Cannabis

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What it Does?
&
Why?

Marijuana

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Cannabis

The Upside:

It's Fun and an Easy Cure for Boredom

The Downside:

Burnout & More Boredom

Cannabis

This talk is Not
about the medical uses for
Cannabis

Cannabis

Yes, MJ has medical uses.

But . . .

So, does Morphine, Oxycontin, Vicodan, Valium, Percodan, . . .

Cannabis

You can get addicted to these drugs because they . . .

GET
YOU
HIGH!

Cannabis

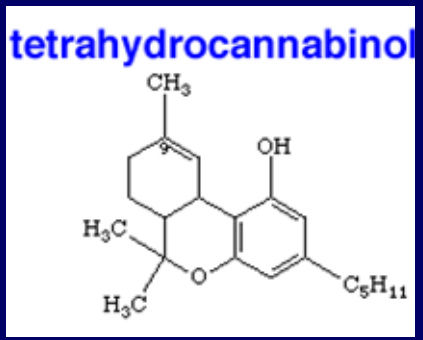
This talk is about how Cannabis

GETS
YOU
HIGH!

And what it does to our brains . . .

What is the Psychoactive Molecule in Cannabis?

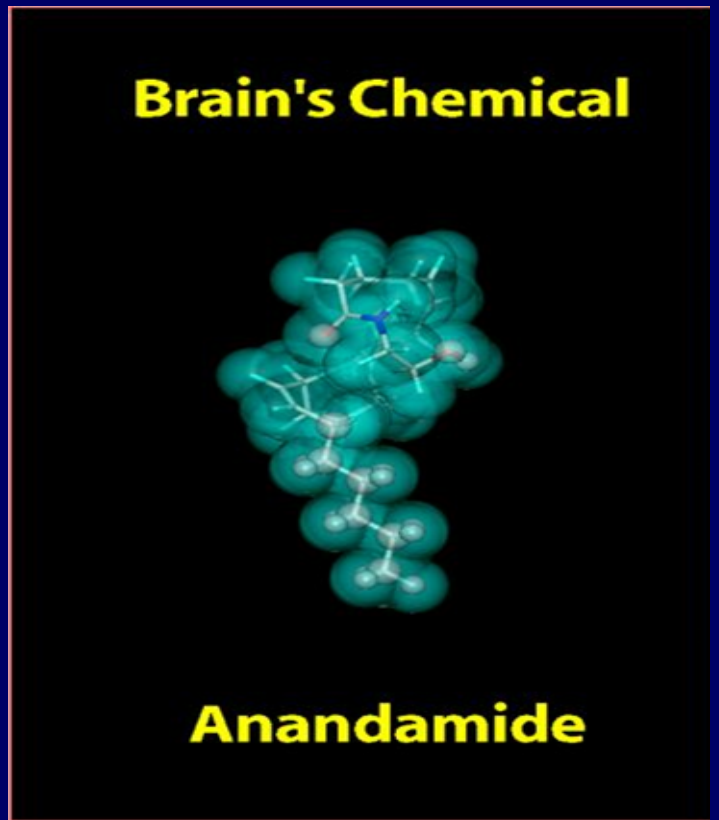
THC

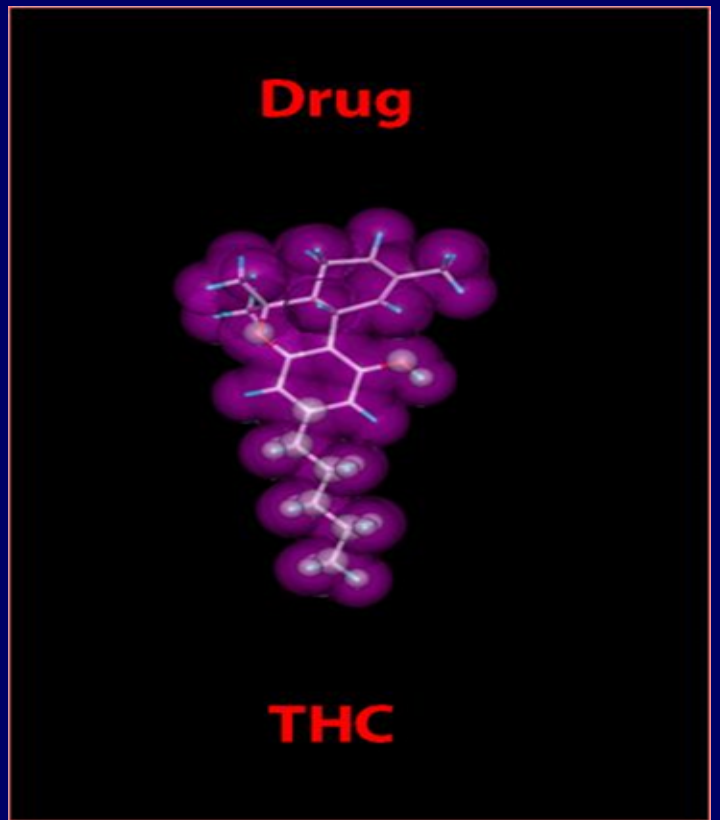


THC

Copies brain's natural THC

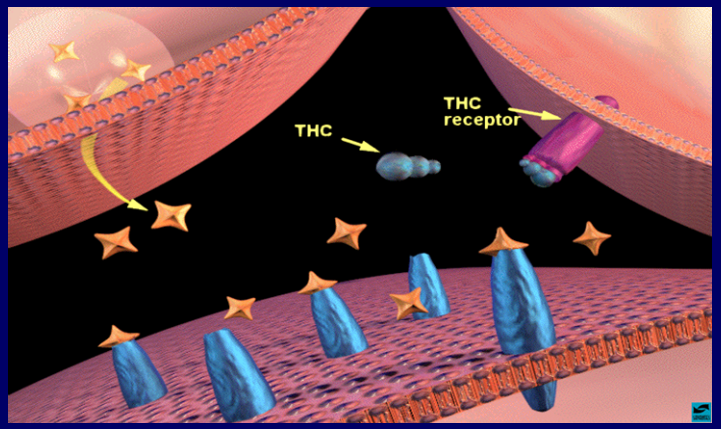
(endocannianoids: anandamide & 2-AG)

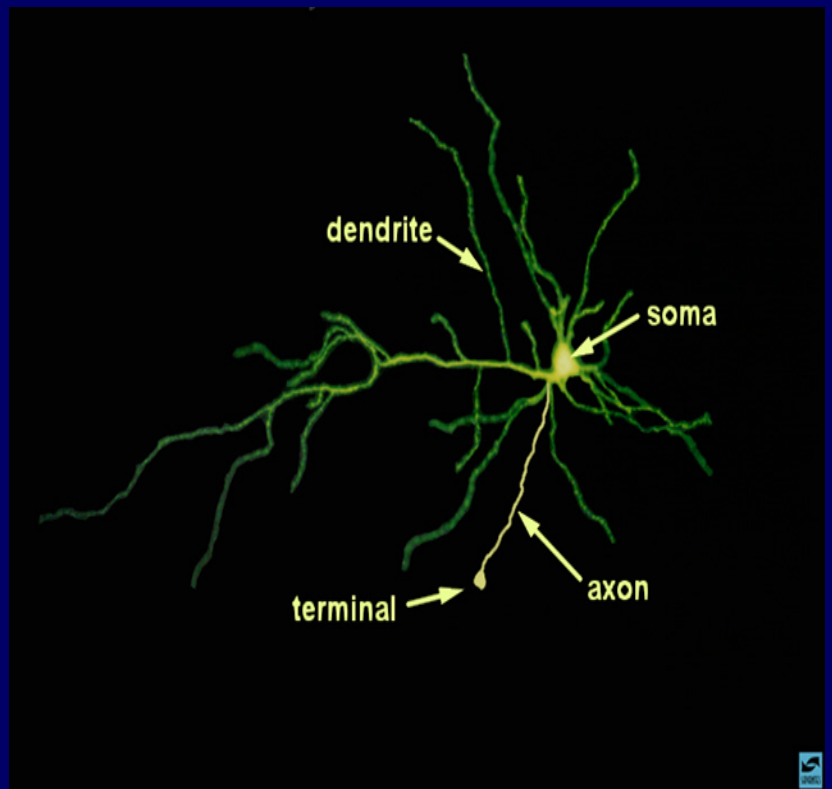


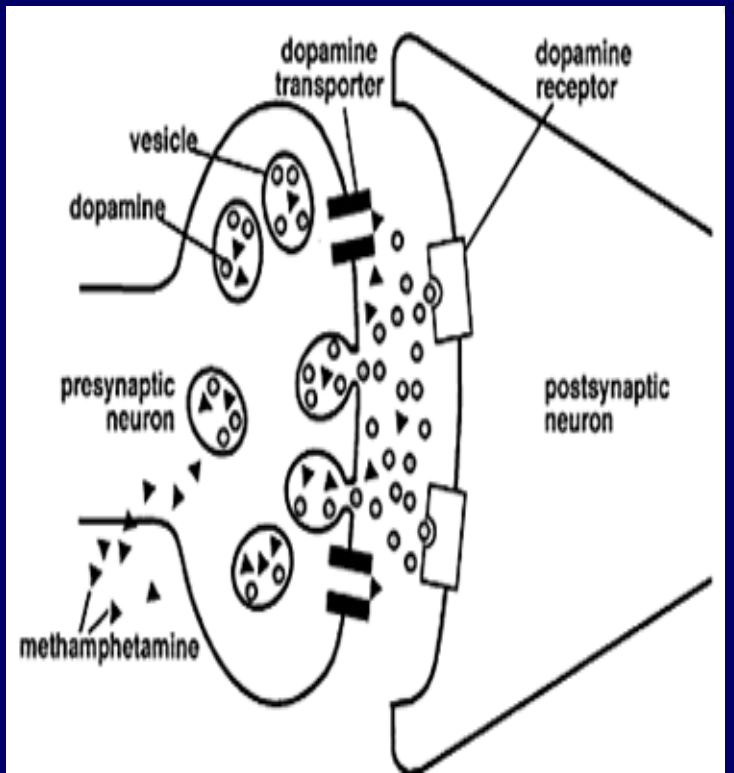


NIDA

Drugs copy natural brain chemicals.



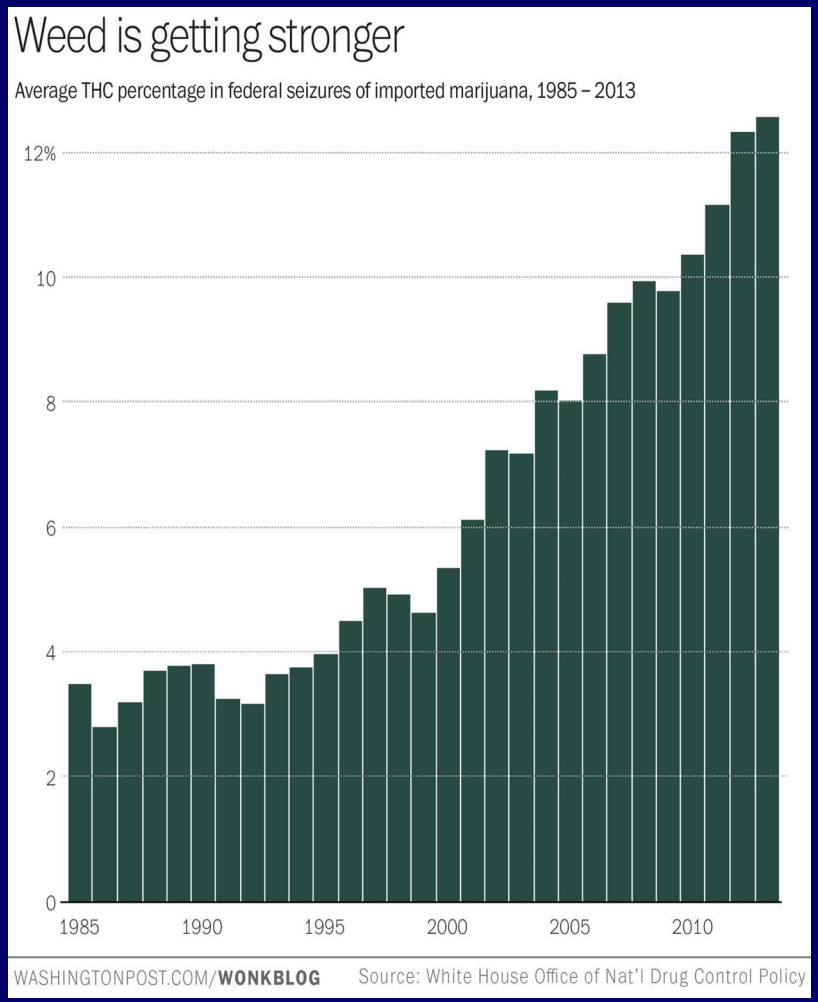




Potency

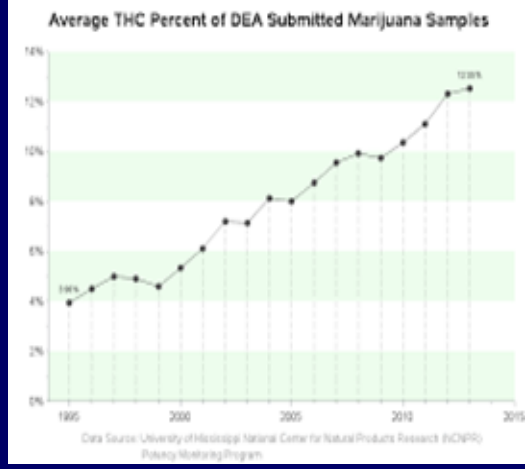
- **Throw away the male plants, female plants aren't fertilized, don't make seeds, all the THC in the bud/flower**

- **Hybridize, cloning: Some MJ 20% to > 25% THC***



https://www.washingtonpost.com/news/wonk/wp/2015/02/17/potent-weed-is-worse-for-you-than-the-mild-stuff-and-its-hard-to-find-anything-else-these-days/?noredirect=on&utm_term=.f1d30be34a58

Potency

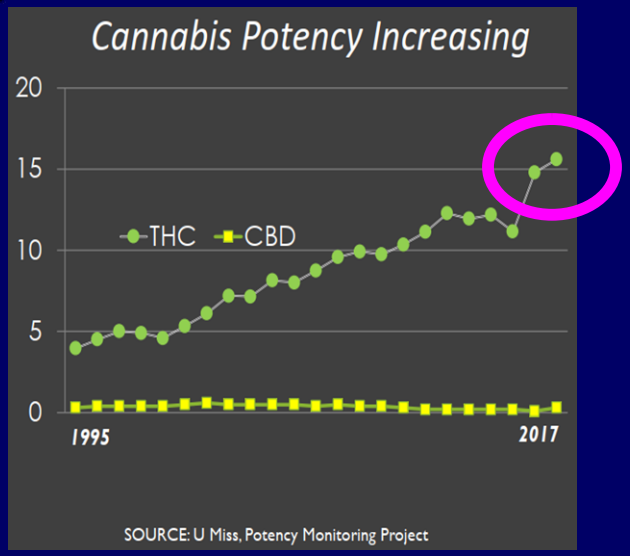


In 2018, average THC > 15% NIDA

Health Experts:

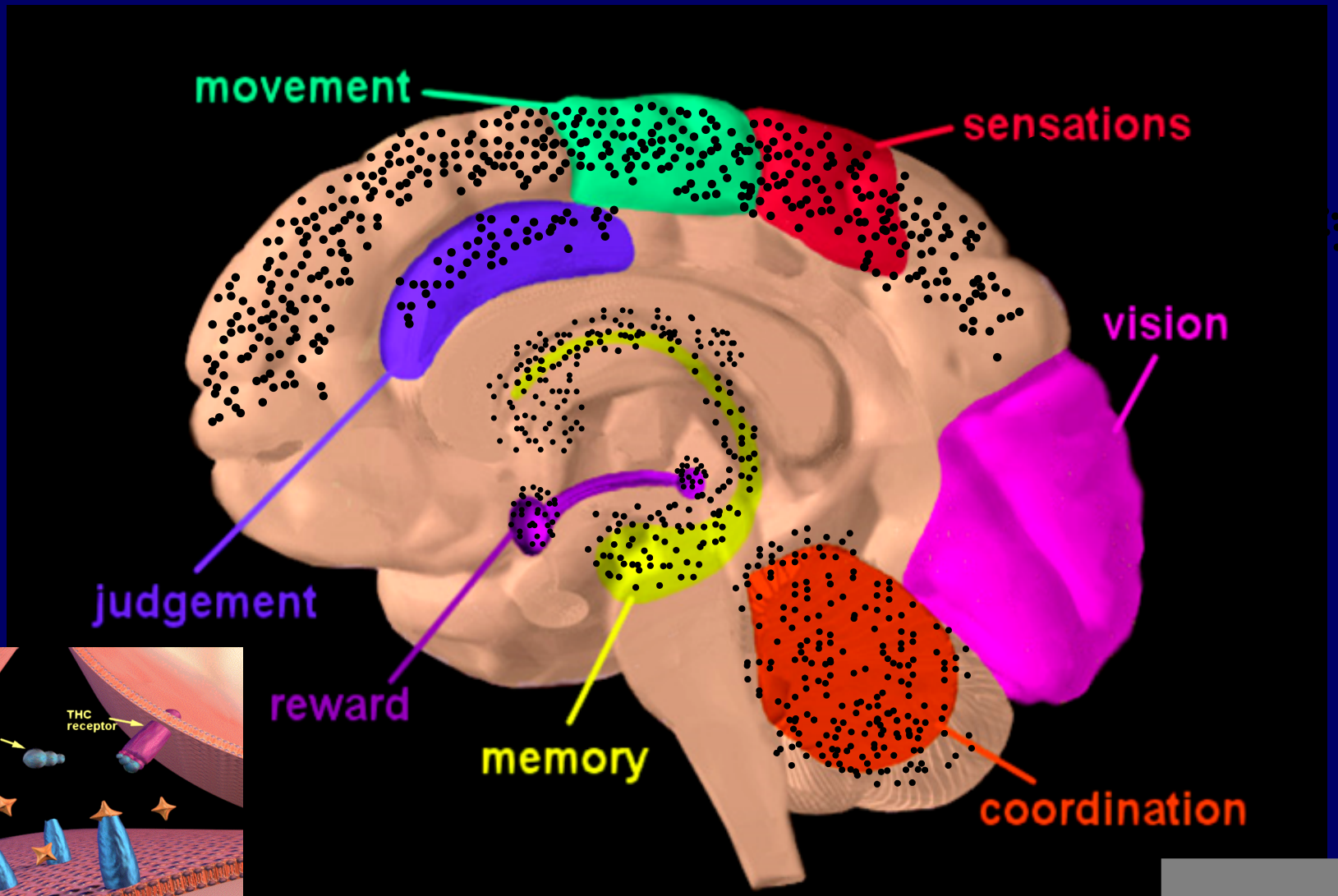
≥ 15% THC

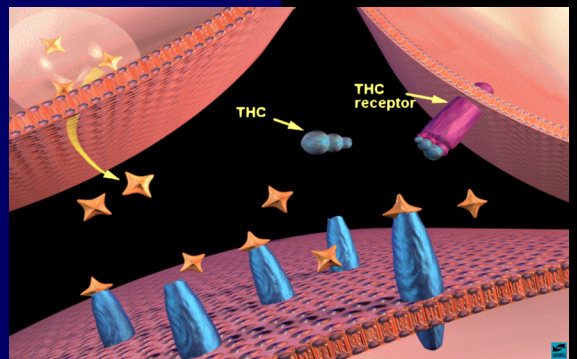
" . . . Should be considered a hard drug, like cocaine . . ."



Laar MV et al. Limitations to the Dutch cannabis toleration policy, assumptions underlying the reclassification of cannabis above 15% THC. In J Drug Policy 2016;34:58-64 https://www.justthinktwice.gov/article/nida-blog-myth-or-fact-%E2%80%9Cmarijuana-stronger-these-days%E2%80%9D ; In J Drug Policy 2016;34:58-64 ; http://www.rethinkpot.org/; https://www.google.com/search?q=increase+in+THC&sxsrf=ALiCzsa6PvcVMomoGg1aWIy3xK7awqeCXA:1654663665932&source=lnms&tbm=isch&sa=X&ved=2ahUKEwj-7Z7Ahp34AhUmlWoFHTYyAQ4Q_AUoAnoECAEQBA&biw=1920&bih=937&dpr=1&safe=active&ssui=on#imgrc=sc45Nt1gg03X1M

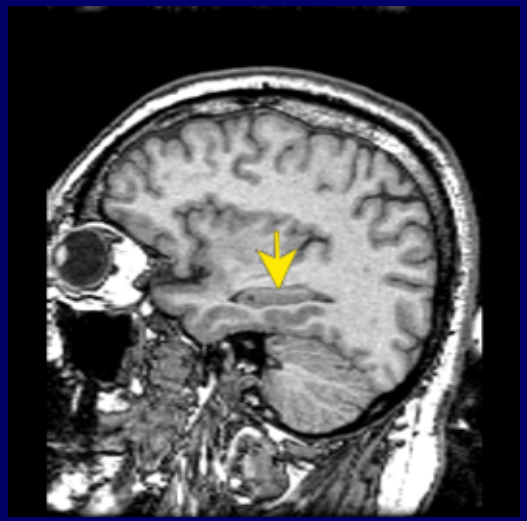
THC Landing (Receptor) Sites

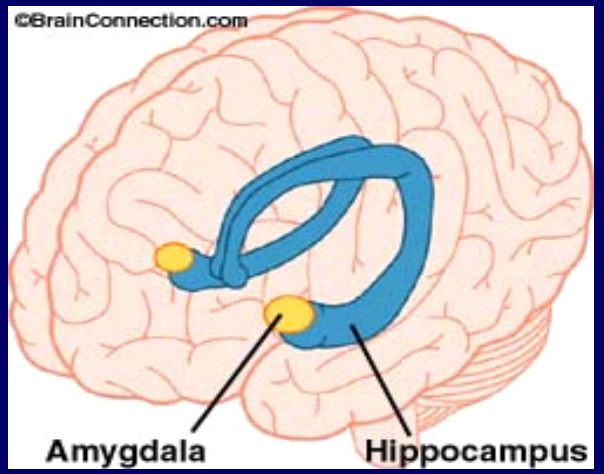




THC & Memory

- HC is like the "save" button on the computer. 23, Kolb
- THC Acts like an eraser in the Hippocampus.

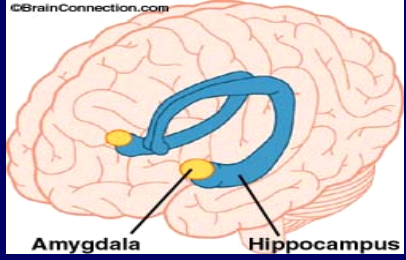




THC & Memory

- Don’t want to and can’t remember everything.
- Like a full hard drive.

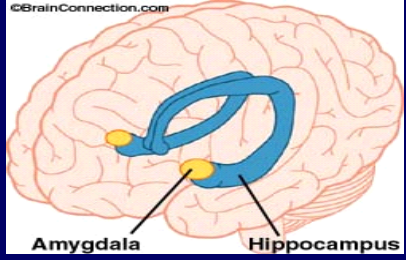
THC & Memory



- Put 2 stranger rats together.
  - Sniff around, get to know each other.

"Is that you, Fred?" "Is that you, Jill?"

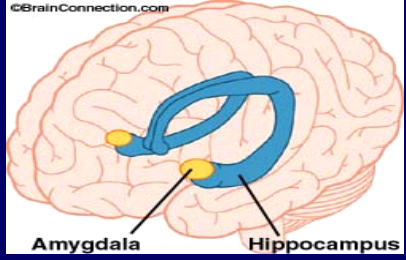
THC & Memory



- Separate for ½ hr., an hr., don't do this.
- 2 hrs. later, start over as if they never met before.

"Is that you, Fred?" "Is that you, Jill?"

THC & Memory

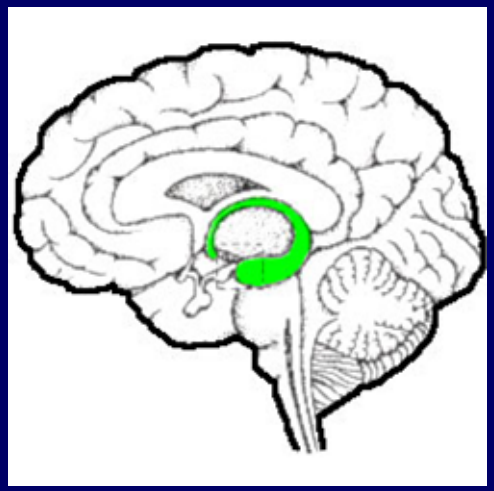


- Get High: separate for ½ hr.
- They have to go through the whole process again.


"I can't complain. Last week they had me on martinis."

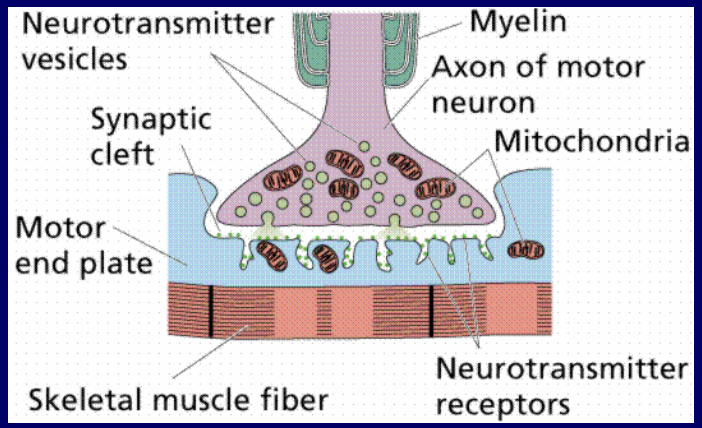
THC & Memory

- Too much natural THC or THC from MJ = Too little memory



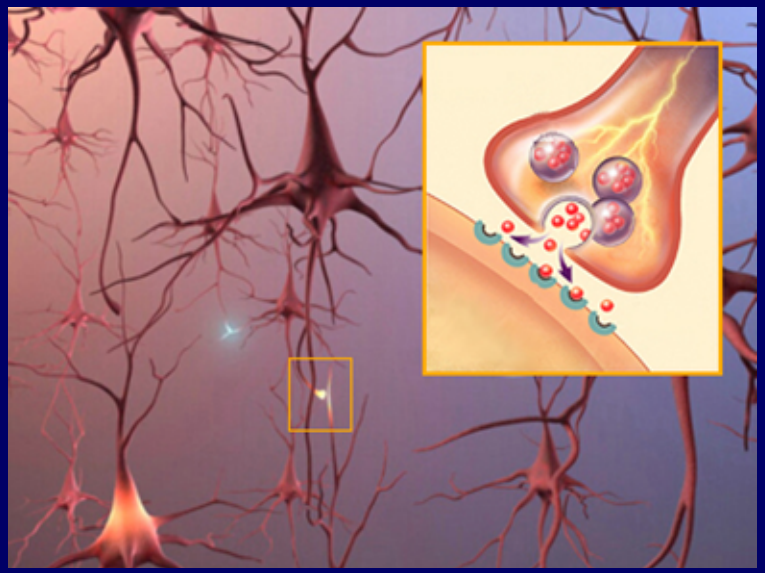
The Downside:

- We're not built to feel - That good,
- That easily,
- That often!



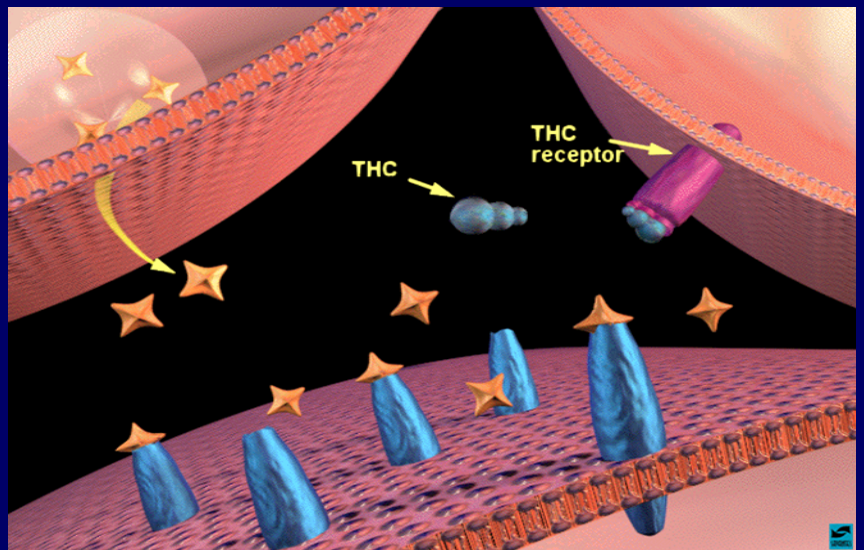
The Downside:

- Using Cannabis, receptor sites immediately begin to dwindle.
- Receptor sites sucked back into the cell.



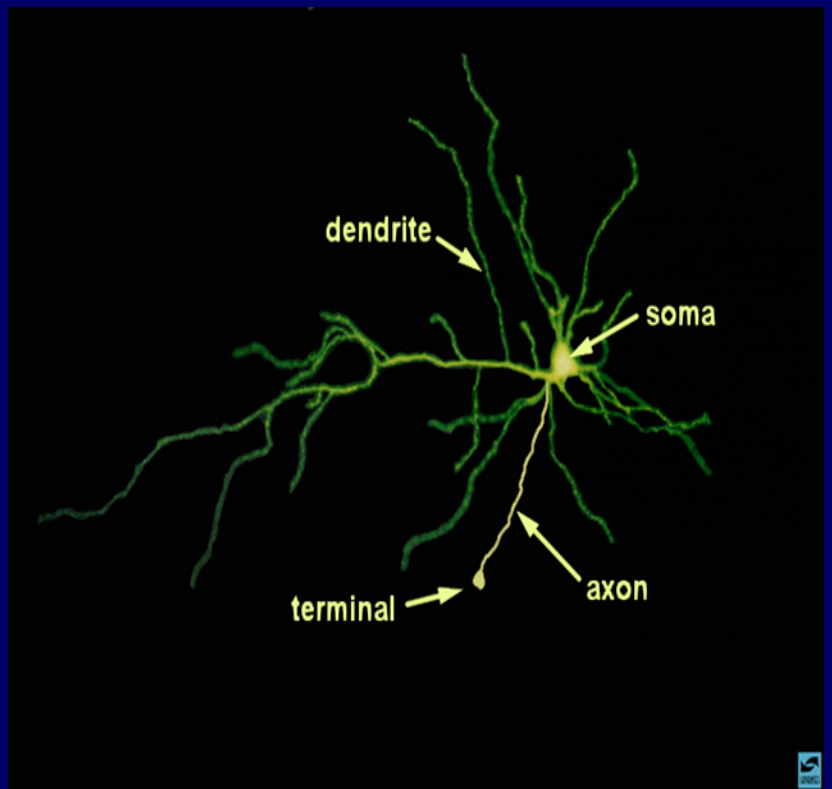
The Downside:

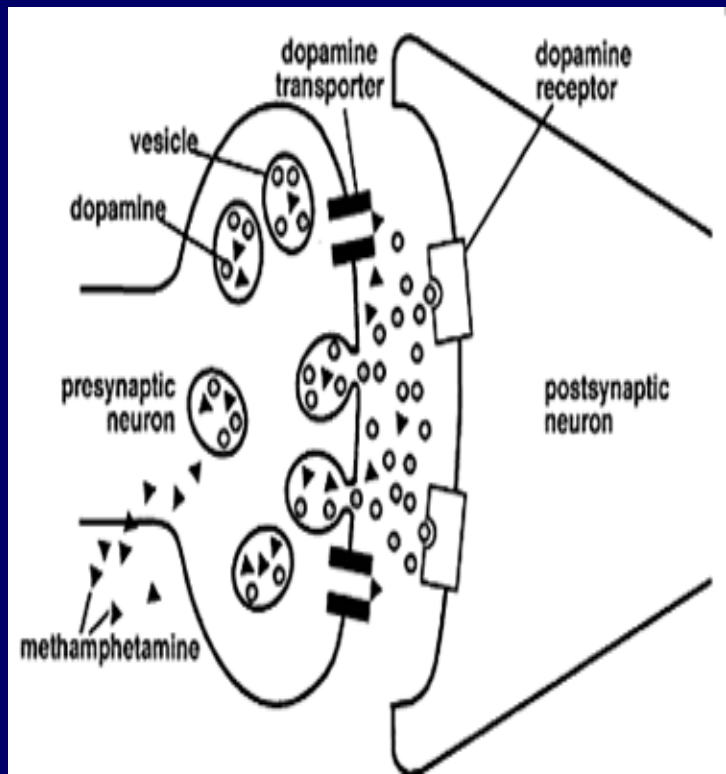
- Reduces 20 - 60% of receptor sites in different areas of the brain with a few weeks of every other day or every 3rd day use.
- Life gets more boring



The Downside: For every action there is an = and opposite reaction.

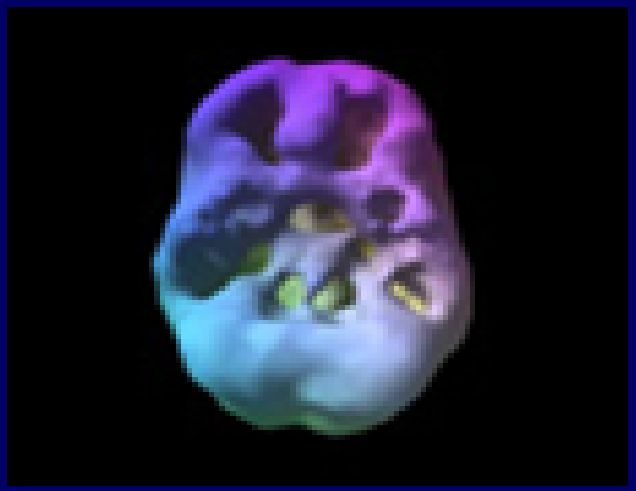
- **The Development of Tolerance:**
- **Receptor Site Degradation**



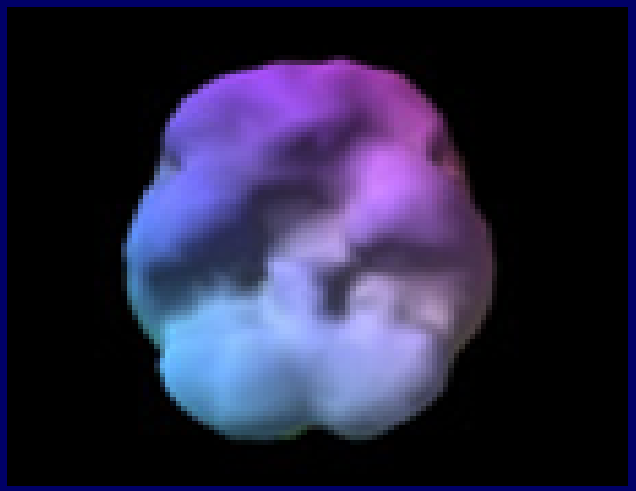


Impact of Chemical Dependency

- WORKING MEMORY
- Cannabis:



16 y.o.
2 year history of daily abuse



Normal

underside surface view of prefrontal and temporal lobe activity

THC (Cannibanoids) – minor pain killers

- Major painkillers?
- Uterus has natural THC receptors. Why?

What MJ Does to the Brain or Why We Use It

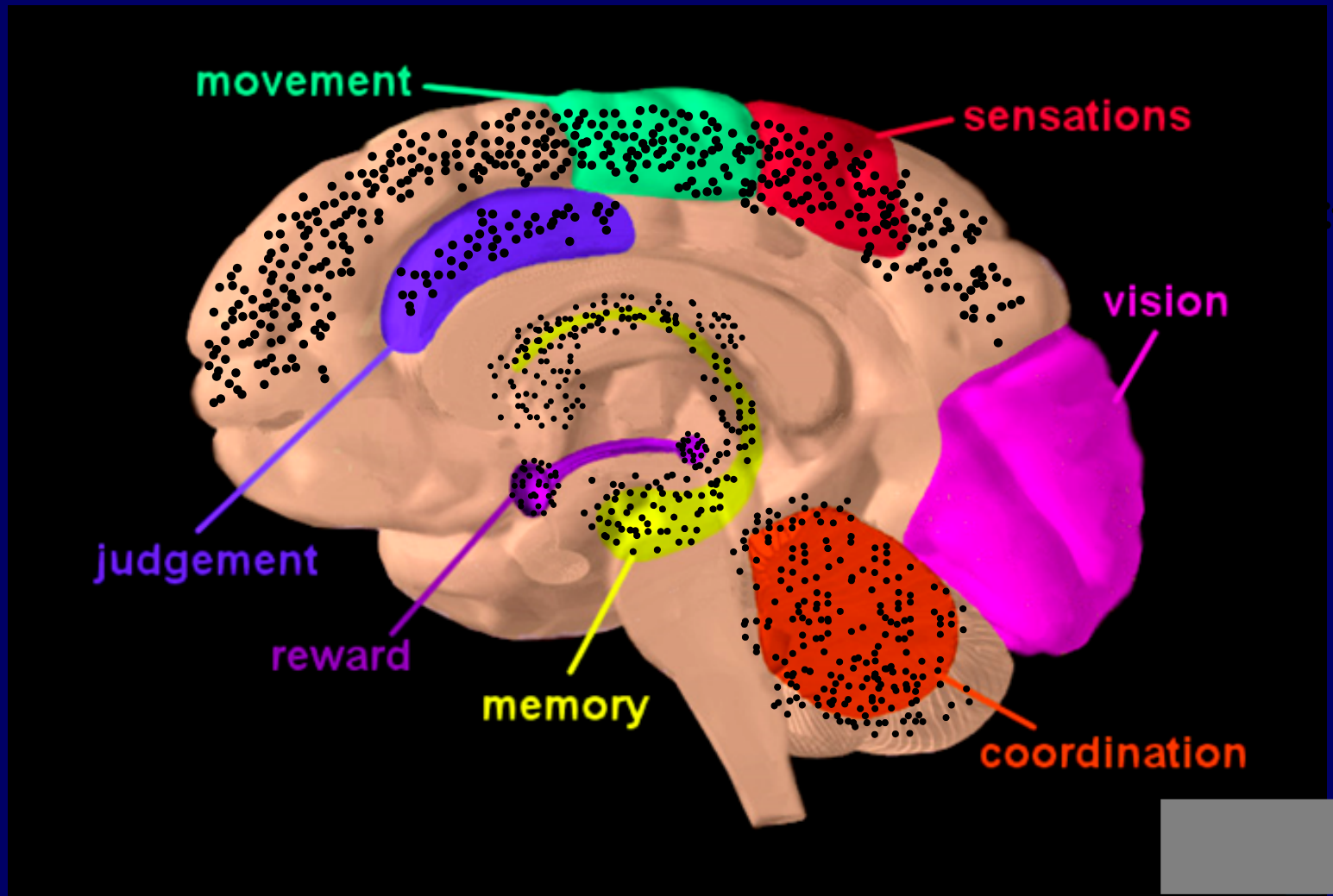
Remember:

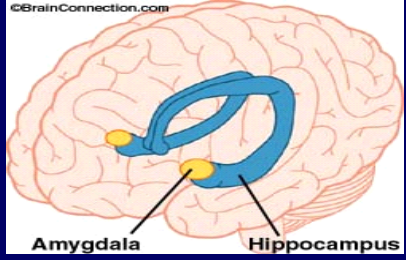
- **Our brains are built for survival.**
- **Still functioning like cave dwellers.**

THC (Cannibanoids) – minor pain killers

- Not good for survival of species if can remember pain.
- Reinforces denial of MJ addiction: don't remember negative experiences.

Other Parts of the Brain that Are Rich in CB1 Receptors that THC Lands In

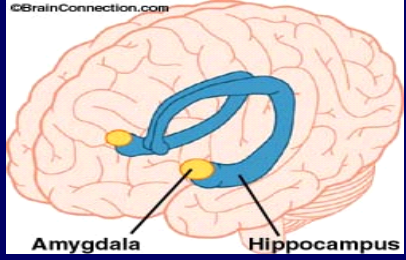




Amygdala

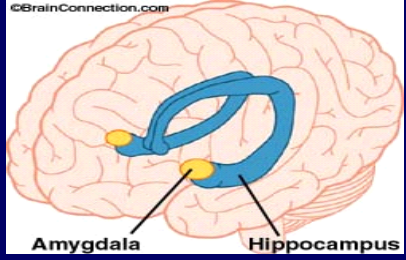
- Several Functions:
- Bonding and nursing.

Amygdala

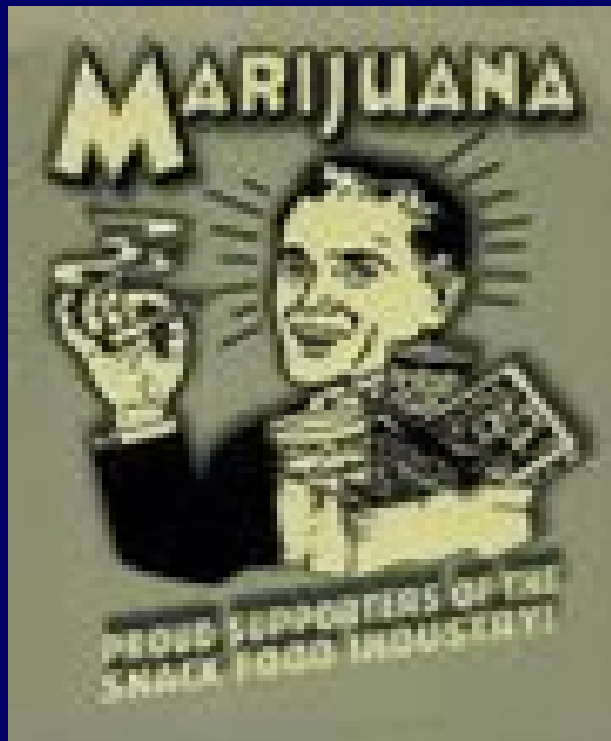


- Give THC blocker to rat pups, they don't nurse and die in 4-8 days.

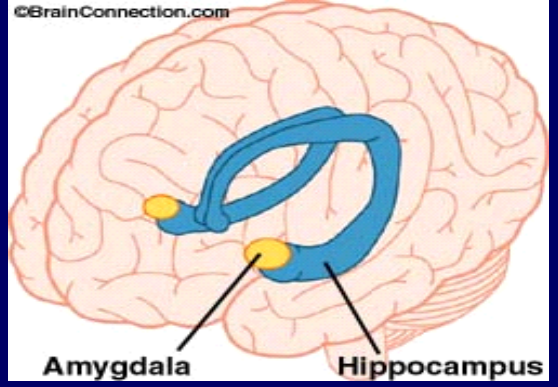
Amygdala



- This bonding and nursing response is part of what gives us the "munchies."

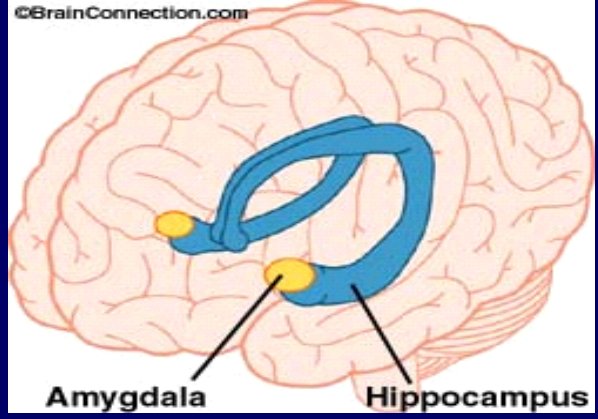


Amygdala



- Assigns emotional importance
- Central to emotional connection with others

Amygdala

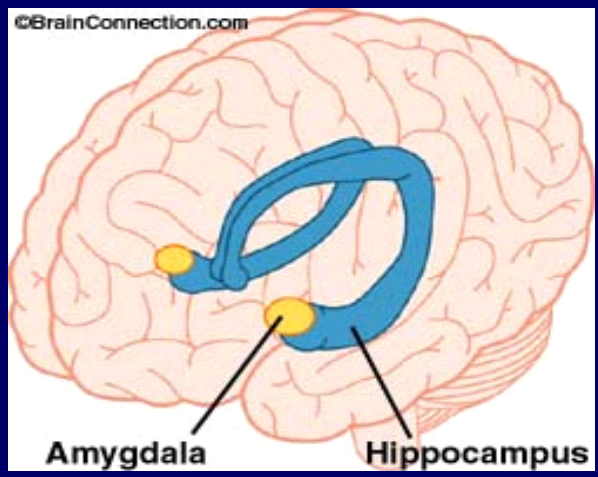


- **Smoke MJ, feel bonded to your friends**

10,000 tokers smoke together on 4/20

Amygdala

- Feelings of awe & spirituality in small area of amygdala



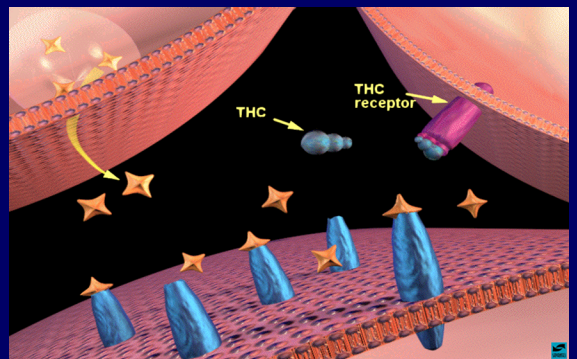
Amygdala

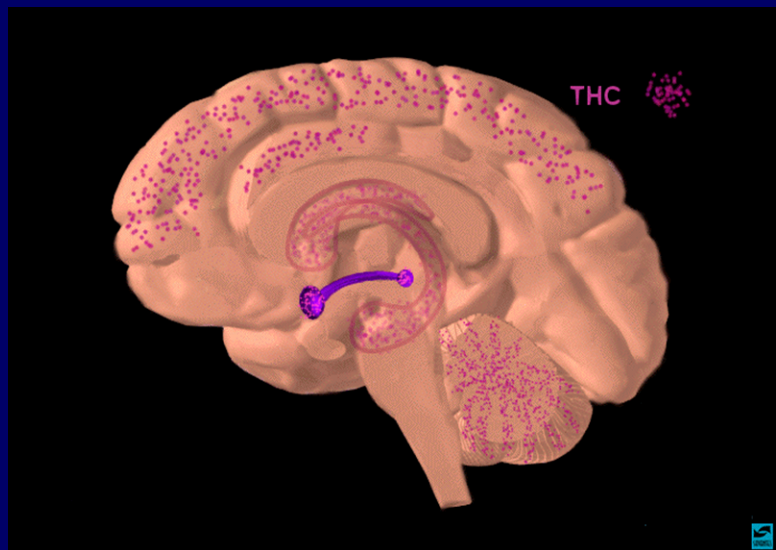
- Monitoring experience:
- When not important for our survival or betterment
- It's quiet . . .
- Bored
- When important . . .
- It's active

Amygdala - Newness/Novelty

Virtual Newness

- THC artificially stimulates novelty.
- MJ turns the boring into the fascinating.



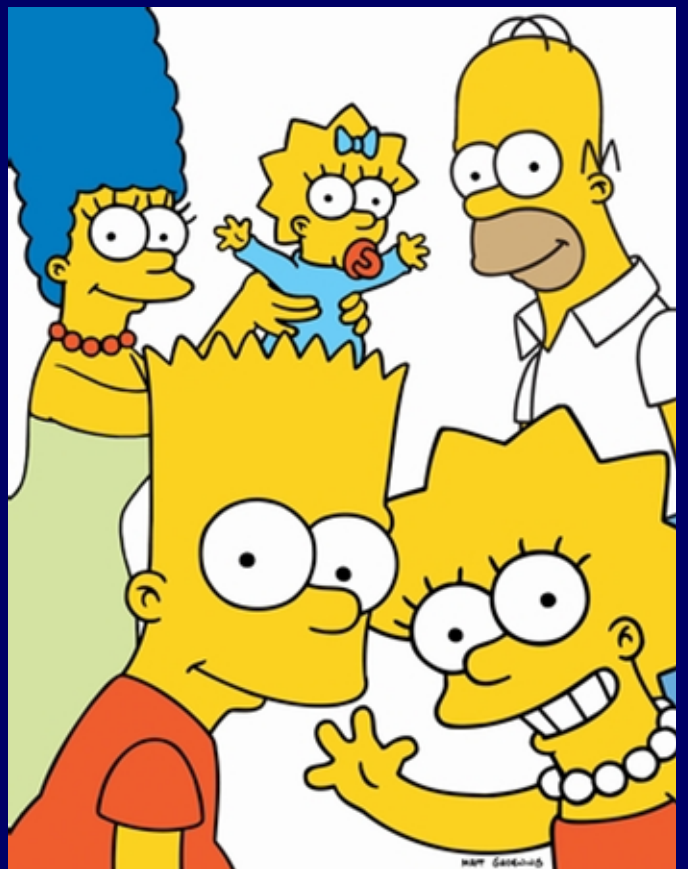


Amygdala - Virtual Novelty

- **Bubbles.**

Amygdala - Virtual Novelty

- Comedies



Amygdala - Virtual Novelty

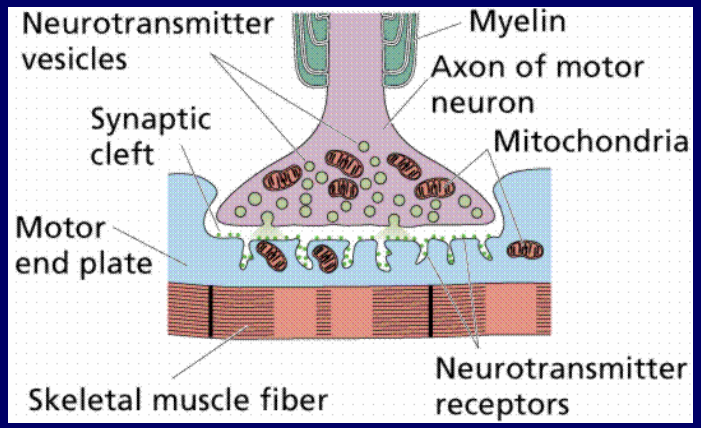
- Familiar foods taste fantastic
- Senses are not actually improved by THC, but the Amygdala is tricked into thinking this is new and exciting . . .

Amygdala - Virtual Novelty

- MJ chemically recreates the child-like experience of discovering the world!

The Downside:

- For every action there is an equal and opposite reaction.



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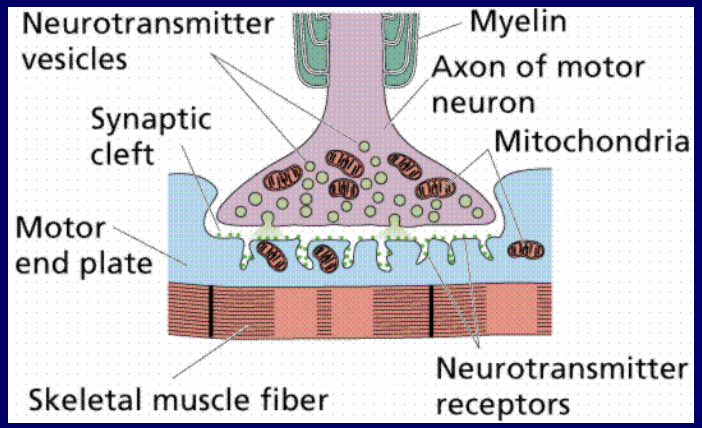
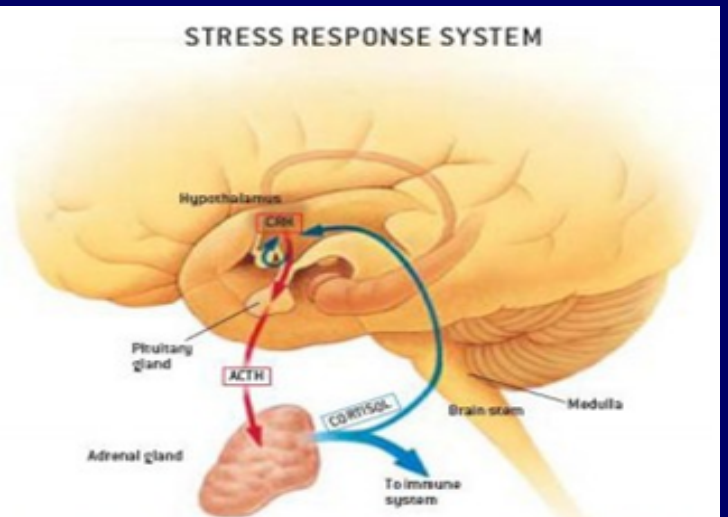


The Dark Side

The Dark Side

The Brain's Anti-Reward System

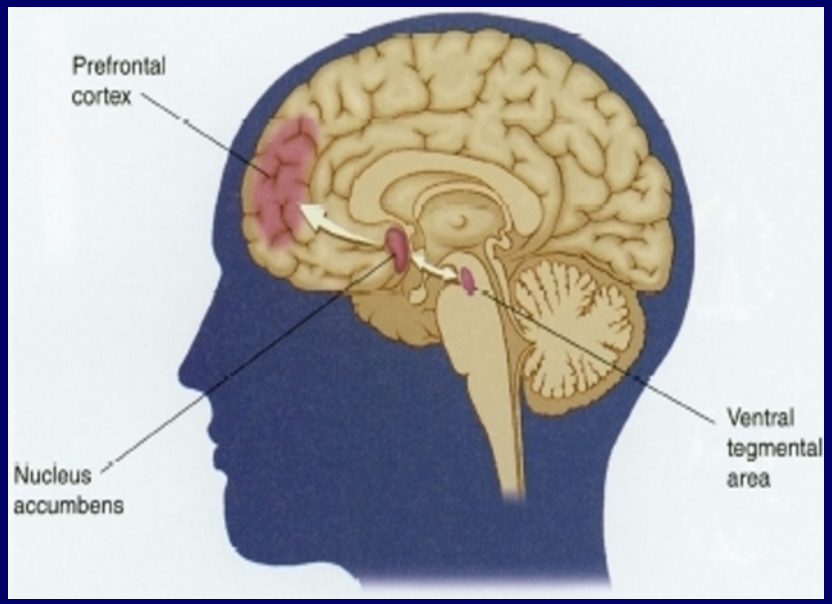
Increased Stress due to increased HPA axis functioning
And Decreased dopamine production from BDNF

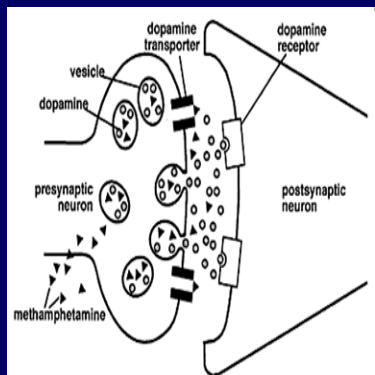


NATURE NEUROSCIENCE, VOL. 8 NUMBER 11 , 11/05 *The Journal of Neuroscience* (Impact Factor: 6.91). 06/2014; 34(23):7899-7909. DOI: 10.1523/JNEUROSCI.3776-13.2014
Vargas-Perez, Hector, et al. "BDNF Signaling in the VTA Links the Drug-Dependent State to Drug Withdrawal Aversions." *The Journal of Neuroscience* 34.23 (2014): 7899-7909.

The Downside: For every action there is an = and opposite reaction.

- Development of Tolerance
- Decreased Reward Functioning
- Decreased Frontal Lobe Functioning

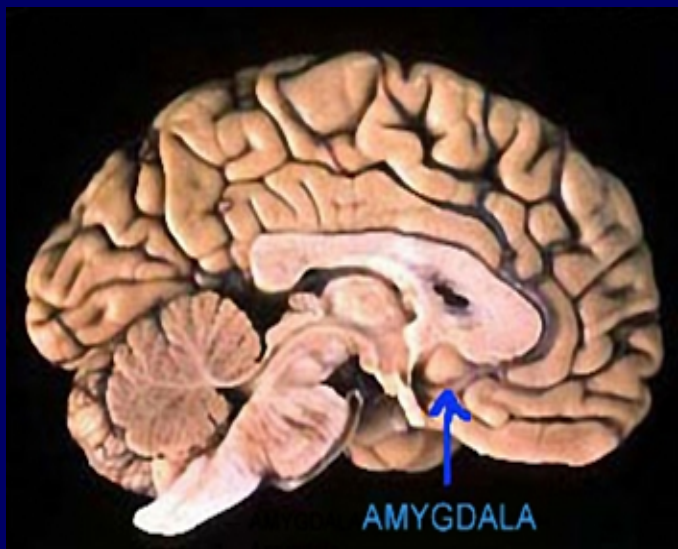




Amygdala - Revisited

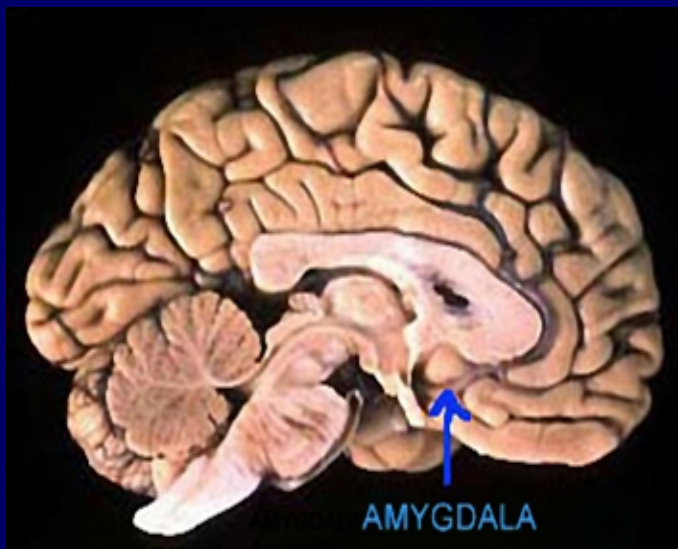
- Novelty Generator is tired:
- Amygdala now has fewer cannabinoid receptor sites.
- Natural experience is not stimulating =
- *School is boring. Nothing interesting ever happens.*

I can't wait to get out of class and smoke a blunt.



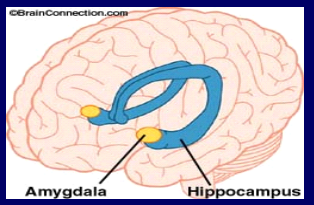
Amygdala - Revisited

- This in combination with being born with lower levels of CB1 receptors in the amygdala =
- More likely to get addicted
- Because Cannabis causes relatively more interest/excitement when have less CB1R . . .



Cermak, T. L. (2020) From Bud to Brain: A Psychiatrist's View of Marijuana

Marijuana & Anxiety

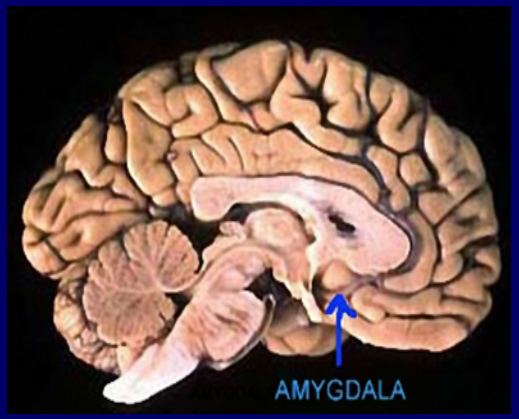


- Genetically different levels of CB1 receptors in the Amygdala:
  - **Low level of CB1 receptors = Less anxiety, higher sensation seeking**
  - **High level of CB1 = Higher anxiety/Wx from novelty**

T. Cermak, (1/20) Lecture.

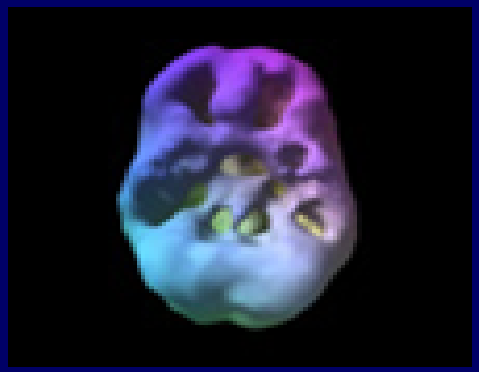
Why Low CB1R?

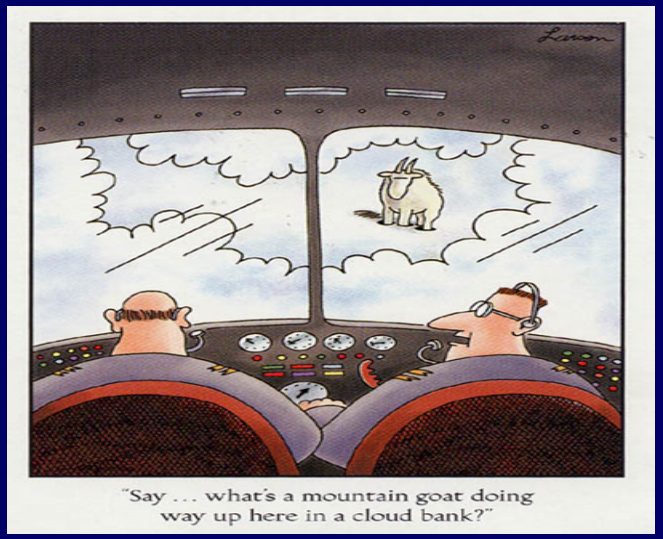
- Low CB1 =
- Will probably like Cannabis
- Explorer, inventor, creator . . .



Less CB1R = Sluggish Amygdala

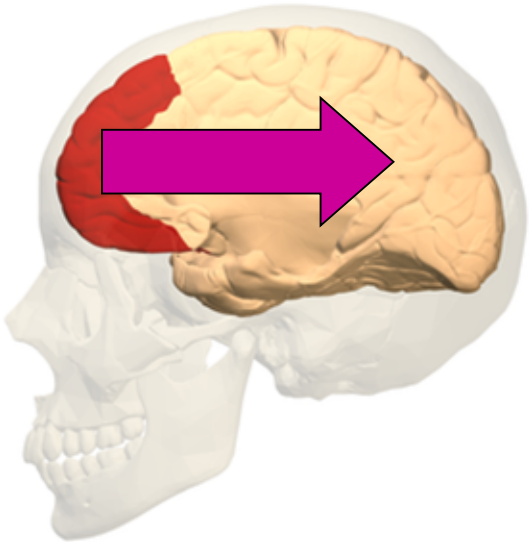
- Slower reactions
  - Airline Pilots

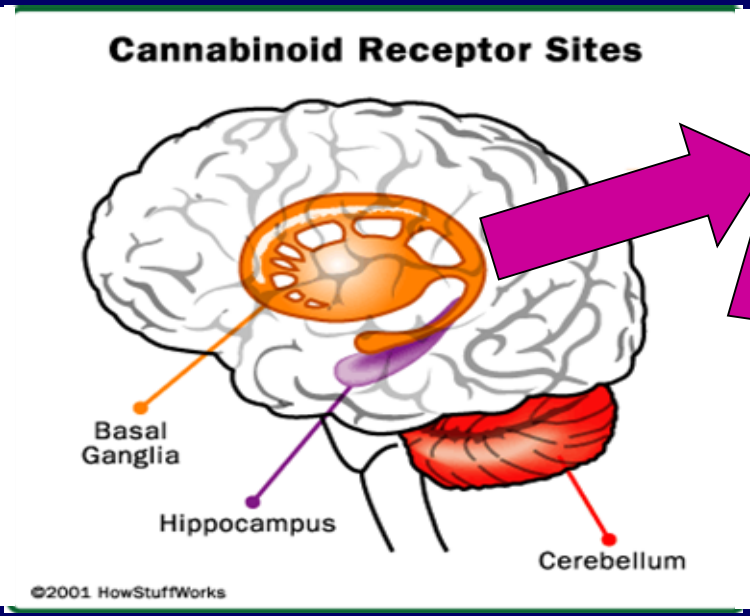


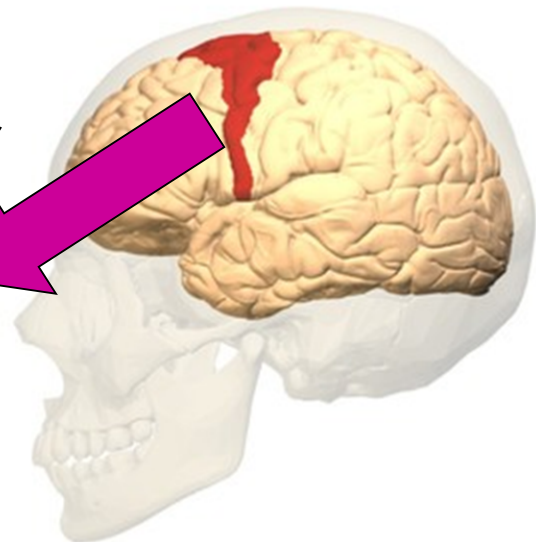


Effects on Action & Motivation

- Go Get It!
- Do It!
- Got a Plan

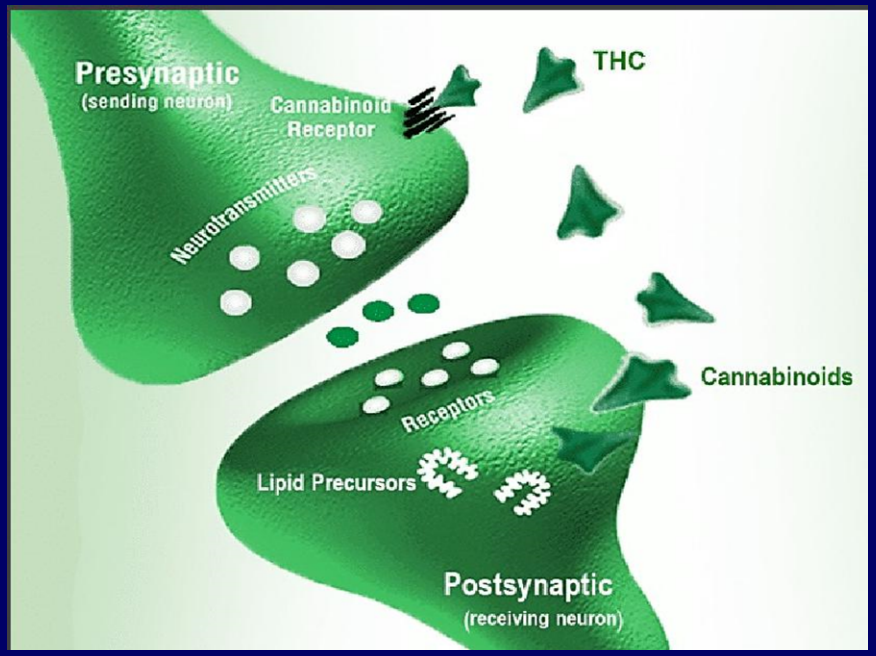


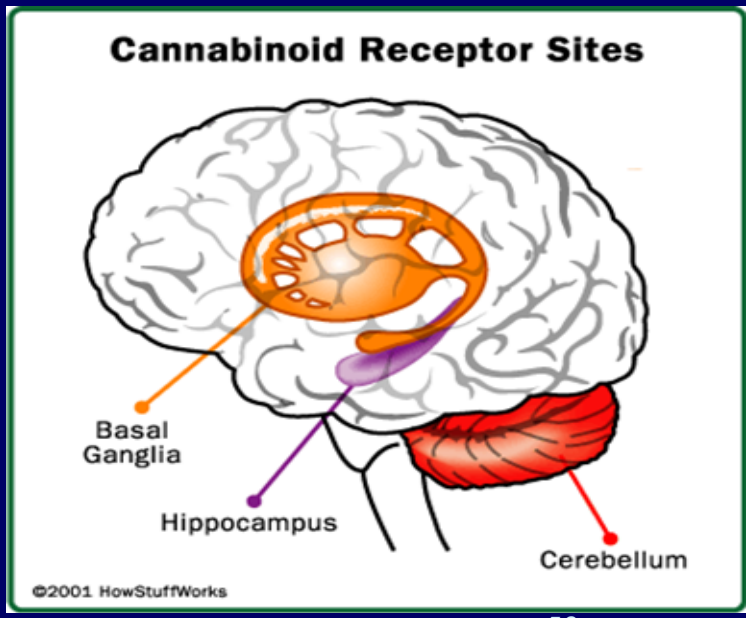




Effects on Action & Movements

- Don't Do It

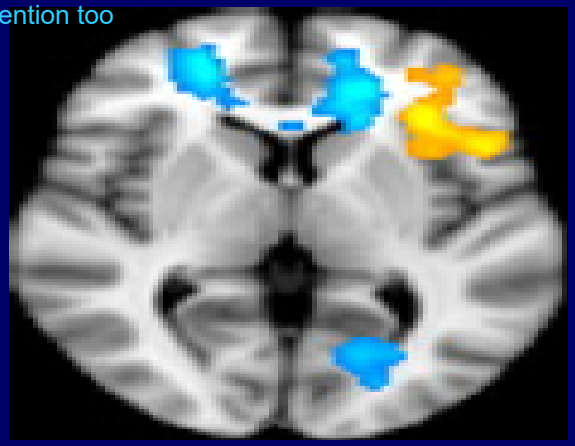


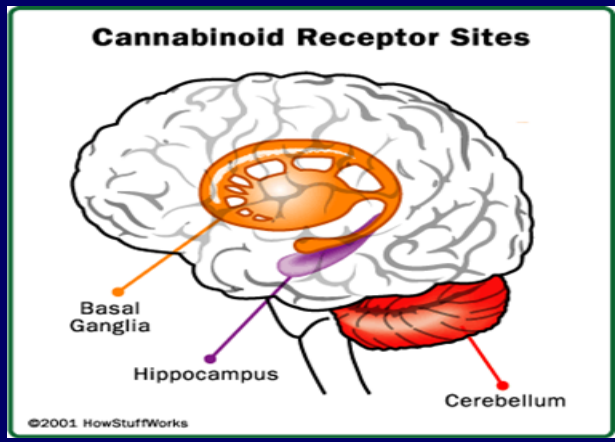


Effects on Action & Movements

- Flood these areas with THC:
- Spontaneous activity diminished.
- Calming effect can be attractive to those w/ADHD
- Doesn't help attention.

Choice of what will pay attention too



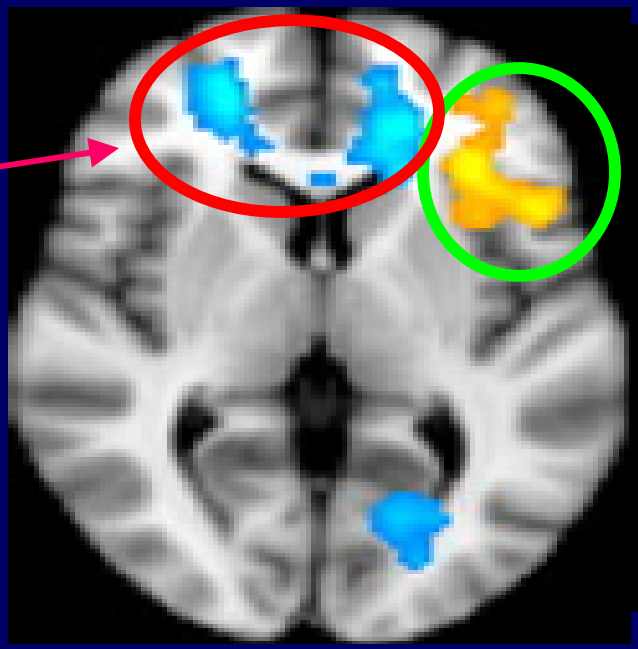


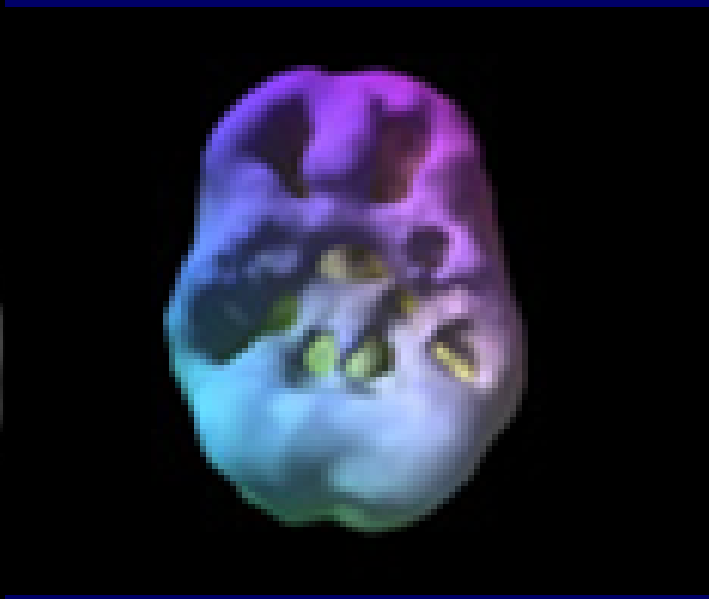
Abdullaev Y, Posner MI, Nunnally R, Dishion TJ. Functional MRI evidence for inefficient attentional control in adolescent chronic cannabis abuse. Behav Brain Res. 2010;215(1):45–57.

Attention with Chronic MJ use:

- **Homework:**
  - **Tired?**
  - **Bored/Hard to Focus?**

Less Active

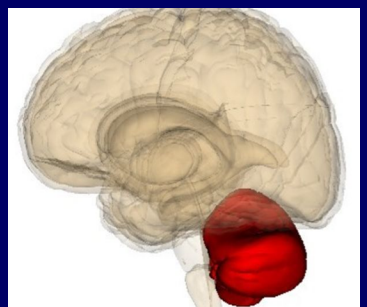




Abdullaev Y, Posner MI, Nunnally R, Dishion TJ. Functional MRI evidence for inefficient attentional control in adolescent chronic cannabis abuse. Behav Brain Res. 2010;215(1):45–57.

Effects on Action & Movements

- Animals become almost motionless with high doses of THC
- Drivers try to compensate for motor impairments by slowing down and being more careful.
- Heightened by distortions in time and space perception (Cerebellum).



Effects on Action & Movements

- 2 grps of drivers on an obstacle course sober then:
- Give 1 grp alcohol –
  - Drive faster, make more mistakes and judge that they did better.
- Give other grp MJ –
- Drive slower, make a few more mistakes, judge themselves as having done worse and . . .
  - They wonder why a car was following them the whole time.

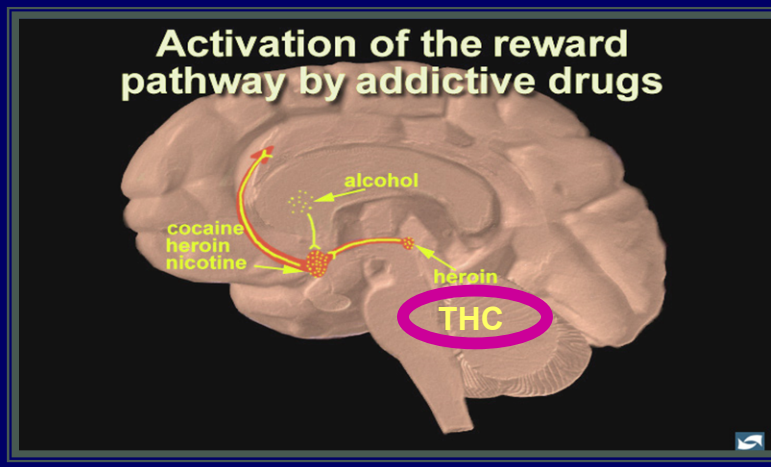
Effects on Action & Movements

- MJ ~Doubles accident risk*
- ~ 4 – 14%** of drivers who sustained injury or death tested + for Cannabis

**In many of these cases, alcohol was detected as well. – NIDA

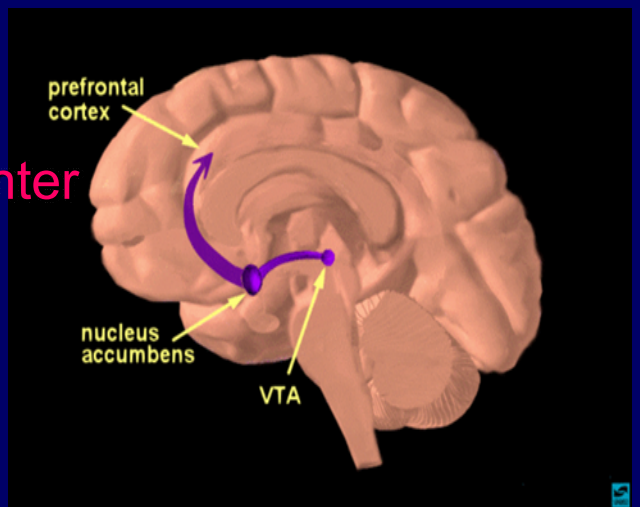
- * for ≥ 2 hrs. - Hartman RL, Huestis MA. Cannabis effects on driving skills Clin Chem. 2013;59(3):478-492.

THC: Reward, Pleasure, Wanting & Addiction



- **Nucleus Accumbens:**
- **Increases DA (dopamine) like other drugs of abuse.**
- **Thinking about MJ causes a release of DA.**

Pleasure Center



MJ: Addiction & Withdrawal Sx

Cannabinoid Deficiency Syndrome

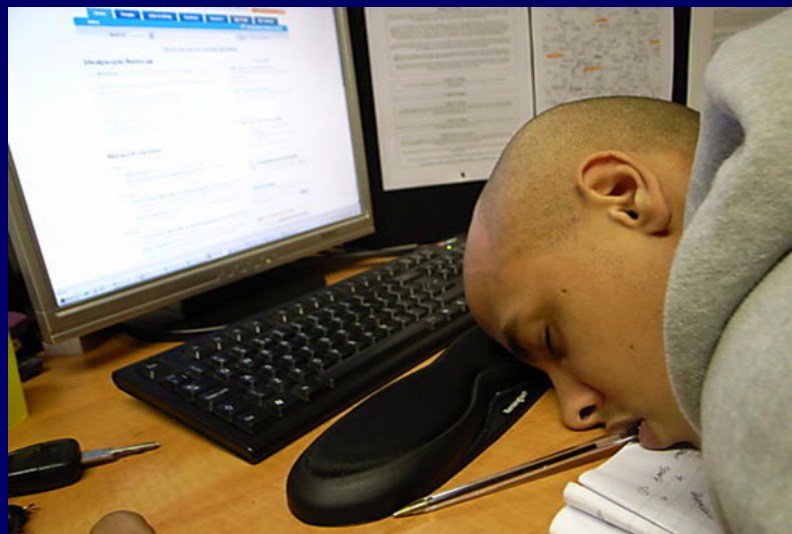
Peak Symptoms 2 – 6 days into withdrawal. Duration for most symptoms is 5 – 21 days.

- **Craving**
- **Anger/Irritability/Aggression**
- **Sleep Disturbances (Up to 6 weeks)**
- **Increased dream sleep including "strange dreams"**
- **Nervousness/anxiety**
- **Decreased appetite or weight loss**
- **Concentration Problems**
- **Restlessness**
- **Aches, Pains and Chills**
- **Sweating**

****Withdrawal from heavy marijuana use (25 days/month) is about as harsh as withdrawal from nicotine addiction (10 cigarettes daily) A within-subject comparison of withdrawal symptoms during abstinence from cannabis, tobacco, and both substances Drug and Alcohol Dependence Volume 92, Issues 1-3, 1 January 2008, 48-54 ,**

THC's Effect on the Frontal Lobes

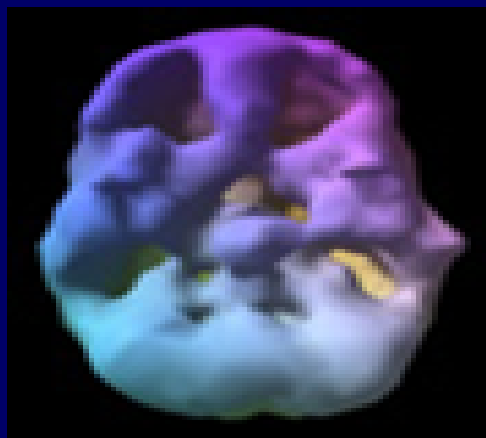
- Frontal lobes: have most cannibanoid receptors.
- AMOTIVATIONAL SYNDROME – Couch potato
  - Can spend years on end in mediocrity. Will lose their passion. . . due to effect of reduced ability to experience novelty: the Amygdala



THC's Effect on the Frontal Lobes

- **"Hashish . . . Gives the power of imagination and takes away the ability to profit from it."**
  Charles Baudelaire (1860) *Les Paradis Artificiel*

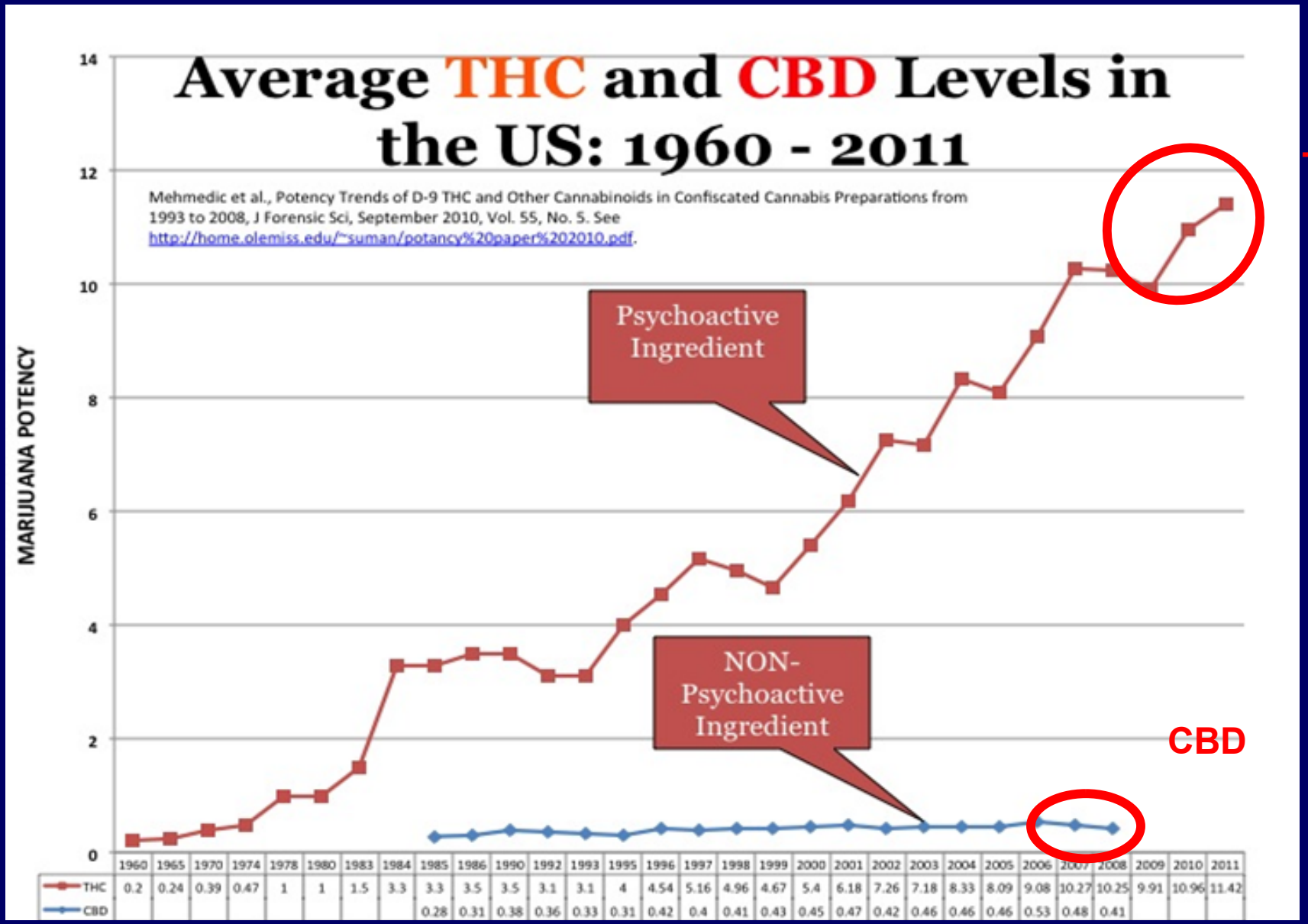
  - Even after a month of abstinence, adolescent MJ users demonstrate subtle deficits in psychomotor speed, complex attention, planning and sequencing, and verbal story memory compared with nonmarijuana using teens.
    J Int Neuropsychol Soc. 2007 September; 13(5): 807–820.

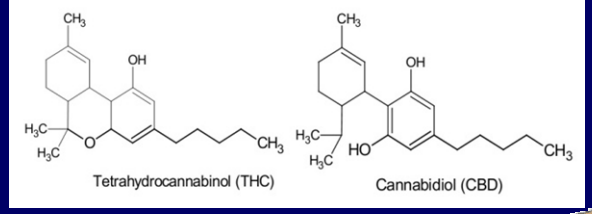


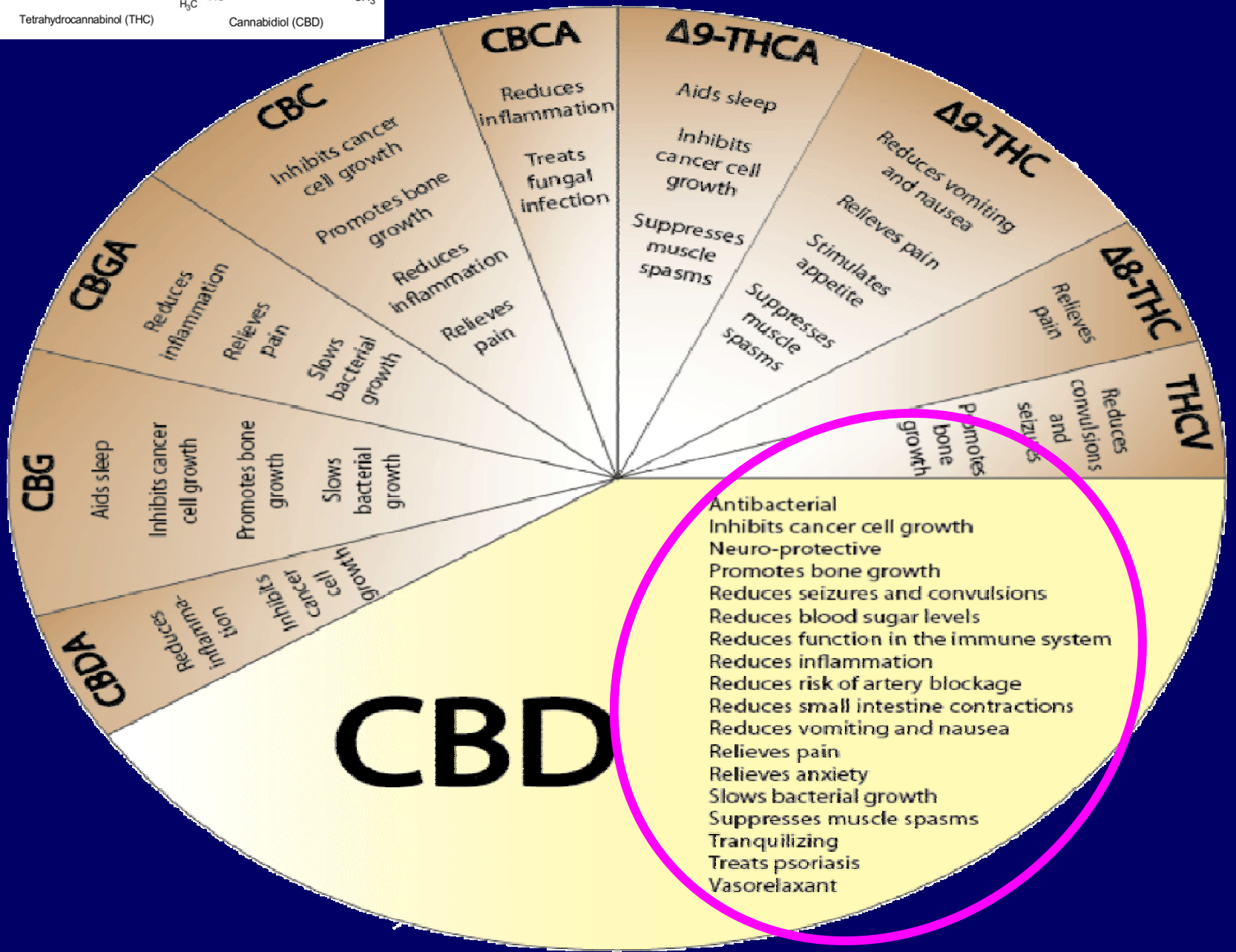
Cannabis Addiction & Denial

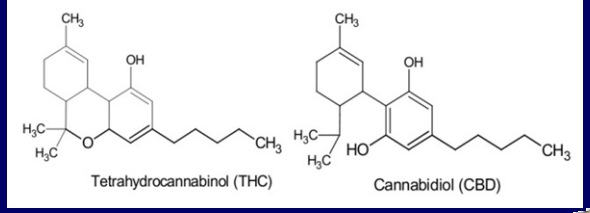
- Denial always present . . .
- Consequences comparatively mild . . .
- Used 2x " . . . to deal w/the jet lag . . . I stopped b/c I noticed that I was getting a little depressed like I used to . . . I was feeling better and positive for the 3 mos. I wasn't using there while I was there . . ."

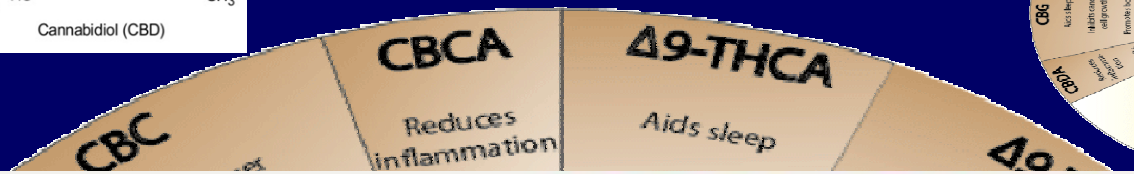
Where's the Medicine?

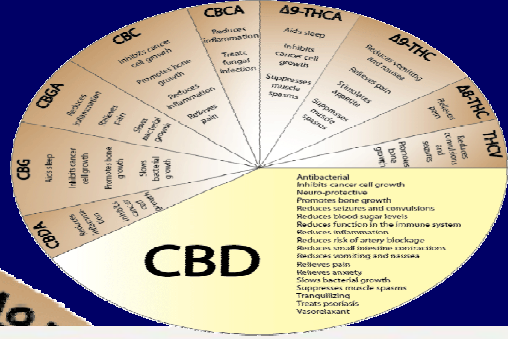



Tetrahydrocannabinol (THC)
Cannabidiol (CBD)


CBCA
Reduces inflammation
Treats fungal infection
Δ9-THCA
Aids sleep
Inhibits cancer cell growth
Suppresses muscle spasms
Δ9-THC
Reduces vomiting and nausea
Relieves pain
Stimulates appetite
Suppresses muscle spasms
Δ8-THC
Relieves pain
THCV
Reduces convulsions and seizures
Promotes bone growth
CBC
Inhibits cancer cell growth
Promotes bone growth
Reduces inflammation
Relieves pain
CBGA
Reduces inflammation
Relieves pain
Slows bacterial growth
CBG
Aids sleep
Inhibits cancer cell growth
Promotes bone growth
Slows bacterial growth
CBDA
Reduces inflammation
Inhibits cancer cell growth
CBD
Antibacterial
Inhibits cancer cell growth
Neuro-protective
Promotes bone growth
Reduces seizures and convulsions
Reduces blood sugar levels
Reduces function in the immune system
Reduces inflammation
Reduces risk of artery blockage
Reduces small intestine contractions
Reduces vomiting and nausea
Relieves pain
Relieves anxiety
Slows bacterial growth
Suppresses muscle spasms
Tranquilizing
Treats psoriasis
Vasorelaxant



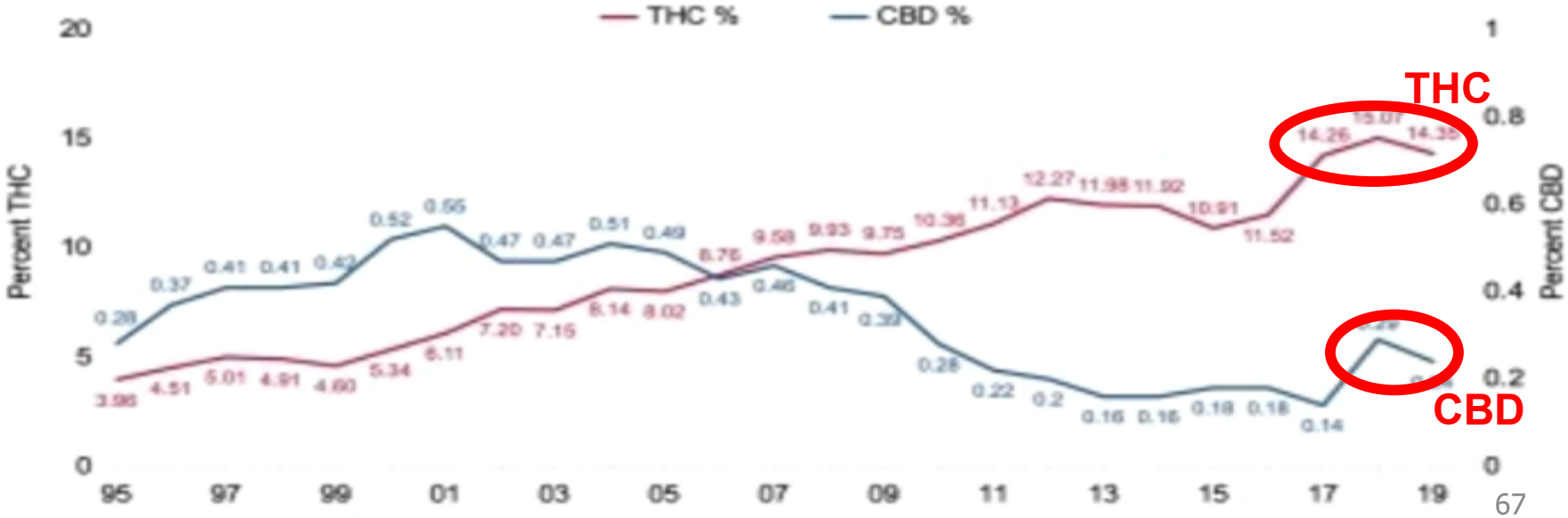




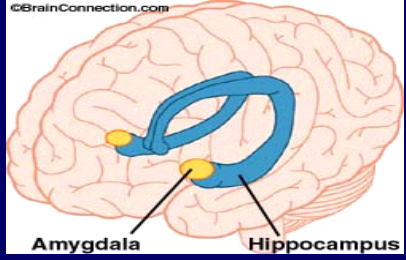
	THC	CBD	CBG	CBN	CBC	THCv	CBGA	CGCA	CBCA	THCA	CBDA
Relieves Pain *Analgesic*	●	●		●	●		●				
Suppresses appetite/Helps with weight loss *Anorectic*						●					
Kills or slows bacteria growth *Antibacterial*		●	●						●		
Reduces blood sugar levels *Anti-diabetic*		●									
Reduces vomiting and nausea *Anti-emetic*	●	●									
Reduces seizures and convulsion *Anti-epileptic*		●				●					
Treats fungal infection *Antifungal*									●		
Reduces inflammation *Anti-inflammatory*		●	●		●		●	●		●	●
Aids sleep *Anti-insomnia*				●							
Reduces risk of artery blockage *Anti-ischemic*		●									
Inhibits cell growth in tumors/cancer cells *Anti-proliferative*		●	●		●					●	●
Treats psoriasis *Anti-psoriatic*		●									
Tranquilizing, used to manage psychosis *Antipsychotic*		●									
Suppresses muscle spasms *Antispasmodic*	●	●		●						●	
Relieves anxiety *Anxiolitic*		●									
Simulates appetite *Appetite Stimulant*	●										
Promotes bone growth *Bone Stimulant*		●	●		●	●					
Reduces function in the immune system *Immunosuppressive*		●									
Reduces contractions in the small intestines *Intestinal Anti-prokinetic*		●									
Protects nervous system degeneration *Neuroprotective*		●									

THE IRONY


Average THC and CBD Levels in the US: 1960 - 2011
Mehmedic et al., Potency Trends of D-9 THC and Other Cannabinoids in Confiscated Cannabis Preparations from 1993 to 2008, J Forensic Sci, September 2010, Vol. 55, No. 5. See
http://home.olemiss.edu/~suman/potancy%20paper%202010.pdf.
MARIJUANA POTENCY
Psychoactive Ingredient
NON-Psychoactive Ingredient
THC
CBD


Percentage of THC and CBD in cannabis samples seized by the DEA from 1995-2019
THC %
CBD %
Percent THC
Percent CBD
THC
CBD
95
97
99
01
03
05
07
09
11
13
15
17
19

Marijuana & Anxiety



Biphasic response:

- Low dose - anxiety mellowing
- High dose - anxiety inducing.

- Genetically different levels of CB1 receptors in the Amygdala:
  - Low level of CB1 receptors: Less anxiety, higher sensation seeking
  - High level, 20% more: Anxiety prone

T. Cermak, (1/20) Lecture.

"Ear Wax, Budder, Dabs, Honey Oil"

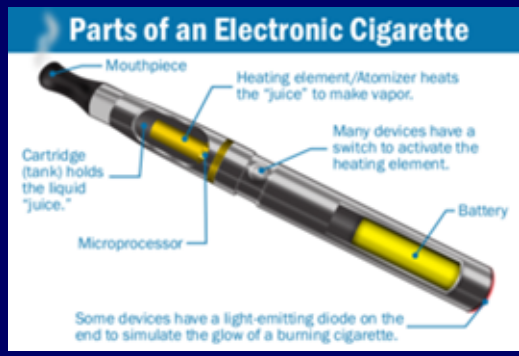
- Looks like honey or butter.

- 40% – 80+% THC
  - Made with butane or other solvents

"Ear Wax, Budder, Dabs, Honey Oil"

Can be ingested in food or drinks,

- But most popular is to smoke or use e-cigarettes or vaporizers
  - Called "Dabbing" or "Vaping"



Possible Acute Negative Side Effects

- Anxiety
- Panic Attacks
- Paranoia
- Increased heart rate & blood pressure
- Psychosis
- Nausea/Vomiting
  - Cannabinoid hyperemesis syndrome
  - [recurrent nausea, vomiting and crampy abdominal pain]
- Withdrawal

The End!

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