!**

# SAVINGS

- If marijuana is decriminalized, it is estimated to save \$1 Billion from the criminal and civil courts



- 500,000 Canadians face travel and employment restrictions due to a criminal record of marijuana possession
- Legalization can produce new investments to growing operations and distribution; a \$10 Billion dollar industry!!!!

# CONCLUSION

- Canadian Medical Association 80,000 members
- Recommends legalization and regulation of marijuana
- Limiting the potency and the amount one person can buy (especially between 21-25 year olds)
- Phase in an educational period before April 2017
- Increase more mental health and substance abuse services
- Reduce the perception of safety for marijuana use in adolescents, pregnant moms and those at risk for psychosis
- Recognize it does have a role for some PTSD, cancer and chronic pain management

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## Adverse Childhood Experience (ACE) Questionnaire

### Finding your ACE Score ra libr 10 24 06

**While you were growing up, during your first 18 years of life:**

1. Did a parent or other adult in the household **often** ...  
Swear at you, insult you, put you down, or humiliate you?  
**or**  
Act in a way that made you afraid that you might be physically hurt?  
Yes No If yes enter 1 \_\_\_\_\_
2. Did a parent or other adult in the household **often** ...  
Push, grab, slap, or throw something at you?  
**or**  
**Ever** hit you so hard that you had marks or were injured?  
Yes No If yes enter 1 \_\_\_\_\_
3. Did an adult or person at least 5 years older than you **ever**...  
Touch or fondle you or have you touch their body in a sexual way?  
**or**  
Try to or actually have oral, anal, or vaginal sex with you?  
Yes No If yes enter 1 \_\_\_\_\_
4. Did you **often** feel that ...  
No one in your family loved you or thought you were important or special?  
**or**  
Your family didn't look out for each other, feel close to each other, or support each other?  
Yes No If yes enter 1 \_\_\_\_\_
5. Did you **often** feel that ...  
You didn't have enough to eat, had to wear dirty clothes, and had no one to protect you?  
**or**  
Your parents were too drunk or high to take care of you or take you to the doctor if you needed it?  
Yes No If yes enter 1 \_\_\_\_\_
6. Were your parents **ever** separated or divorced?  
Yes No If yes enter 1 \_\_\_\_\_
7. Was your mother or stepmother:  
**Often** pushed, grabbed, slapped, or had something thrown at her?  
**or**  
**Sometimes or often** kicked, bitten, hit with a fist, or hit with something hard?  
**or**  
**Ever** repeatedly hit over at least a few minutes or threatened with a gun or knife?  
Yes No If yes enter 1 \_\_\_\_\_
8. Did you live with anyone who was a problem drinker or alcoholic or who used street drugs?  
Yes No If yes enter 1 \_\_\_\_\_
9. Was a household member depressed or mentally ill or did a household member attempt suicide?  
Yes No If yes enter 1 \_\_\_\_\_
10. Did a household member go to prison?  
Yes No If yes enter 1 \_\_\_\_\_

**Now add up your "Yes" answers: \_\_\_\_\_ This is your ACE Score**