

# Cognitive Impairment: A Seldom Discussed Complication of Substance Use Disorders

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[www.atlantahealingcenter.com](http://www.atlantahealingcenter.com)



# Faculty Disclosures

- **Susan K. Blank, MD**  
Founder & Chief Medical Officer of Atlanta Healing Center and Atlanta Wellness Center
- President - Georgia Society of Addiction Medicine
- Board of Directors-Georgia Council on Alcohol and Drugs
- Board of Directors- Let's Be Clear Georgia
- Consultant-Libertas Tobacco Healing Center, Ontario, Canada
- Appointee to Georgia's State Commission on Narcotics Treatment Programs 2016
- Fellow of the American Psychiatric Association
- Fellow of American Board of Forensic Examiners
- Fellow of American Academy of Anti-Aging Regenerative Medicine
- Fellow of American Society Addiction Medicine
- Diplomate ABPN, ASAM, ABAM, AAAAM
- Certified Medical Review Officer
- Chapter : *Tobacco Addiction*, 2013 ASAM Criteria
- Chapter: Responsible, safe, and effective prescription of opioids in chronic non-cancer pain. ASIPP Guidelines 2017, Pain Physician, March 2017.
- Weekly Radio Show: "*Detailing Addiction with Dr. Susan Blank*" on America's Web Radio.

# Atlanta Healing Center

*helping you find your path*

State of the art outpatient addiction recovery program  
Highest quality, evidence based, integrated treatment

## Services include:

- Thorough Evaluation
- Neurofeedback  
*Craving Reduction and Mental Fluidity*
- Hormonal Rebalancing
- Medication Assisted Recovery



An abstract painting with vibrant colors like blue, red, and yellow, featuring a large white circular shape in the center. In the foreground, a purple orchid plant is visible.

# Atlanta Wellness Center

State-of-the-Art Approach to a Healthy and Fulfilling Life


## Services include:

- Acupuncture
- Brain Mapping & Neurofeedback  
*Mental Clarity and Improved Performance*
- Hormone Balancing
- Smoking Cessation
- Weight Management

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**ATLANTA  
HEALING  
CENTER**

# Topics for today

- Definition of Addiction
- Neurocognitive Effects of Addiction
- How can you test for these in your office?



# Confusing Terms



# Definitions

- Proper Use
  - Taking Medications as per doctor's Instructions
- Drug MisUse
  - Taking a psychoactive substance for non-medical purposes, out of curiosity
- Drug Abuse
  - Drug use that leads to problems (e.g. loss of effectiveness in society; behavioral psychopathology, criminal acts)
- Drug Dependence
  - The state of needing a drug to function within 'normal limits'
- Addiction:
  - A maladaptive pattern of drug use leading to clinically-significant impairment or distress, associated with difficulty in controlling drug-taking behavior, withdrawal, and tolerance

**ADDICTION: CONTINUED USE IN SPITE OF CONSEQUENCES**

# Definitions: Expected Outcomes from Prescription Medications

- Proper Use
  - Taking Medications as per doctor's Instructions
- Drug Dependence
  - The state of needing a drug to function within 'normal limits'



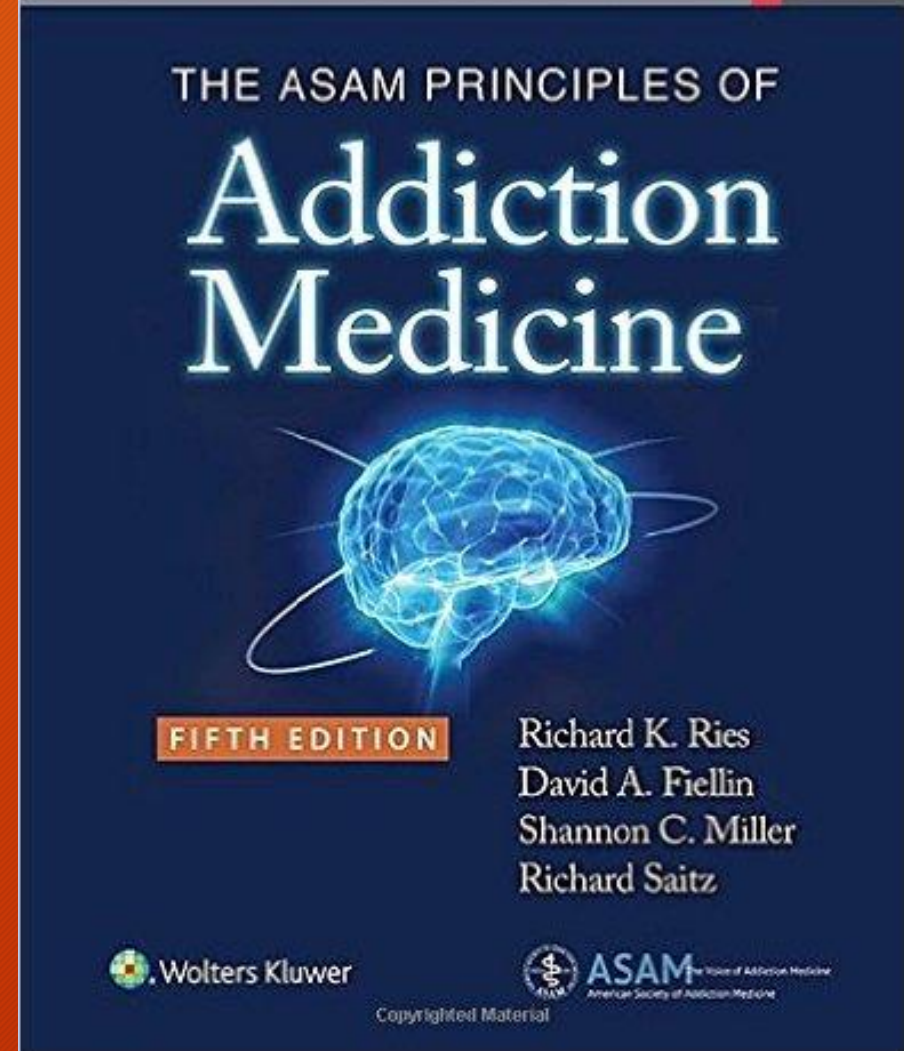
# Definitions: Improper Use

- Drug Misuse
  - Taking a psychoactive substance for non-medical purposes, out of curiosity for “recreational” uses
- Drug Abuse
  - Drug use that leads to problems (e.g. loss of effectiveness in society; behavioral psychopathology, criminal acts)



# Classic Models of Addiction

<b>Model</b>	<b>Emphasized Causes</b>	<b>Example Interventions</b>
Moral	Personal responsibility; self-control	Moral suasion; social/legal sanctions
Spiritual	Spiritual defect	Prayer; 12-step faith-based treatment (e.g. AA)
Temperance	Drugs	Control of supply; calls for abstinence
Educational	Ignorance	Education
Conditioning	Classical/operant conditioning	Counterconditioning; extinction



American Society of Addiction Medicine

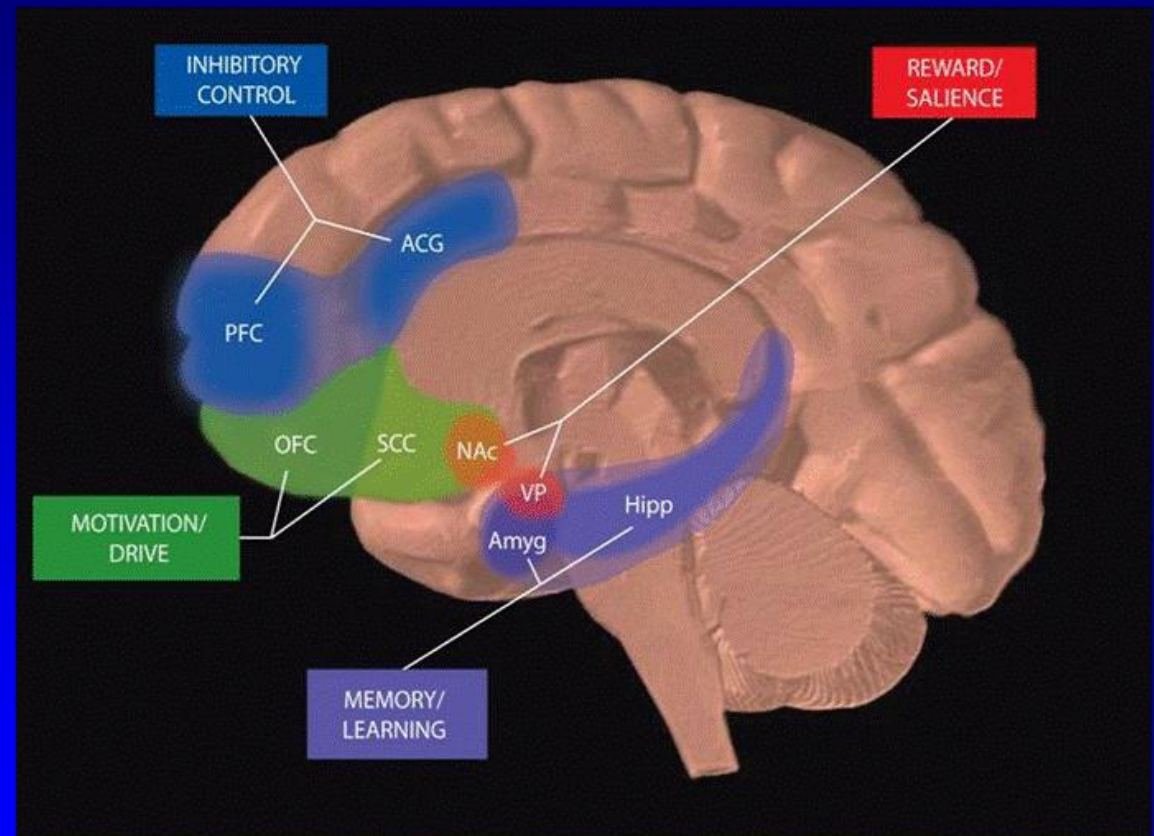
# American Society of Addiction Medicine

- **Addiction is a Primary**
- **Chronic disease of brain**
- **Reward Pathway**
- **Motivation Pathway**
- **Memory Network and related circuitry.**

## Drug Addiction involves 4 circuits

1. Reward – nucleus accumbens(NAc)  
ventral pallidum
3. Motivation/drive- orbitalfrontal cortex (OFC)  
subcallosal cortex
5. Memory and learning- amygdala  
hippocampus
7. Control- prefrontal cortex  
anterior cingulate gyrus

## *Circuits Involved In Drug Abuse and Addiction*



**All of these brain regions must be considered in developing strategies to effectively treat addiction**



# American Society of Addiction Medicine

- Dysfunction in these circuits leads to characteristic Biological
- Psychological
- Social
- Spiritual manifestations.

# American Society of Addiction Medicine

- This is reflected in an individual pathologically pursuing Reward and/or
- Relief by substance use and other behaviors.

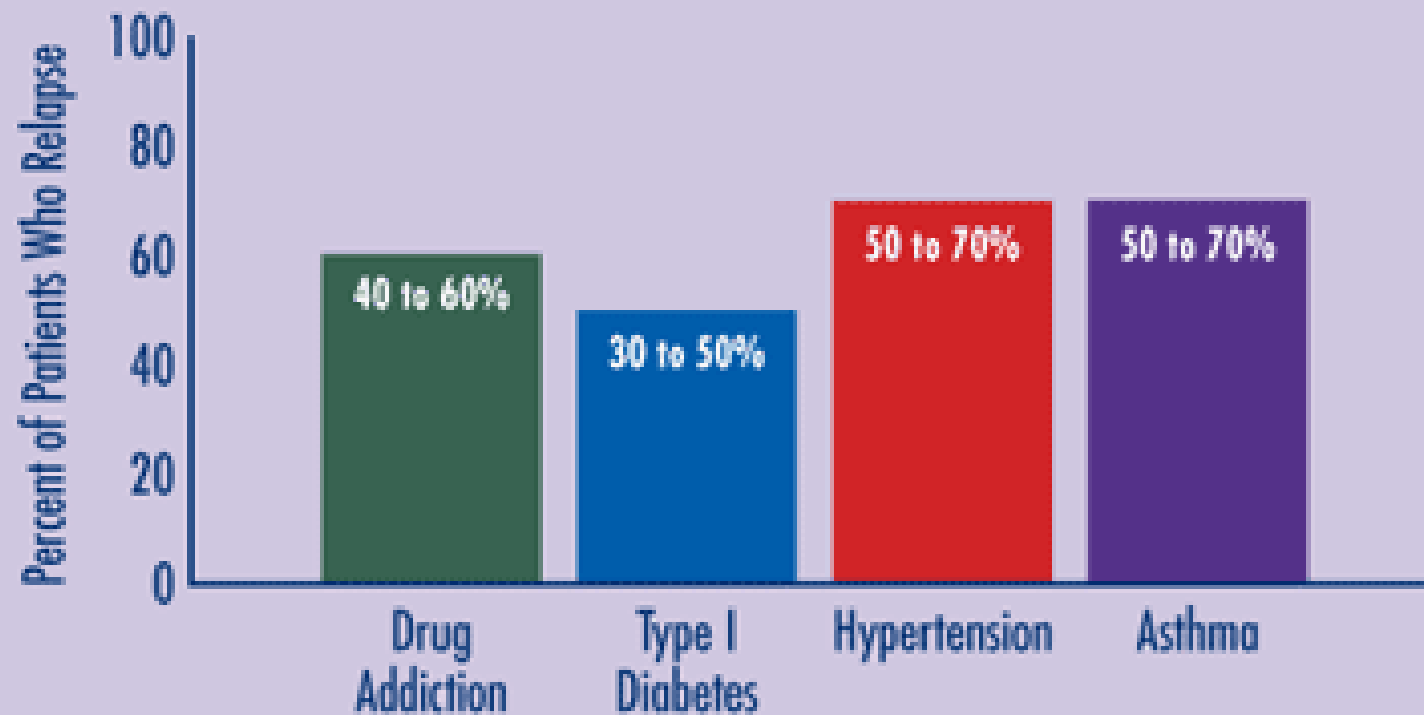
# American Society of Addiction Medicine

- Addiction is characterized by inability to consistently abstain
- Impairment in behavioral control
- Craving
- Diminished recognition of significant problems with one's behaviors and interpersonal relationships
- A dysfunctional emotional response.

# American Society of Addiction Medicine

- Like other chronic diseases,
- Addiction often involves cycles of
- Relapse and Remission.

## COMPARISON OF RELAPSE RATES BETWEEN DRUG ADDICTION AND OTHER CHRONIC ILLNESSES



# American Society of Addiction Medicine

- Without treatment or engagement in recovery activities,
- Addiction is progressive and
- Can result in disability or premature death.



# Evolutionary advantage of sugar

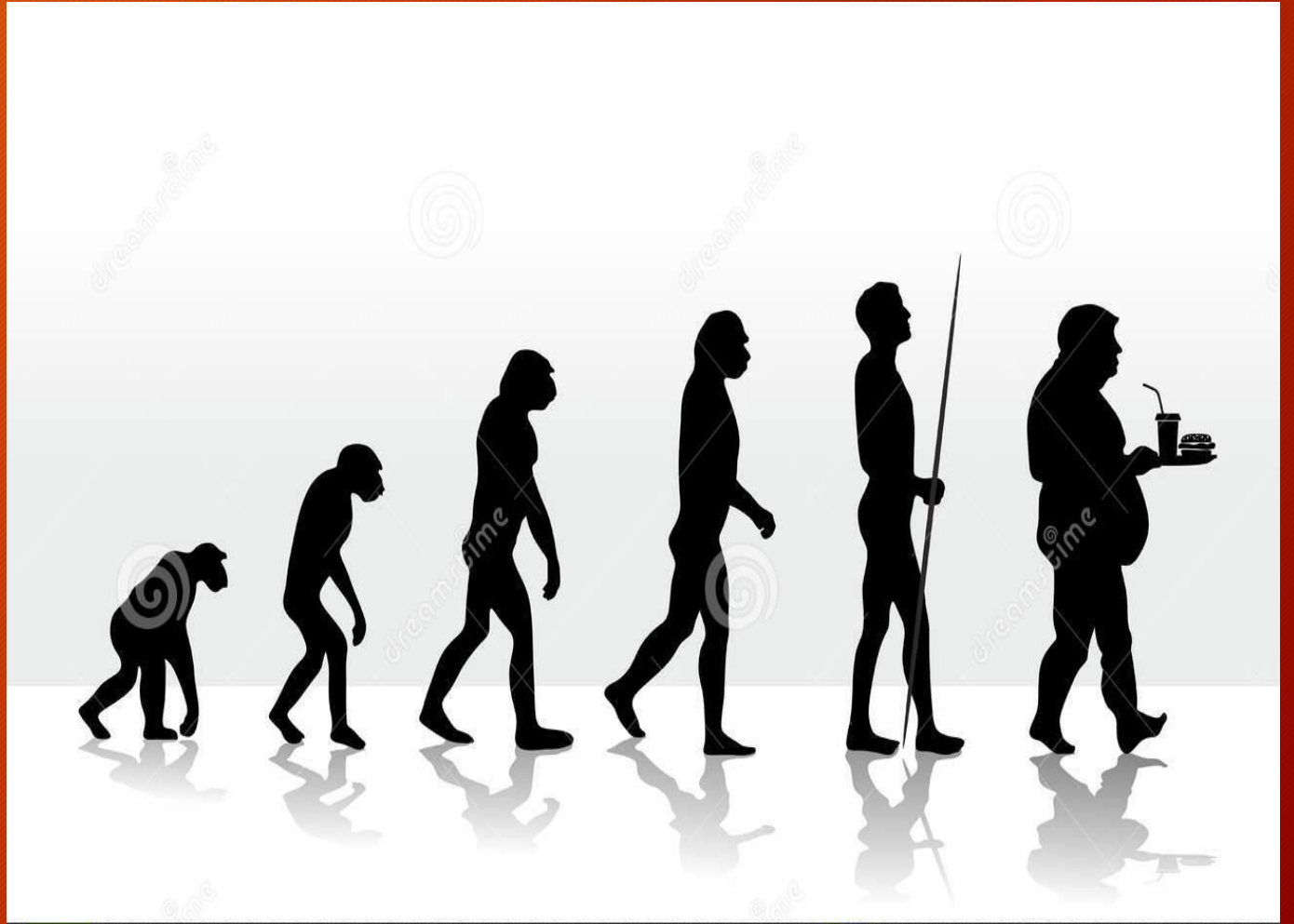
The only food that our brain is hard wired for is SUGAR

Early man was wired for finding sources of sugar, such as honey or ripe fruit

Glucose for energy

Fructose to help us store fat

Storing fat was life saving during times of famine or drought.





# Why Not Broccoli? Answer: Incentive Salience

- Salience is a deep and even unconscious wanting, rooted in our biological and genetic need for food, water, reproduction and connection to others.
- One group of researchers puts it this way: “Core ‘wanting’ does not require conscious awareness, perhaps because it is chiefly a product of subcortical structures involving... dopamine systems (Robinson, Robinson & Berridge, 2013).
- This kind of wanting is deep, and creates a magnetic and attention-commanding aspect to certain activities or substances.

# Why Not Broccoli? Answer- Dopamine

- This transformation is incentive salience. Incentive salience is guided by the neurotransmitter dopamine and is more than simply liking something. Now, most of us have had ice cream and the dopamine reward we get from eating it is familiar.
- If you try methamphetamine, the amount of dopamine reward is about 10 times greater than ice cream.
- If you are addicted to Methamphetamine, ice cream is no longer salient (important), unfortunately, nothing in real life will be as rewarding to your brain.



FEB 5 2013

THE PARAMOUNT

SPECIAL GUEST  
Andrew McMahon

TICKETS & INFO AT  
STOPPRESENTS.ORG

etc  
PRESENTS

FUN.

# Why Not Broccoli?

- If you eat ice cream for the first time, some dopamine is released in your brain and you like it.



admit it. you  
love me.

And then they hear it.....



# SUGAR ADDICTION

You eat an ice cream cone.



Massive release of dopamine in the brain.



You feel pleasure.



Brain is like "woah too much dopamine" so it turns off some receptors.



The next day, you eat another ice cream cone.



You don't feel the same pleasure because there are less dopamine receptors.



So you eat more ice cream to feel the same pleasure you felt the first time.



And the addiction begins.



- Addictive drugs produce long-lasting changes in brain organization
- The brain systems that are changed include those normally involved in the process of incentive motivation and reward.
- Addiction renders these systems hypersensitive (“sensitized”) to drugs and drug-associated stimuli
- These sensitized systems mediate a component of reward termed incentive salience or “wanting” (not pleasure or “liking”).

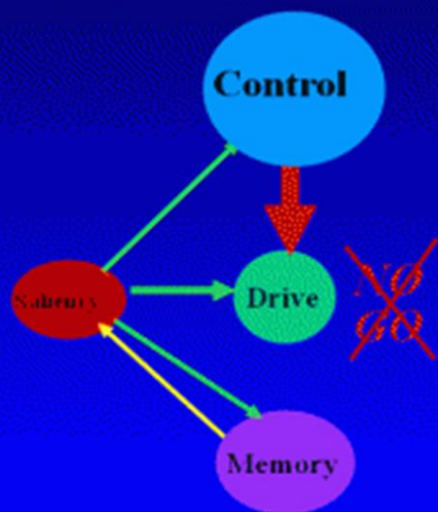
## Reward and Salience

- Addictions are in a sense “end-stage” diagnoses because at the time diagnosis is made potentially irreversible neuroadaptive changes have occurred—changes that were preventable at an early point of the trajectory of the illness.



## Why Can't Addicts Just Quit?

Non-Addicted Brain

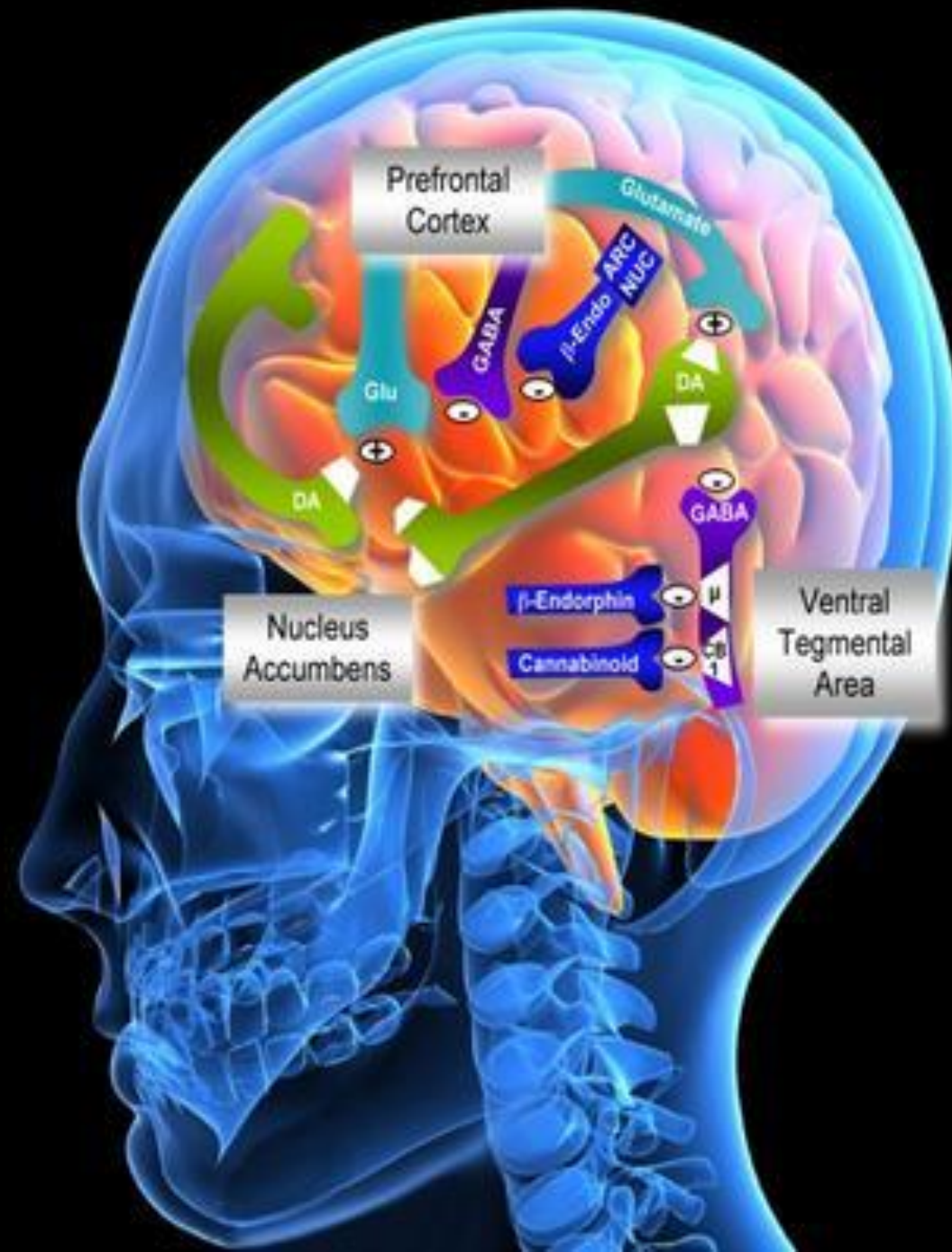


Addicted Brain

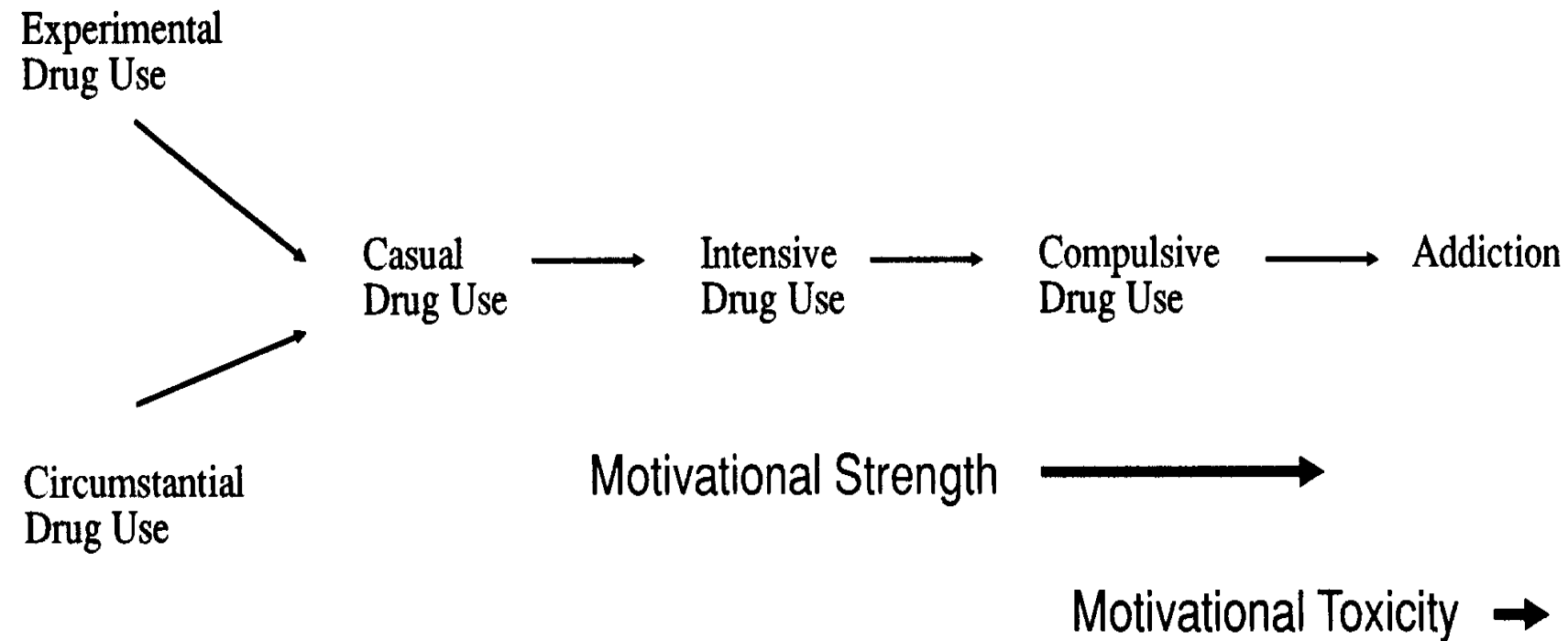


*Because Addiction Changes Brain Circuits*

NIDA



# Nature of Addiction - a continuum of use?



*However, addiction is more than mere drug use...*

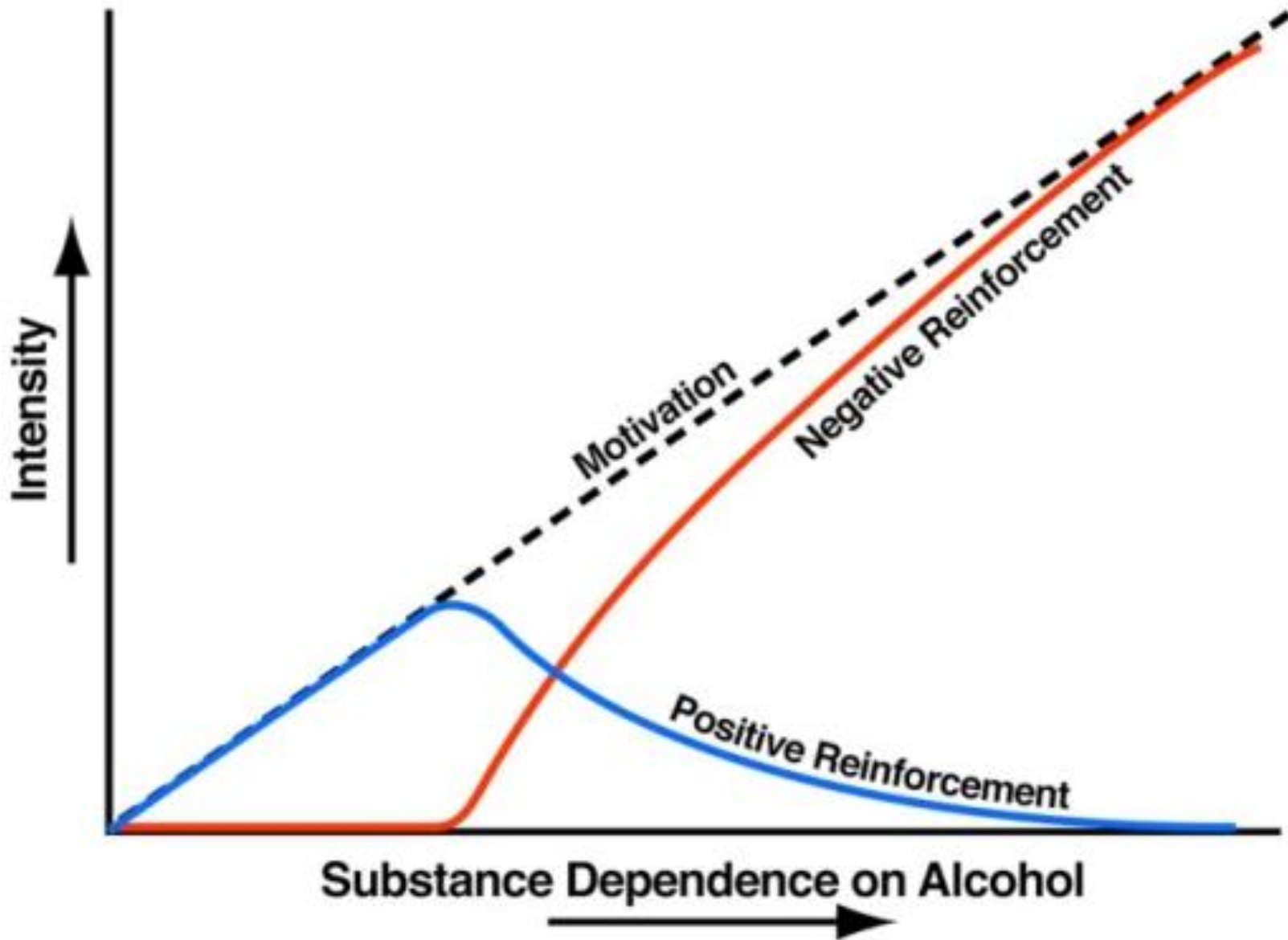
# Positive and Negative Reinforcement-



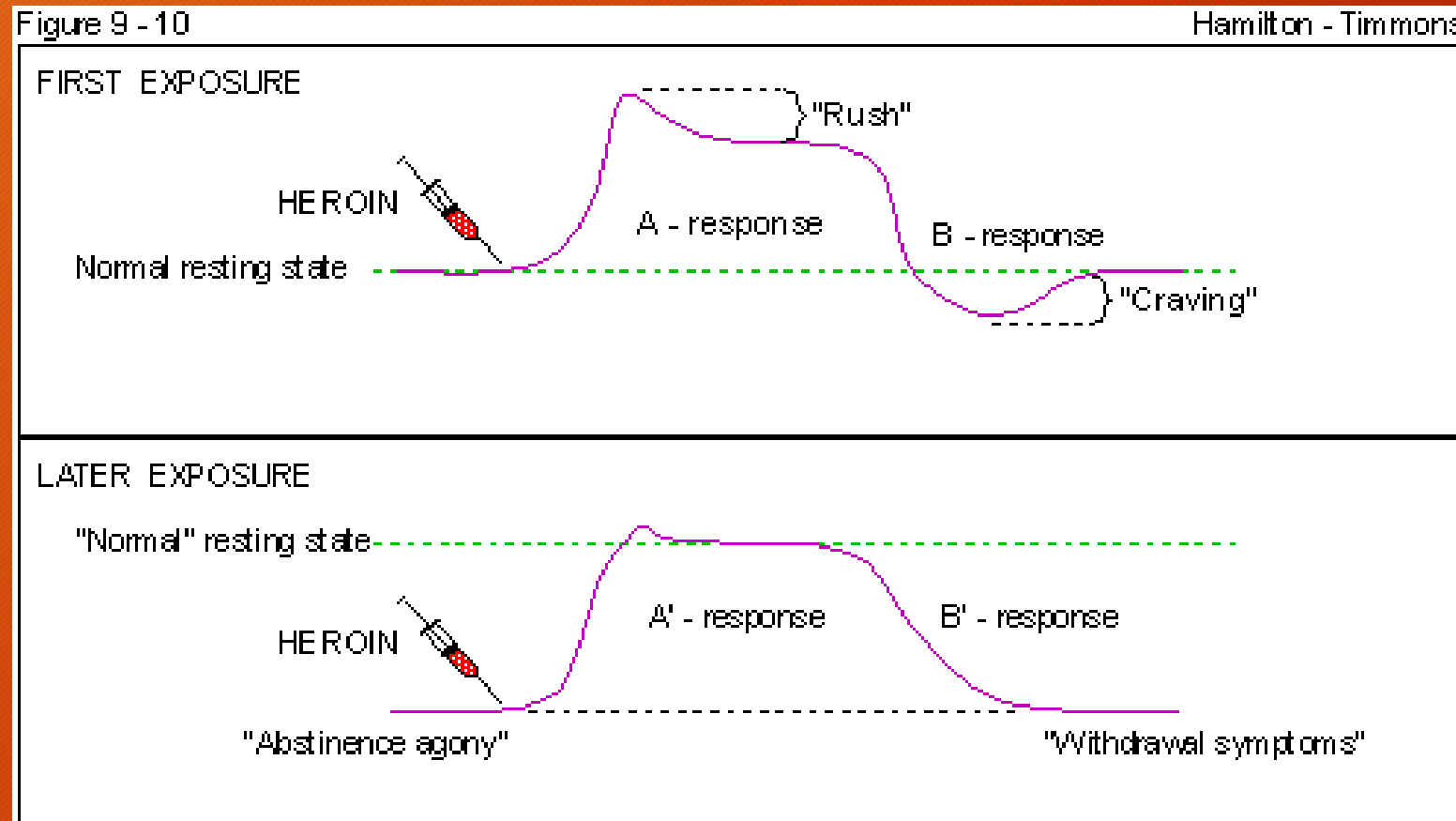
- Initial Use (for pleasure or pain relief)  
Positive Reinforcement – defined as the process by which presentation of a stimulus (drug) increases the probability of a response (non dependent drug taking paradigms-appropriate use, misuse, abuse).
- Negative Reinforcement (addiction)– defined as a process by which removal of an aversive stimulus (negative emotional state of drug withdrawal) increases the probability of a response (dependence-induced drug taking)



SCABS, HALLUCINATIONS, AND BODY SORES.  
THEN THINGS REALLY GO DOWNHILL.

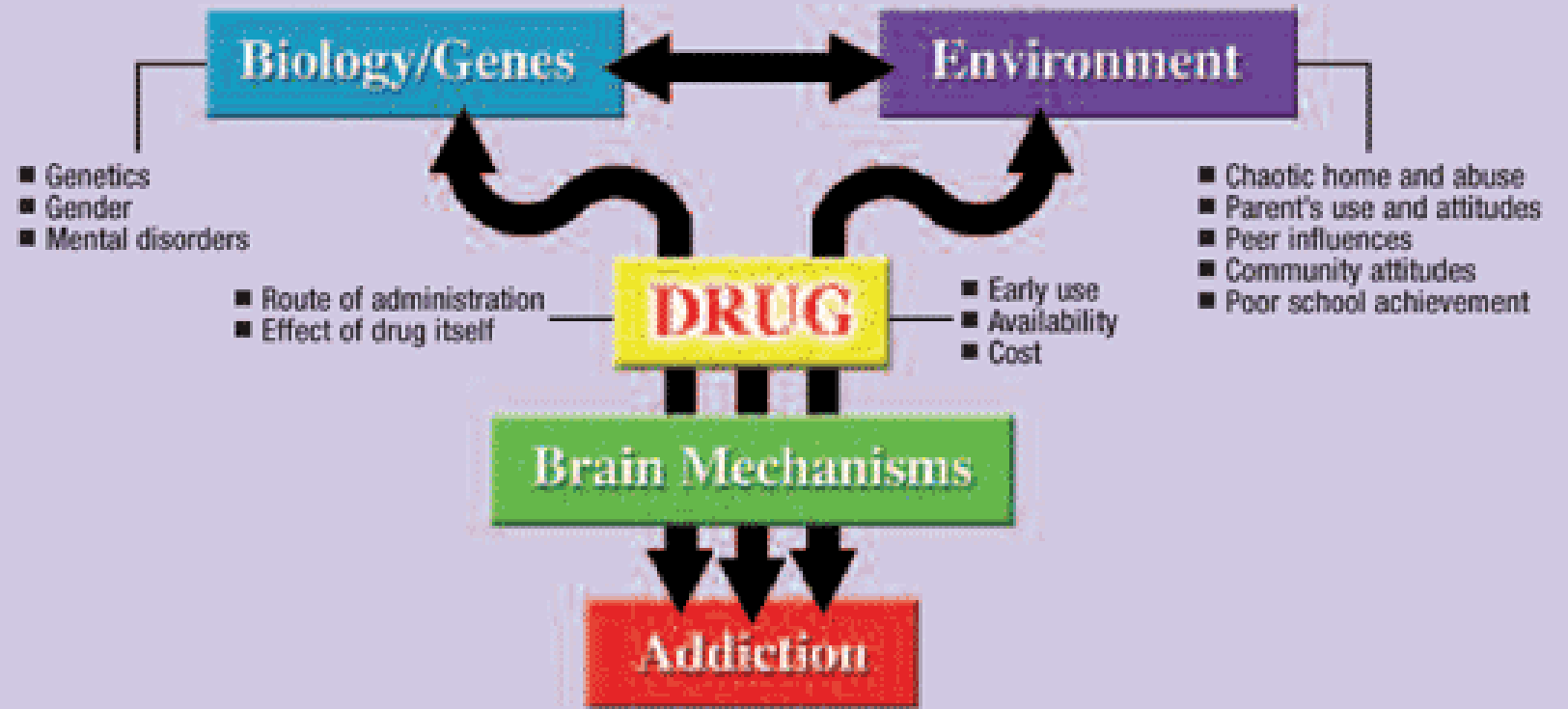


- Drug-use initially motivated by positive reinforcement
- Over time, tolerance develops to rewarding effects
- Abstinence leads to withdrawal
- Drug use ultimately maintained by negative reinforcement

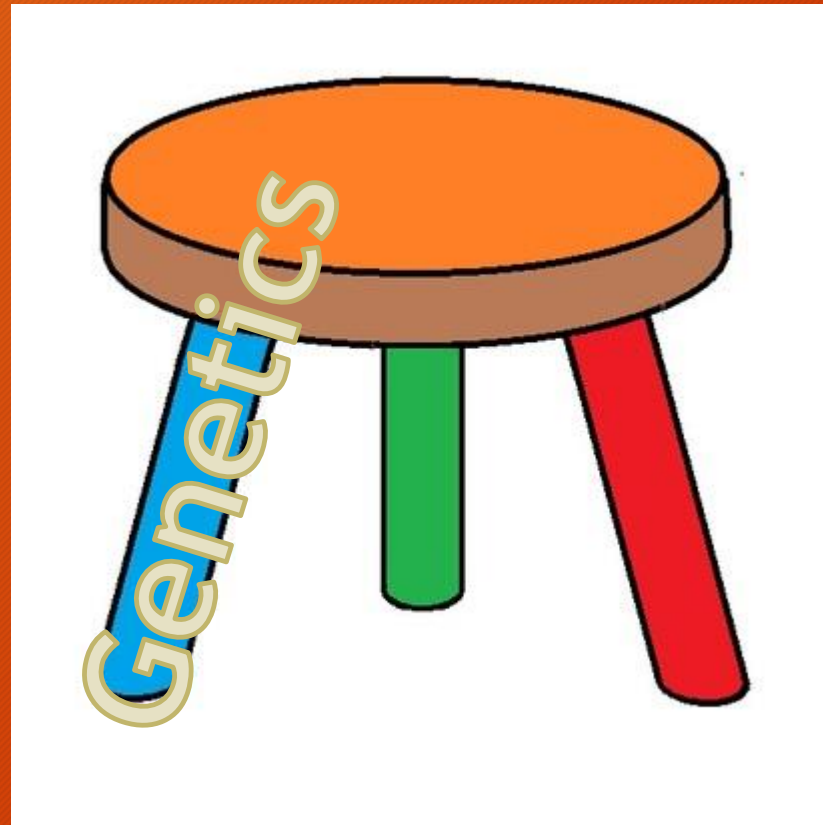




## RISK FACTORS



# First Leg Essential to all Addiction: Genetics



# General Population DSM 5

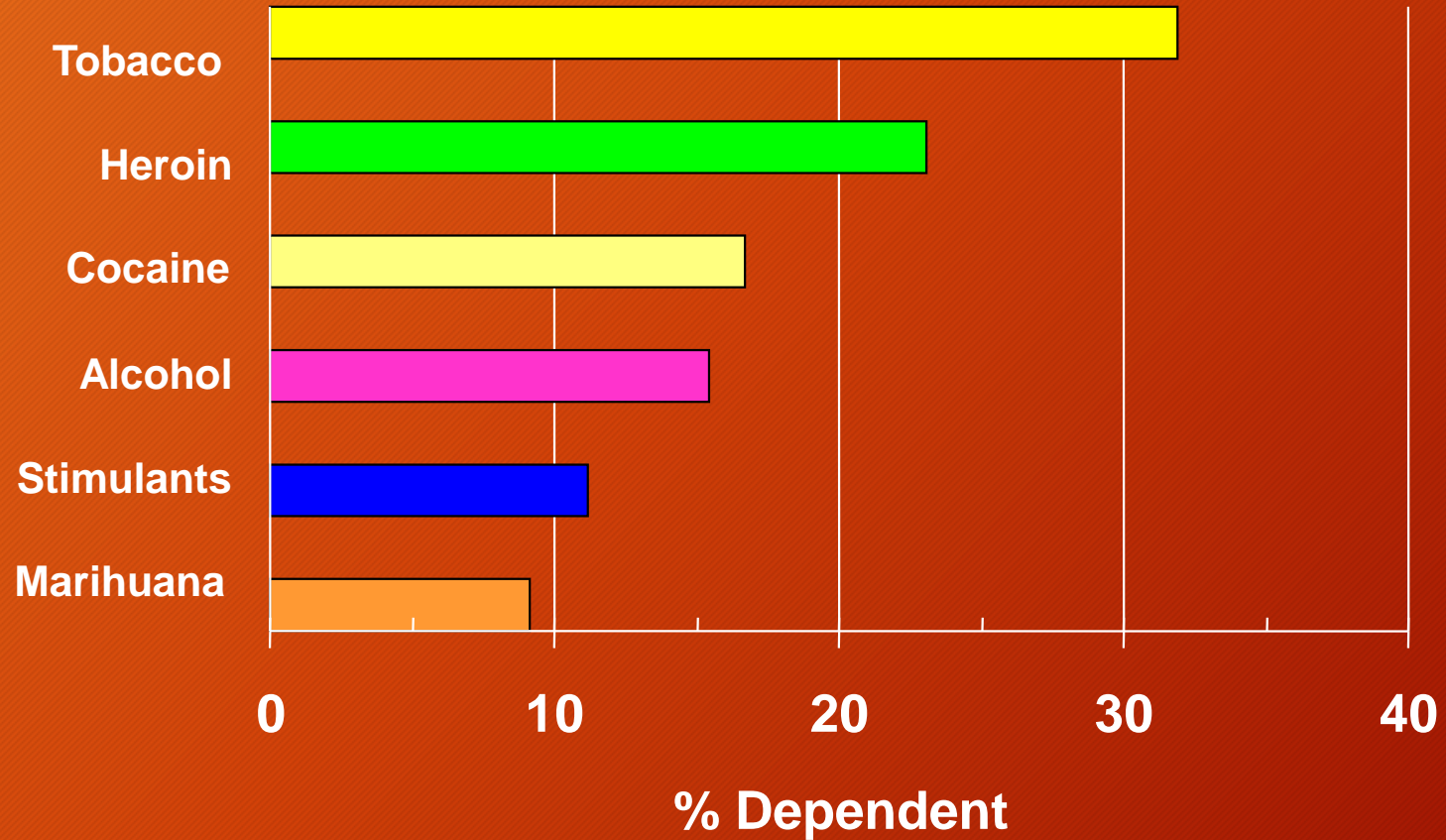
❖ Any Substance Use Disorder (excluding Tobacco)	
• 1 month	3.8 %
• 6 months	6.0 %
• Lifetime	35.0 %
❖ Alcohol Use Disorder	
• 1 month	2.8 %
• 6 months	4.7 %
• Lifetime	29.1 %
❖ Other Drug Use Disorder	
• 1 month	1.3 %
• 6 months	2.0 %
• Lifetime	5.9 %



# NSDUH 2013: Non-Medical Use Ages 12 & Older

Drug	Ever Used	Dependence
Tobacco	75.6%	24.1%
Cannabis	46.3	4.2
Cocaine	16.2	2.7
Stimulants	35.5	1.7
Anxiolytics	12.7	1.2
Hallucinogens	15.1	0.5
Analgesics	13.5	1.0
Inhalants	8.0	0.4
Heroin	1.8	0.3

# Drug Dependence Among Ever-Users



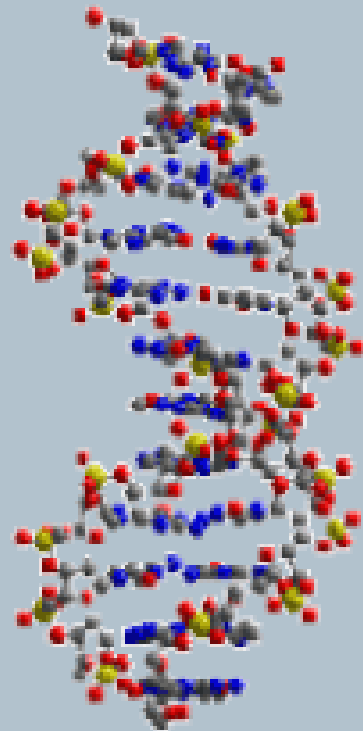
# Addiction, Like Cardiovascular Disease, Has Genetic Contributions

## Drug Abuse

CYP2A6 (nicotine metabolism) tobacco dependence

FAAH (endogenous cannabinoid regulator) problem drug use

Mu-opioid receptor in heroin addiction



## Cardiovascular Disease

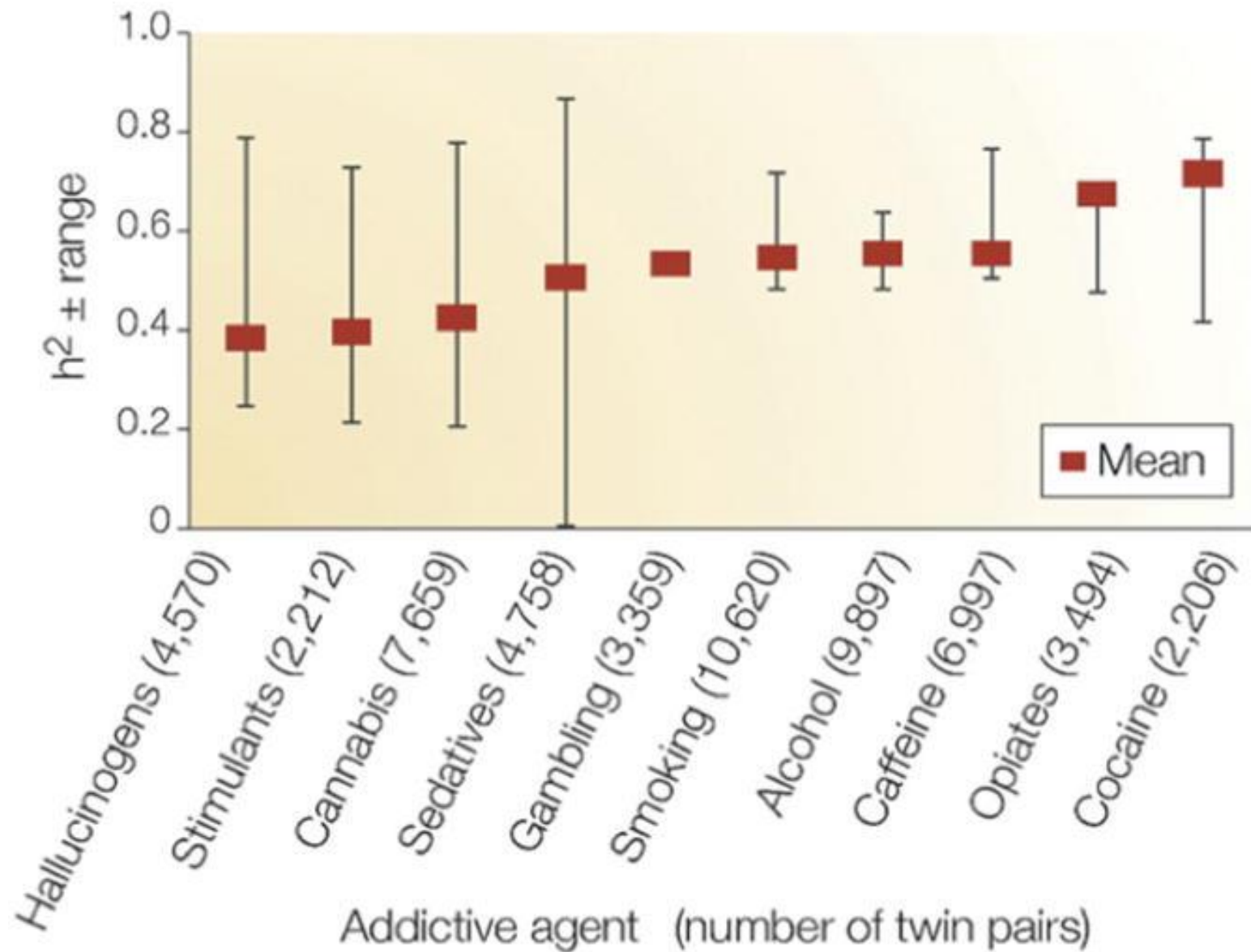
APO-E (Apolipoprotein E) coronary artery disease

LOX 1 (lectin-like oxidized low density lipoprotein receptor) coronary artery disease in Caucasian women

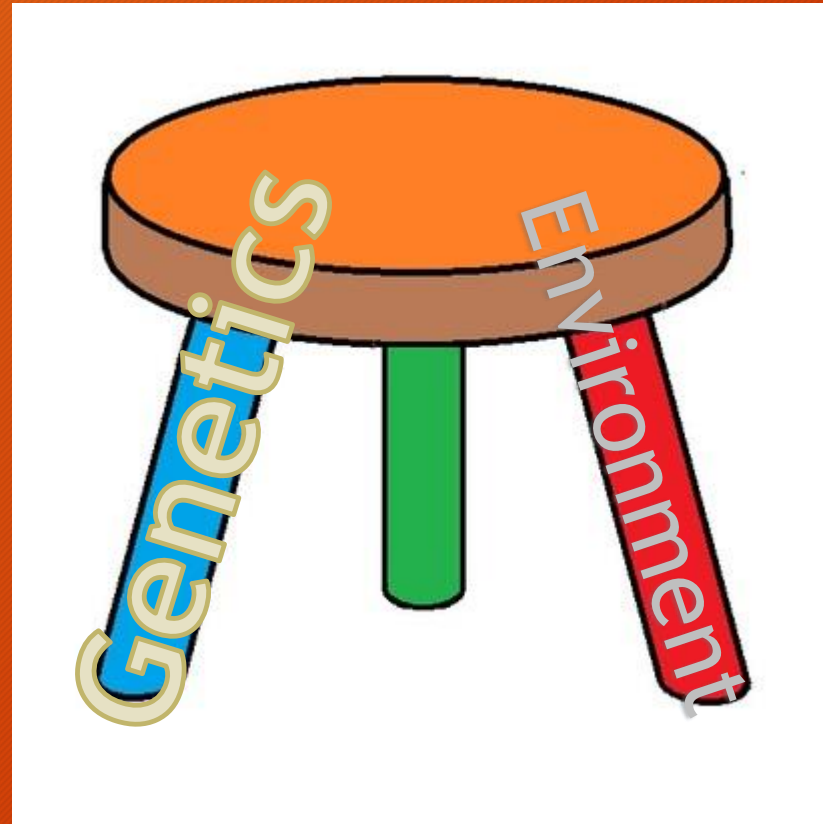


# Genetic Studies and Cocaine Addiction

- Genetic studies estimate that 65-78% of the vulnerability risk for cocaine dependence is heritable (Kendler et al 2000; Kendler and Prescott 1998);
- COMT gene breaks down Dopamine, Norepinephrine and Serotonin. VAL/VAL combination breaks down these neurotransmitters most rapidly.
- VAL/VAL is associated with cocaine addiction, heroin addiction, ADHD, aggression, bipolar disorder and Parkinsons Disease.



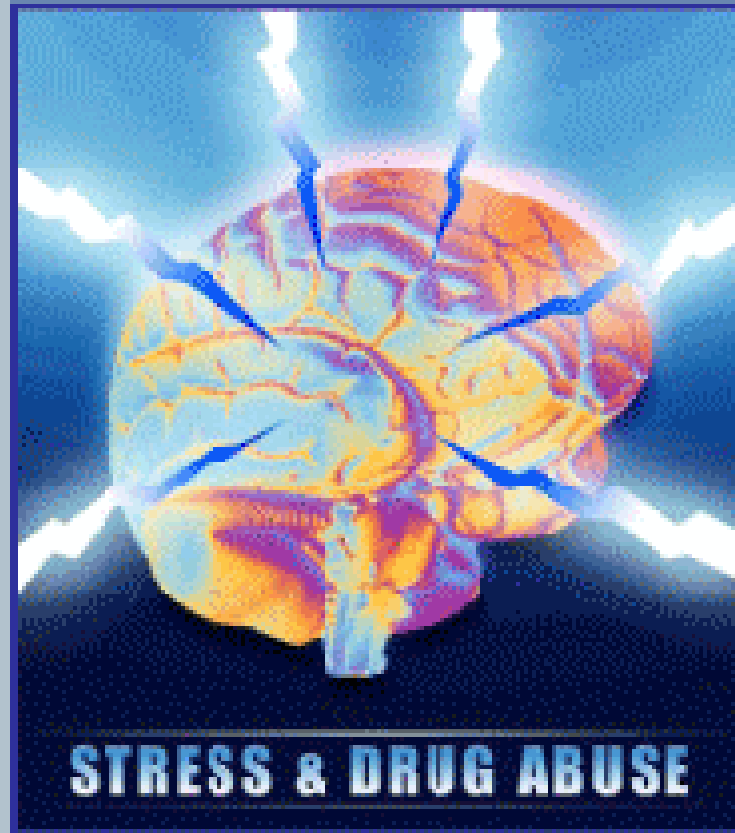
# Second Leg Essential to all Addiction: Environment



## Addiction, Like **Cardiovascular Disease**, Has Environmental Contributions

### **Drug Abuse:**

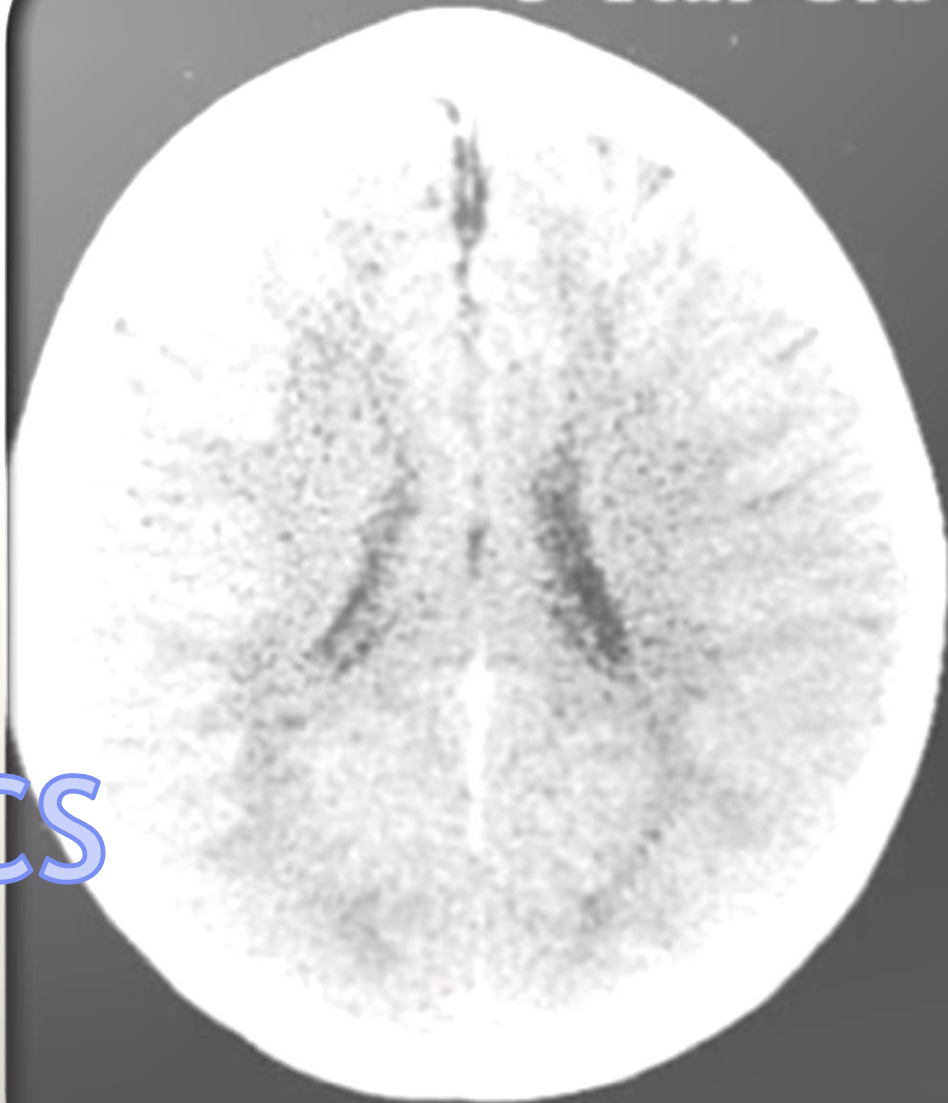
- Early Physical or Sexual Abuse
- Witnessing Violence
- Stress
- Peers Who Use Drugs
- Drug Availability



### **Cardiovascular Disease:**

- Obesity
- Sedentary Lifestyle
- Stress
- Drug and Alcohol Abuse

### 3-Year-Old Children



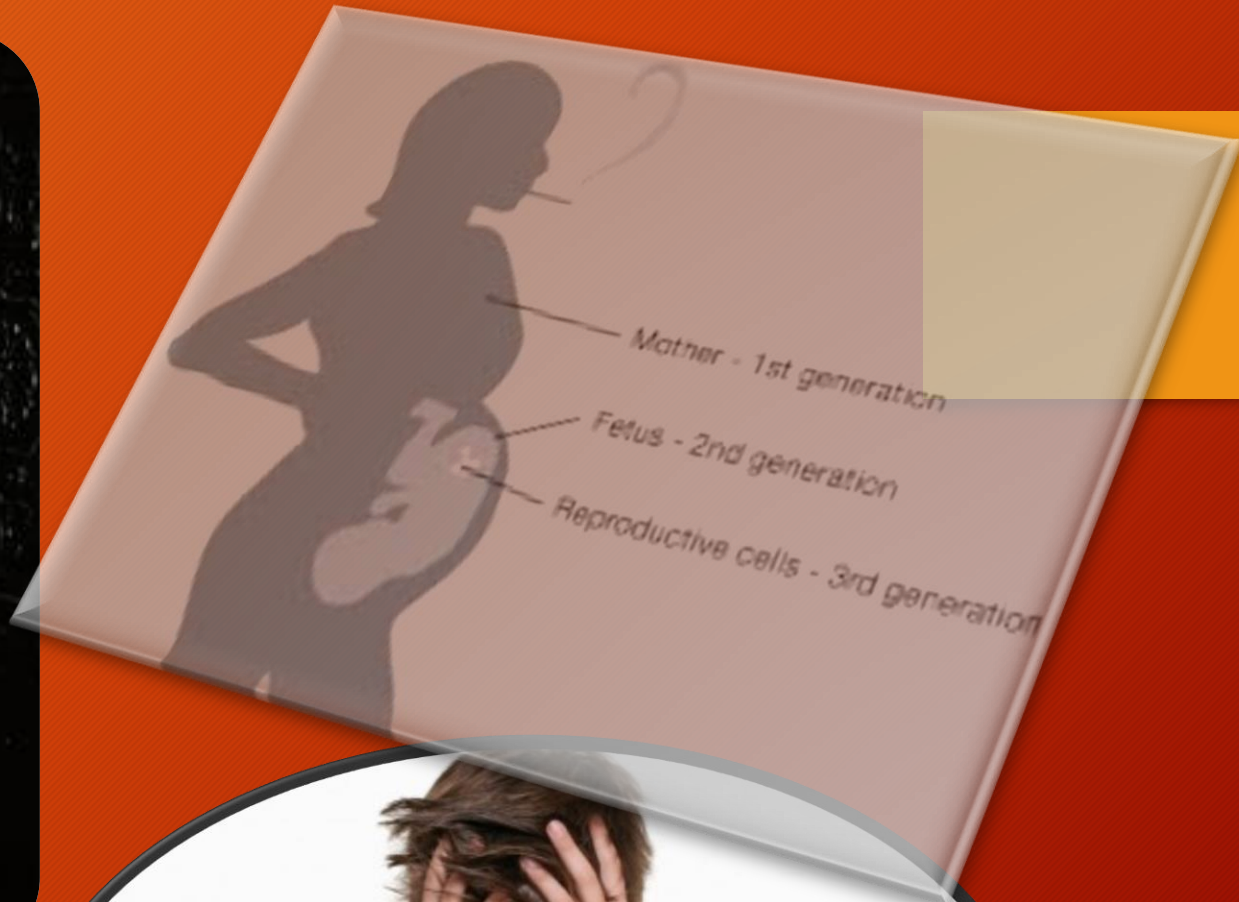
Normal



Extreme Neglect

EPIGENETICS  
or  
Environment



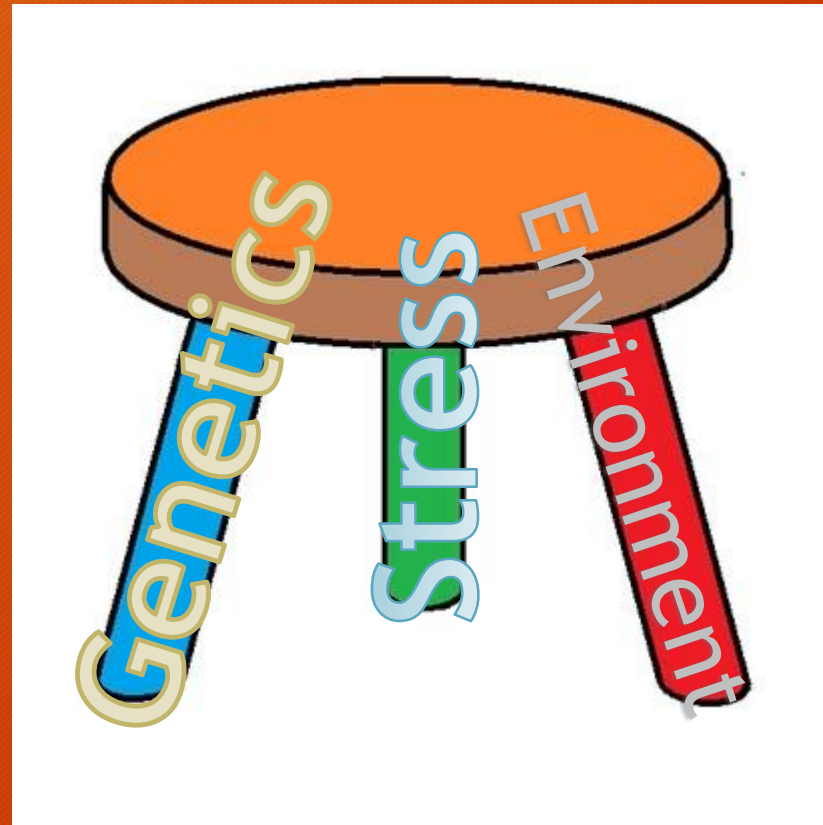


Source: Randy Jirtle, Ph.D., Duke University Medical Center. Used with permission.

These inbred mice are genetically identical. They are each about a year old and both are male. Their different characteristics result from differences in the epigenome. The mother of the mouse on the left received a normal mouse diet. The mother of the mouse on the right received a diet supplemented with genistein, the phytoestrogen found in soy products. Genistein increases the incidence of brown offspring by altering the epigenome rather than by mutating the genome — an example of nature via nurture.



# Third Leg Essential to all Addiction: Stress



# *Why Do People Take Drugs in The First Place?*

## To Feel Good

### **To have novel:**

feelings  
sensations  
experiences

**AND**

to share them

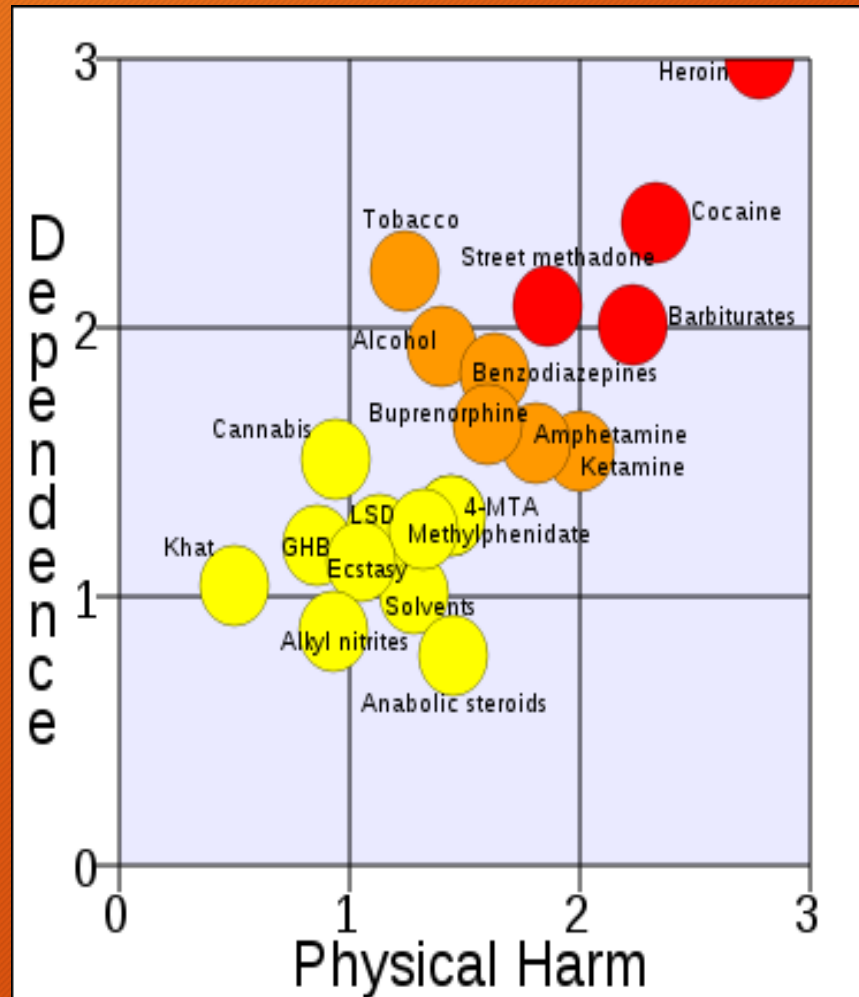


## To Feel Better

### **To lessen:**

anxiety  
worries  
fears  
depression  
hopelessness

# Heroin, Cocaine, Nicotine and Alcohol



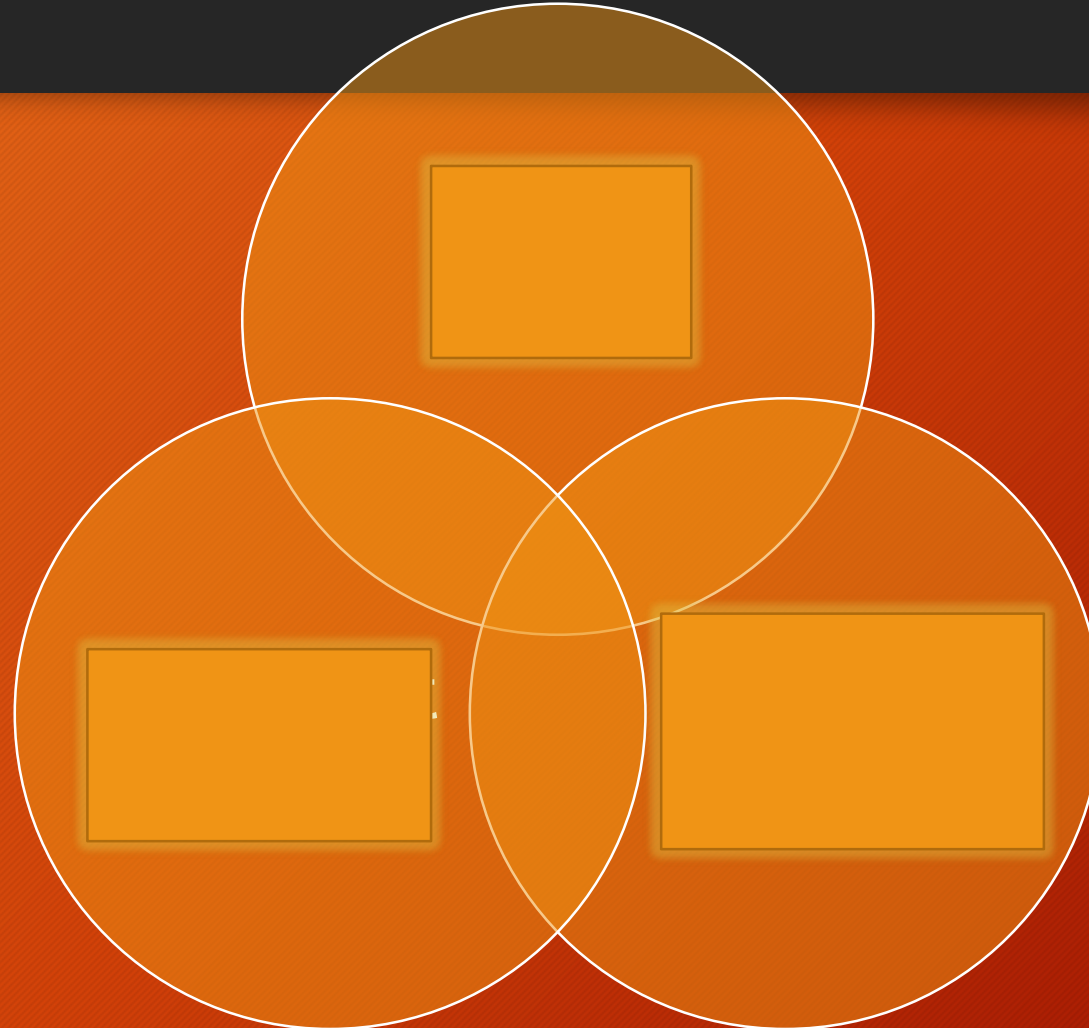
- Profoundly alter the Stress Response
- There are Acute Effects with use and opposite effects with withdrawal.
- These short acting substances cause the brain to be in constant flux creating a very unstable hormonal environment.

# Case Study: Megan

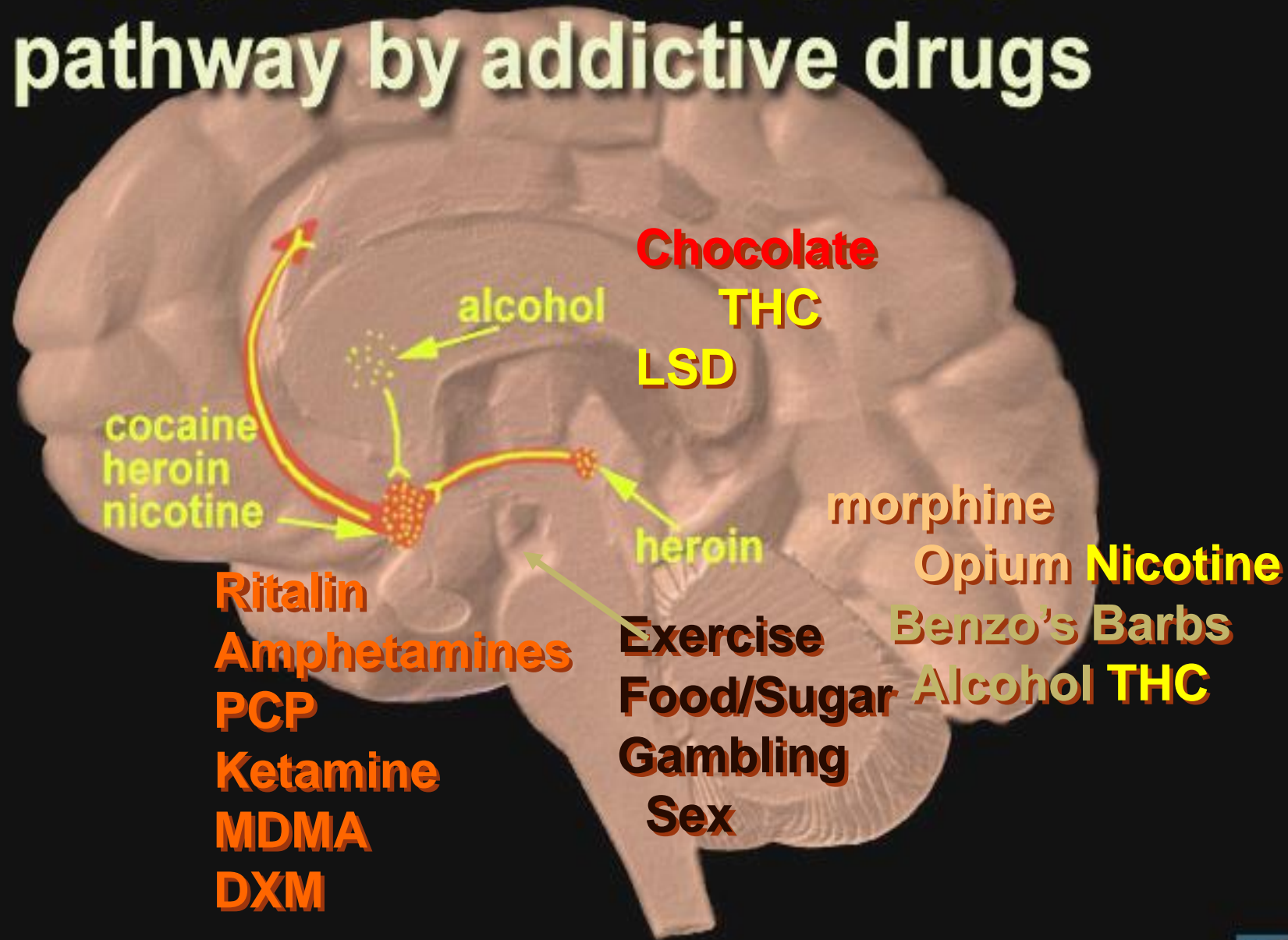
- Megan is a 45 year old woman, she is recently divorced, has 3 children and works 12 hour shifts as an ER Nurse
- Strong Family History of Addiction in both of her parents, so Megan vowed never to use drugs or alcohol
- Megan has some financial stress due to divorce
- Children are acting out at school and her oldest son has been caught stealing at the local convenience store
- Megan hurt her back at work.....Doctor prescribed Opiates



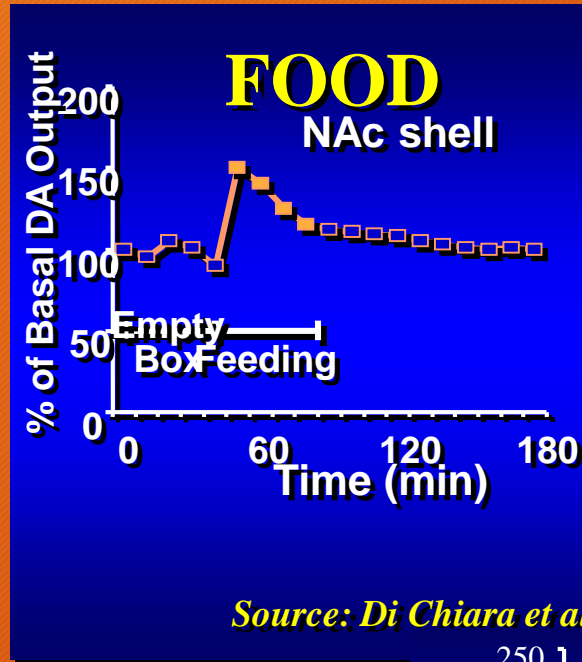
# Megan's The Three Legged Stool:



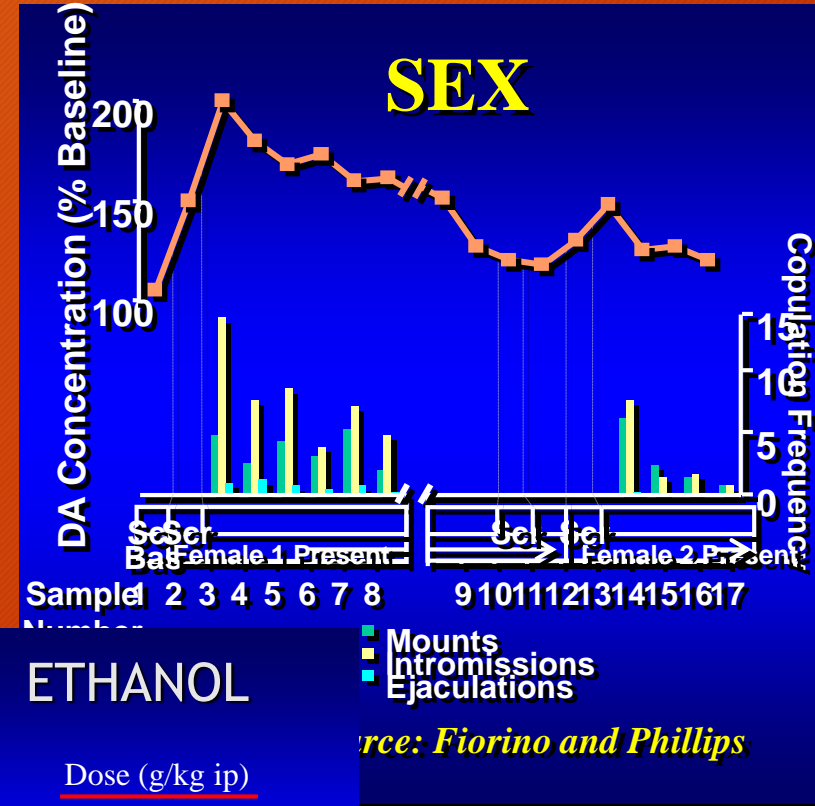
# Activation of the reward pathway by addictive drugs



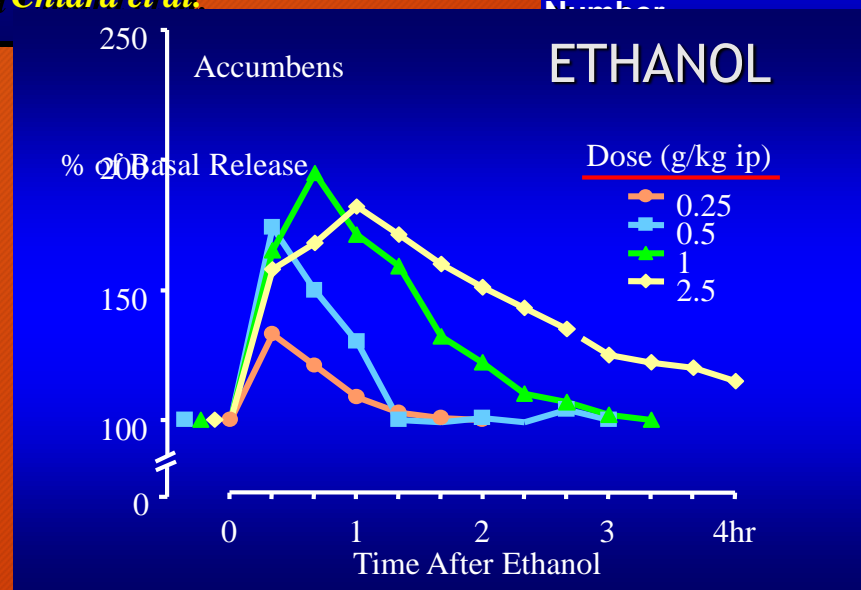
# Natural Rewards Elevate Dopamine Levels



Source: Di Chiara et al.

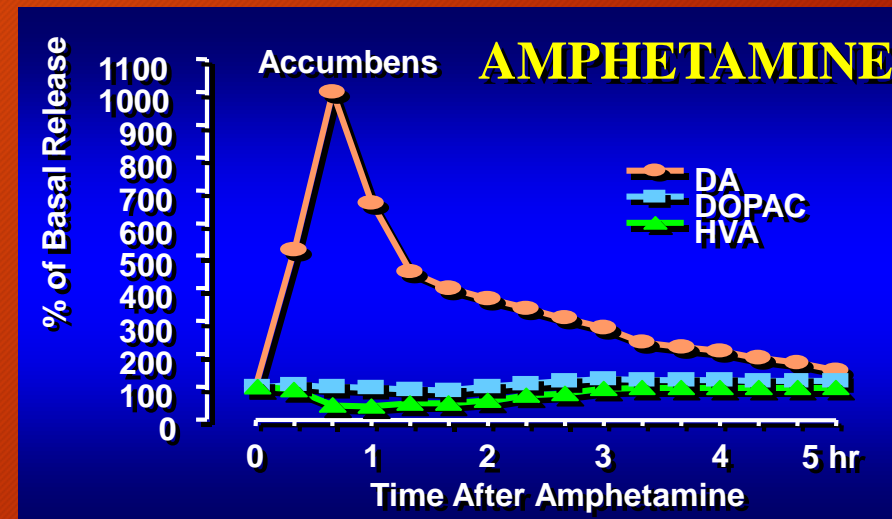
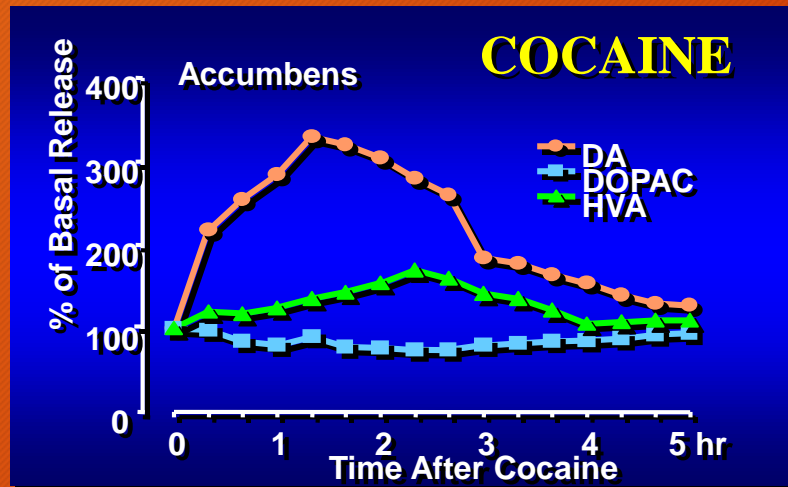
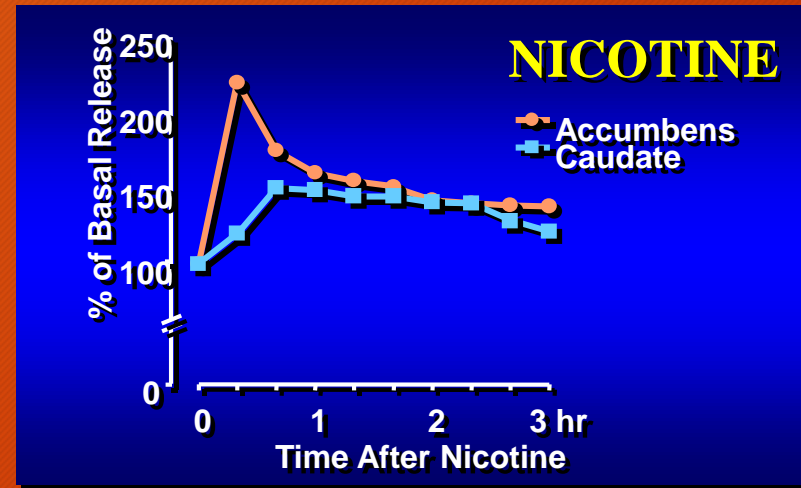
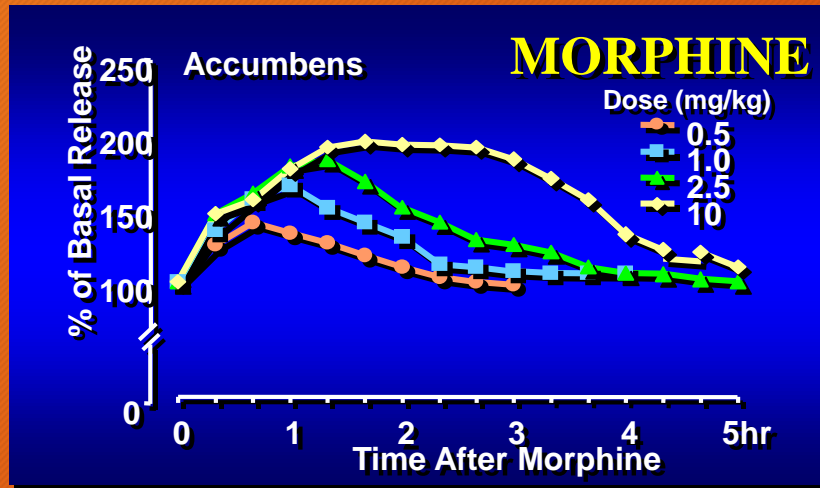


Source: Fiorino and Phillips

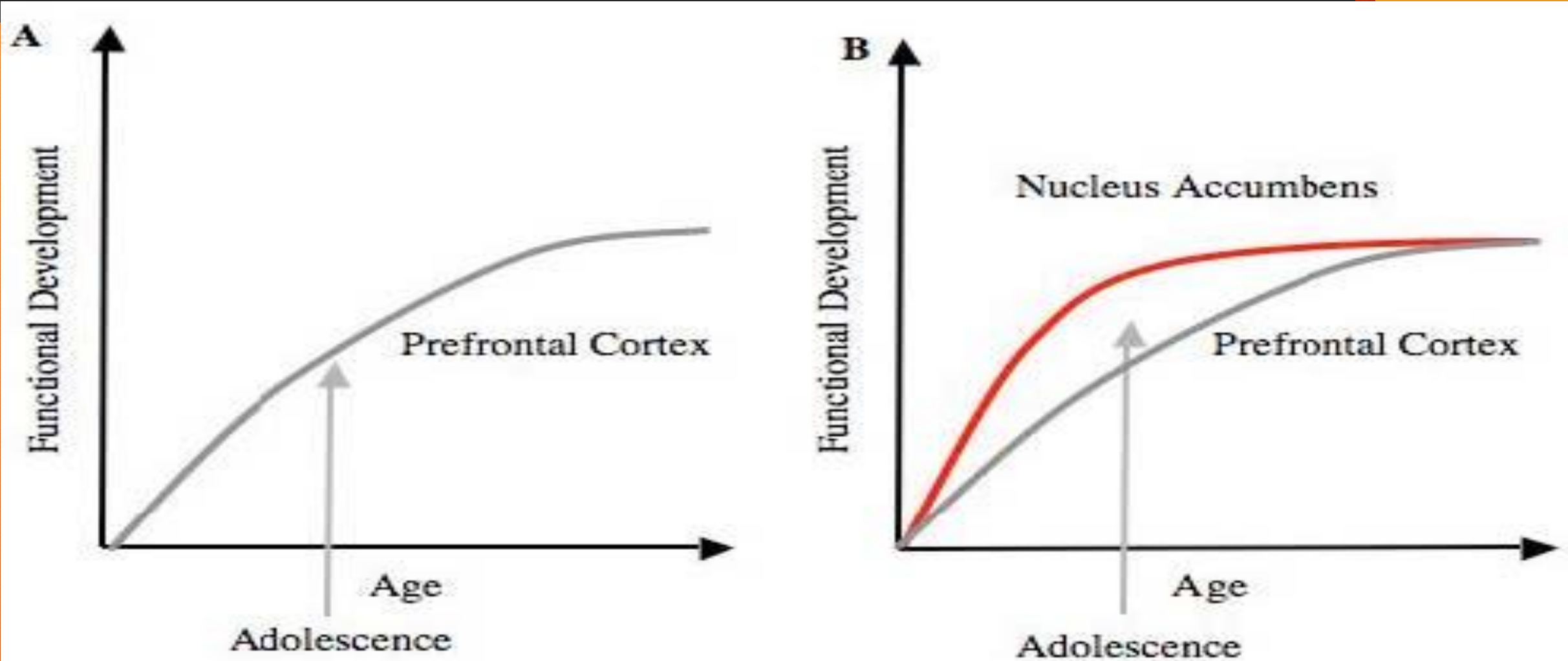




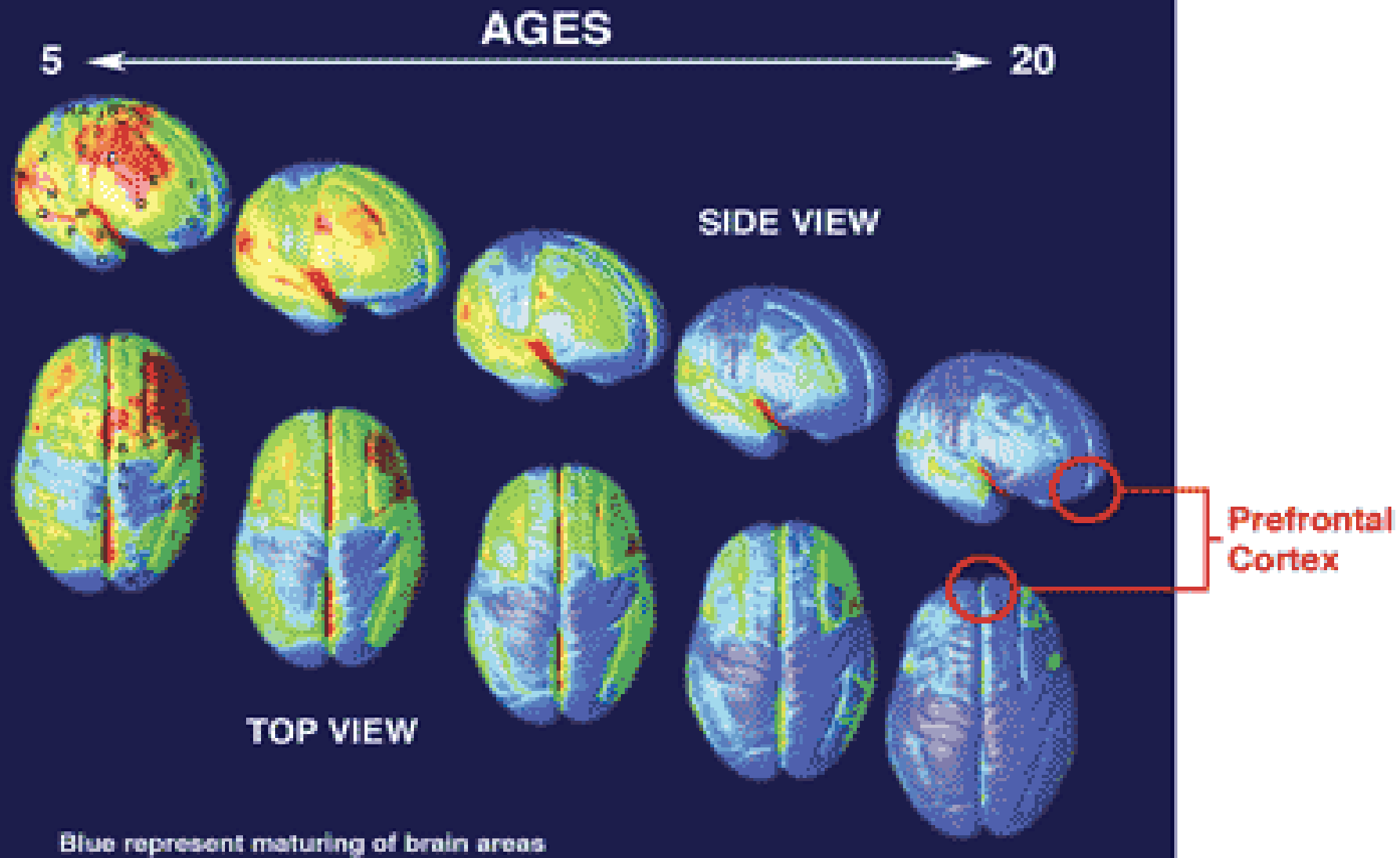
# Effects of Drugs on Dopamine Levels



# What causes Adolescents to experiment-role of early development of the Nucleus Accumbens- seek out exciting things

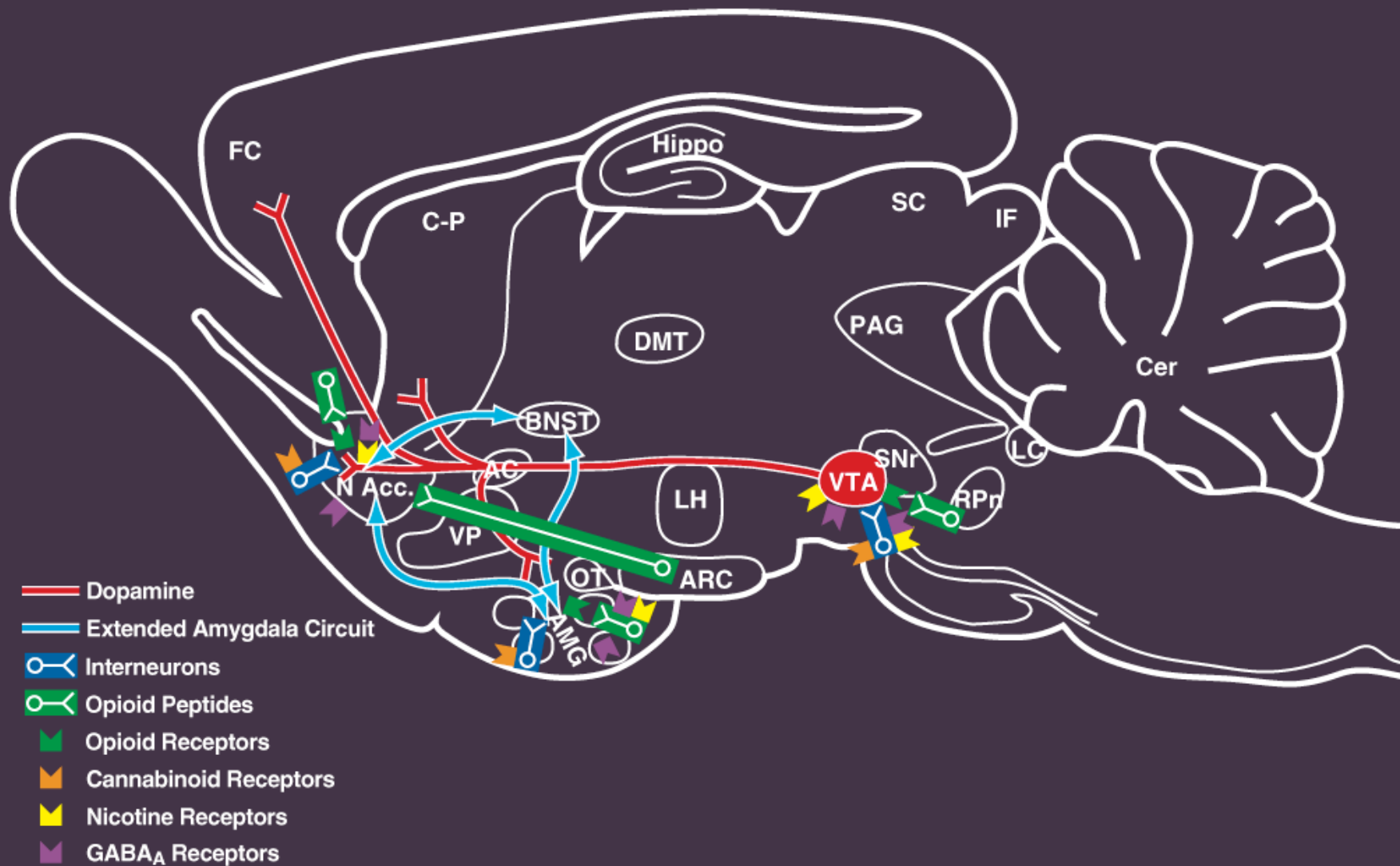


# IMAGES OF BRAIN DEVELOPMENT IN HEALTHY CHILDREN AND TEENS (AGES 5-20)

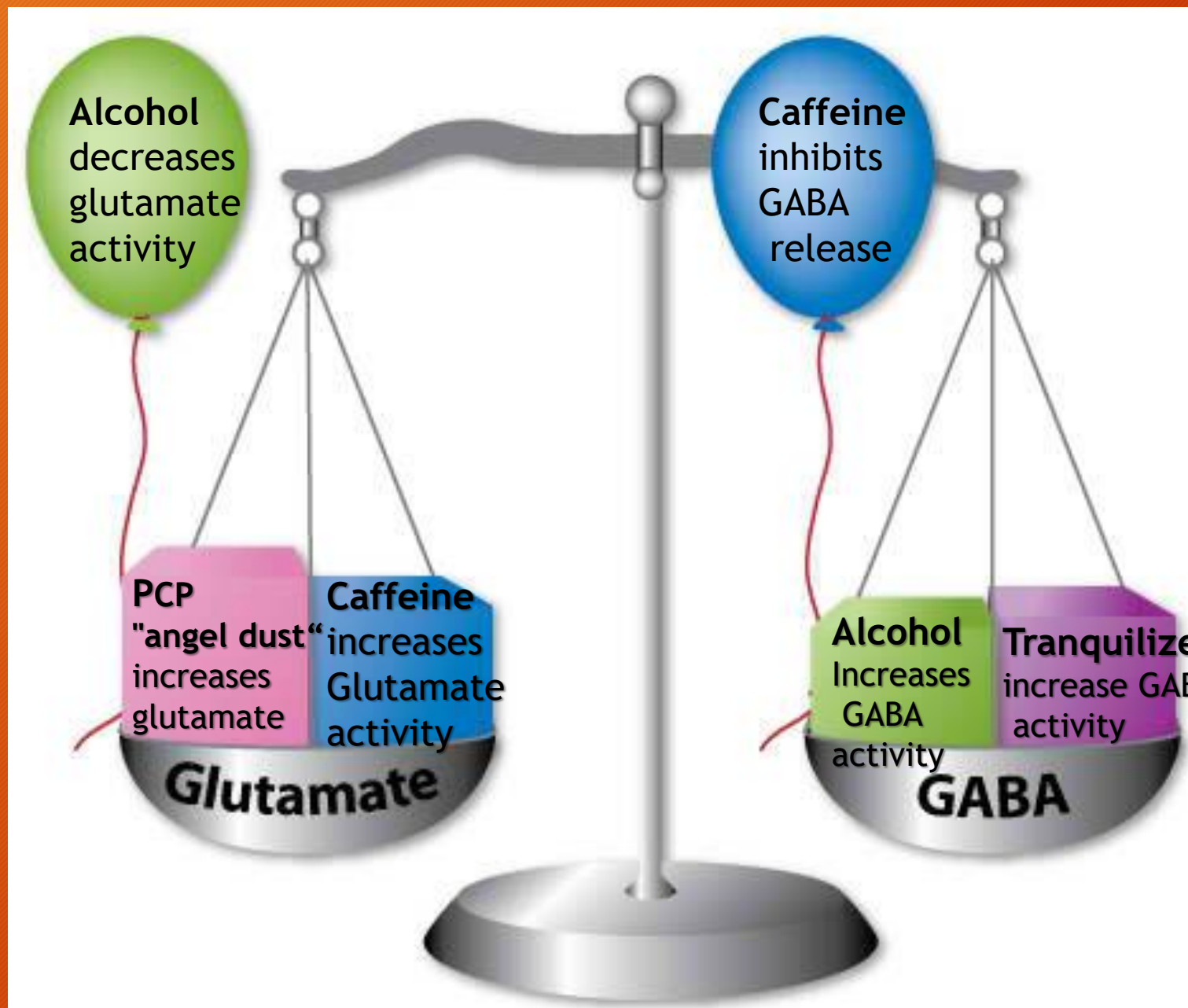


Blue represent maturing of brain areas

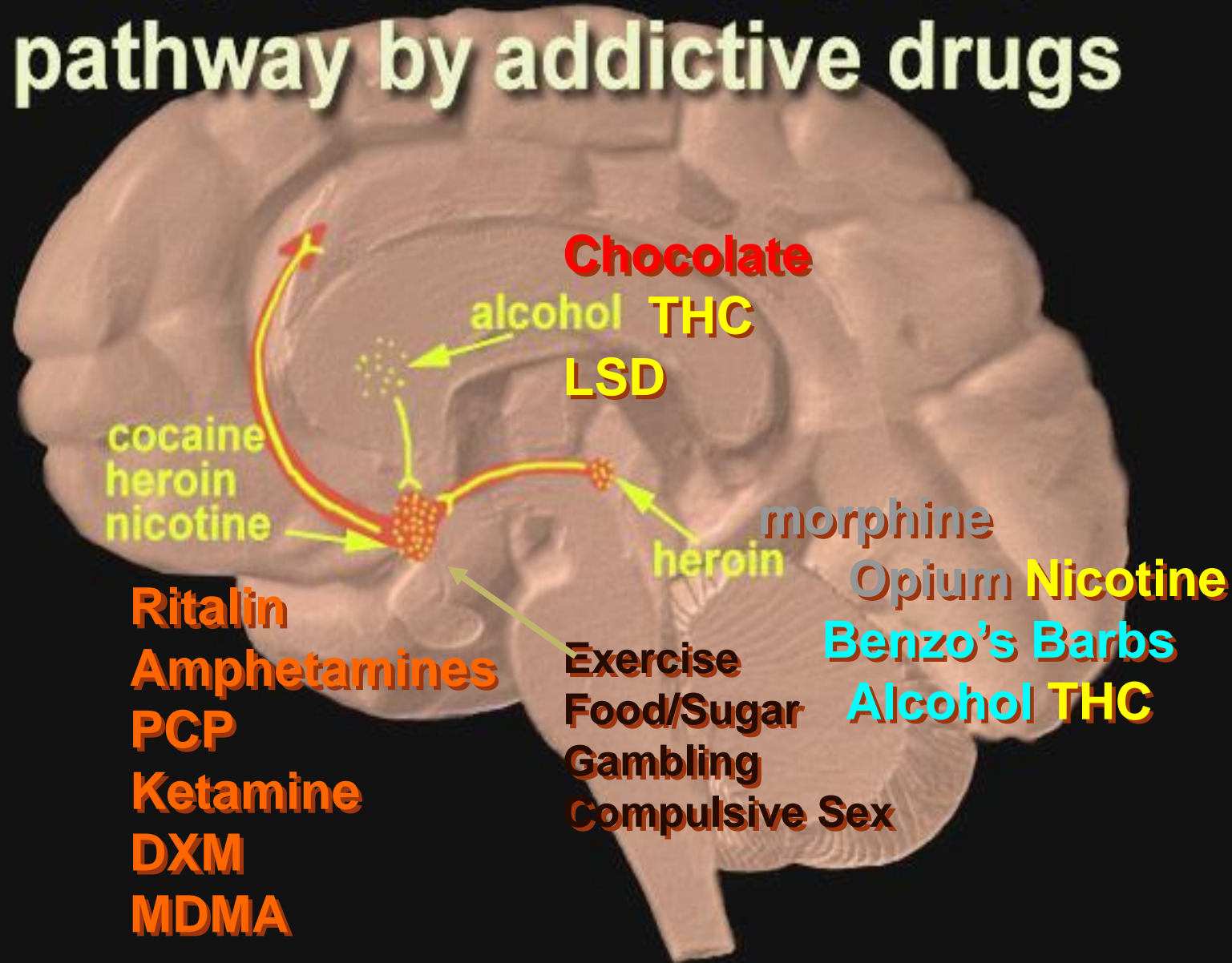
# Neurochemical Circuitry in Drug Reward



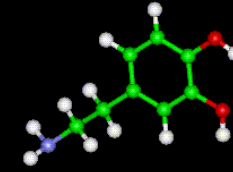
From: Koob GF, Clin Neurosci Res, 2005, 5:89-101.



# Activation of the reward pathway by addictive drugs



# Dopamine



Found widely in many areas of the Brain

Reinforcing effects of Drugs of abuse

Effects immediate pleasure centers

Lack of D2/5HT feedback loop results in the disease of Addiction

# Dopamine Dysfunction

- Dopamine Feedback loop- Normal Brain





# Dopamine Dysfunction

- Dopamine Brain Diseases: Schizophrenia

Dopamine produced



Too Much  
Dopamine:  
hallucinations,  
paranoia

# Dopamine Dysfunction

- Dopamine Brain Diseases: Parkinson's Disease



# Dopamine Dysfunction

- Dopamine Brain Diseases: Addiction

Dopamine produced



No Feedback:  
Dopamine production  
continues

*\*a little is good, more is better*

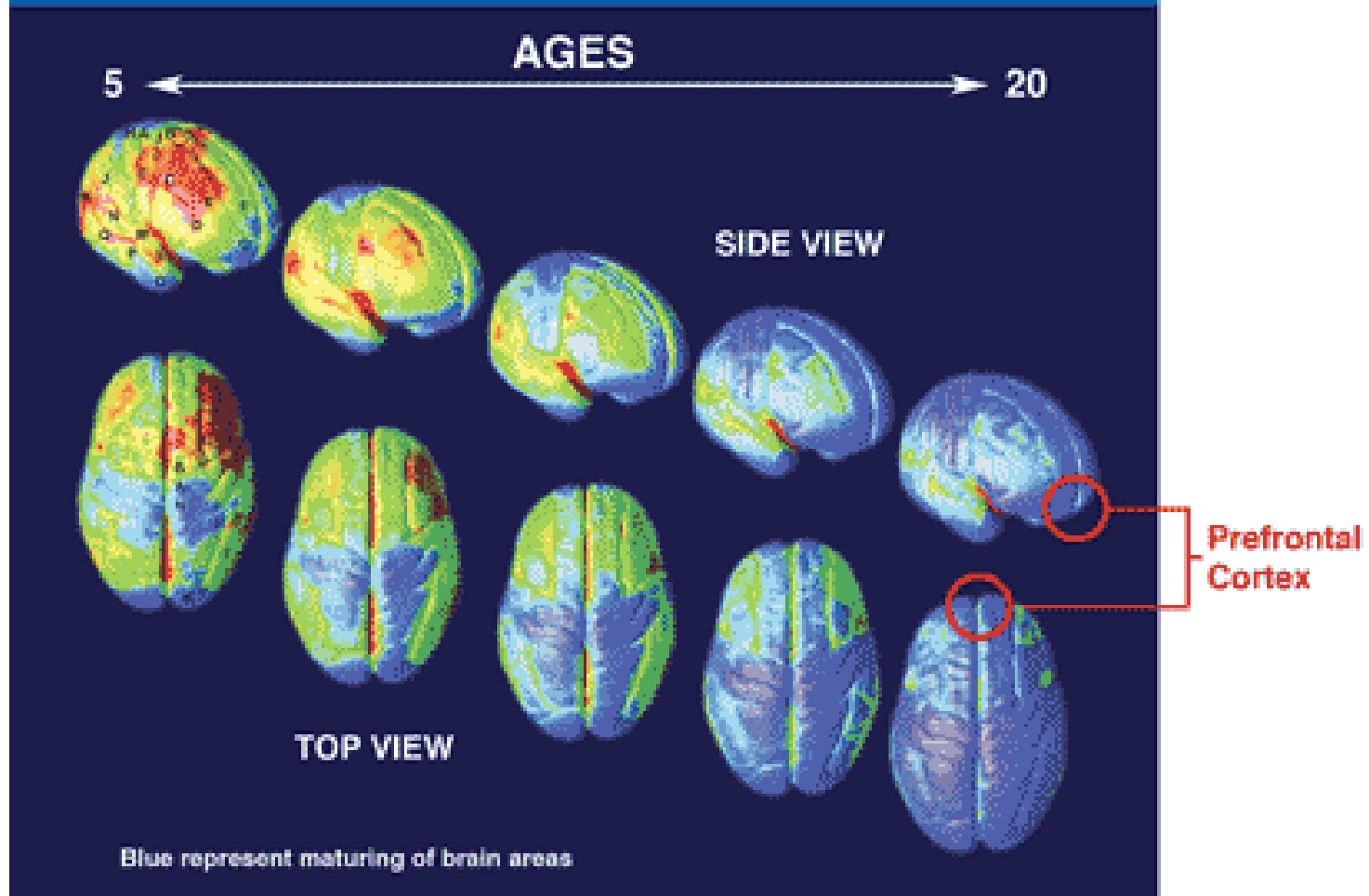
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# Cognitive Impairment



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



Source: Copyright PNAS ;101(21):8174-9, 2004

# Brain: Most Complex Organ

- 100 Billion Neurons
- 1,000,000,000,000,000 connections in your brain
- 2% of body's weight
- Uses 20-30% of the total calories consumed

I AM THE  
LEFT BRAIN

Decisions!  
011001011 LOGIC

Accurate  
ANALYTIC

REASON  
1 2 3 4 5 6 7 8 9  
PRACTICAL  
Strategic

CONTROL

SCIENCE  
Realistic  
PRACTICAL  
VIVID



I AM the  
Right Brain!

YOU LOVE LOVE LOVE  
that Art  
Betty

FREE DOM

Passion  
vivid

creative

YEARNING

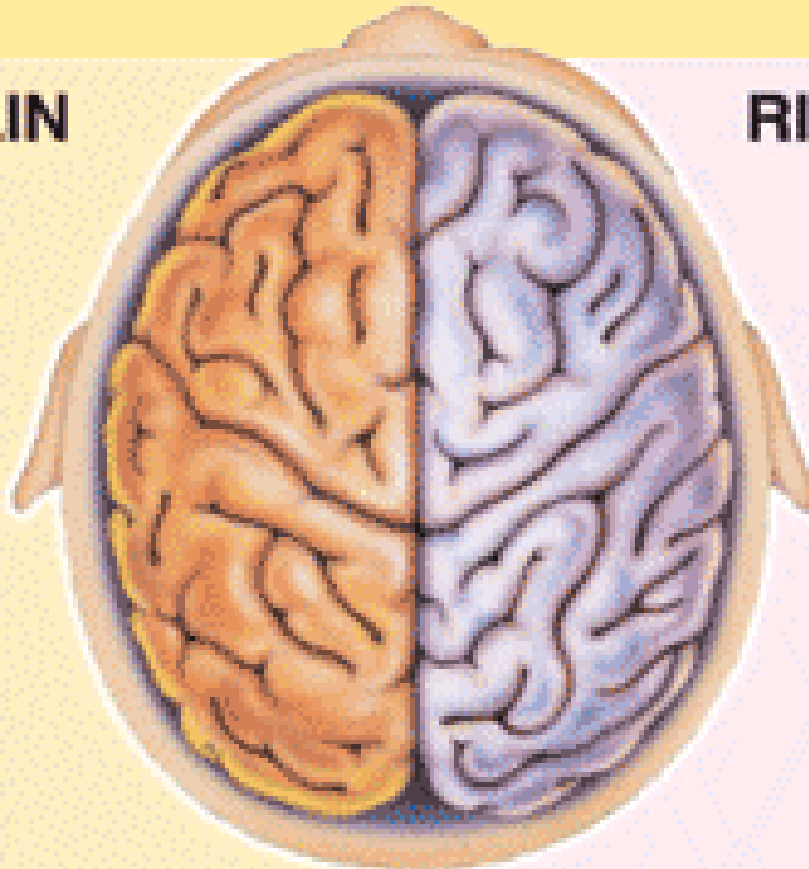
PEACE



# We can divide the brain in a number of ways

## LEFT BRAIN

LOGIC  
ANALYSIS  
SEQUENCING  
LINEAR  
MATHEMATICS  
LANGUAGE  
FACTS  
THINK IN WORDS  
WORDS OF SONGS  
COMPUTATION



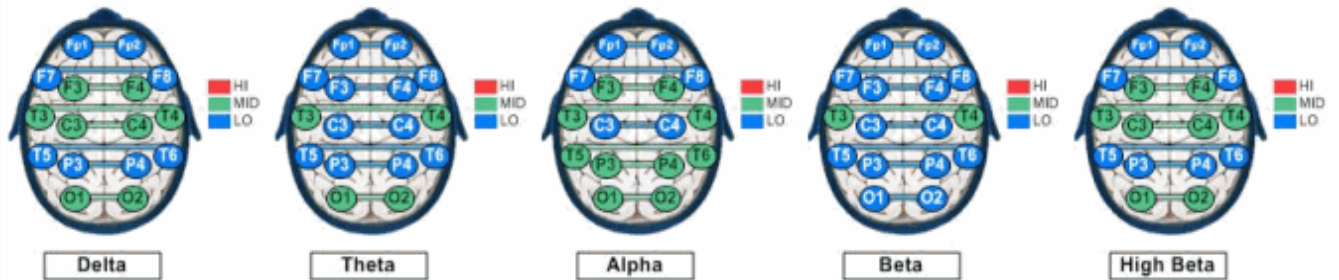
## RIGHT BRAIN

CREATIVITY  
IMAGINATION  
HOLISTIC THINKING  
INTUITION  
ARTS (Motor skill)  
RHYTHM (Beats)  
NON-VERBAL  
FEELINGS  
VISUALISATION  
TUNE OF SONGS  
DAYDREAMING

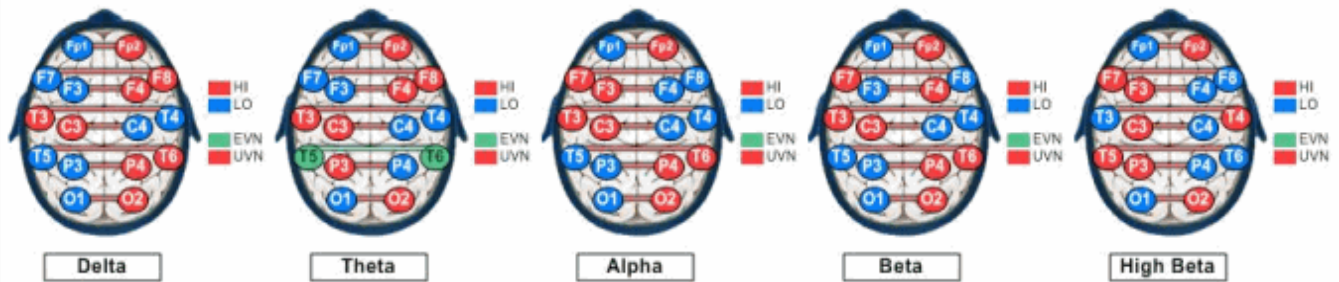
### Dominant Frequency



### Inter-Connectivity



### Asymmetry



## Executive Center

*"The Thinking Brain"*

Developmental shifts around ages 5-6, 11 & 15.  
Handles logic, empathy compassion, creativity,  
self-regulation, self-awareness, predicting,  
planning, problem-solving, attention.

**PREFRONTAL  
CORTEX**

**LIMBIC  
SYSTEM**

## Emotional Center

*"The Emotional Brain"*

Developmental focus is during  
ages 0-5. Processes emotions,  
memory, response to stress,  
nurturing, caring, separation  
anxiety, fear, rage, social  
bonding and hormone control.

**REPTILIAN  
BRAIN**

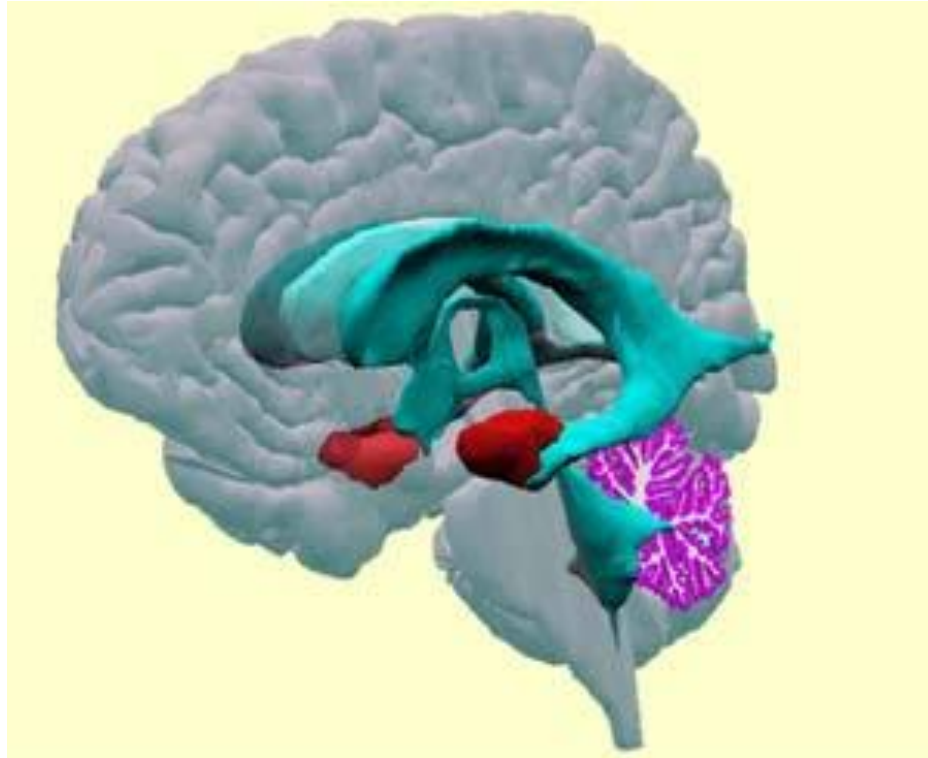
## Survival Center

*"Fight, Flight or Freeze"*

Developed at birth. Regulates autonomic  
functions: breathing, digestion, heart rate,  
sleep, hunger, instinctual behaviors &  
behaviors that sustain life.

# Reptilian Brain

- Basic Survival Brain
- Developed at Birth
- Not under conscious control
- Reward Center: Part of the brain where addiction lives
- Burglar Alarm System to keep us safe



**Amygdala= Greek for Almond**

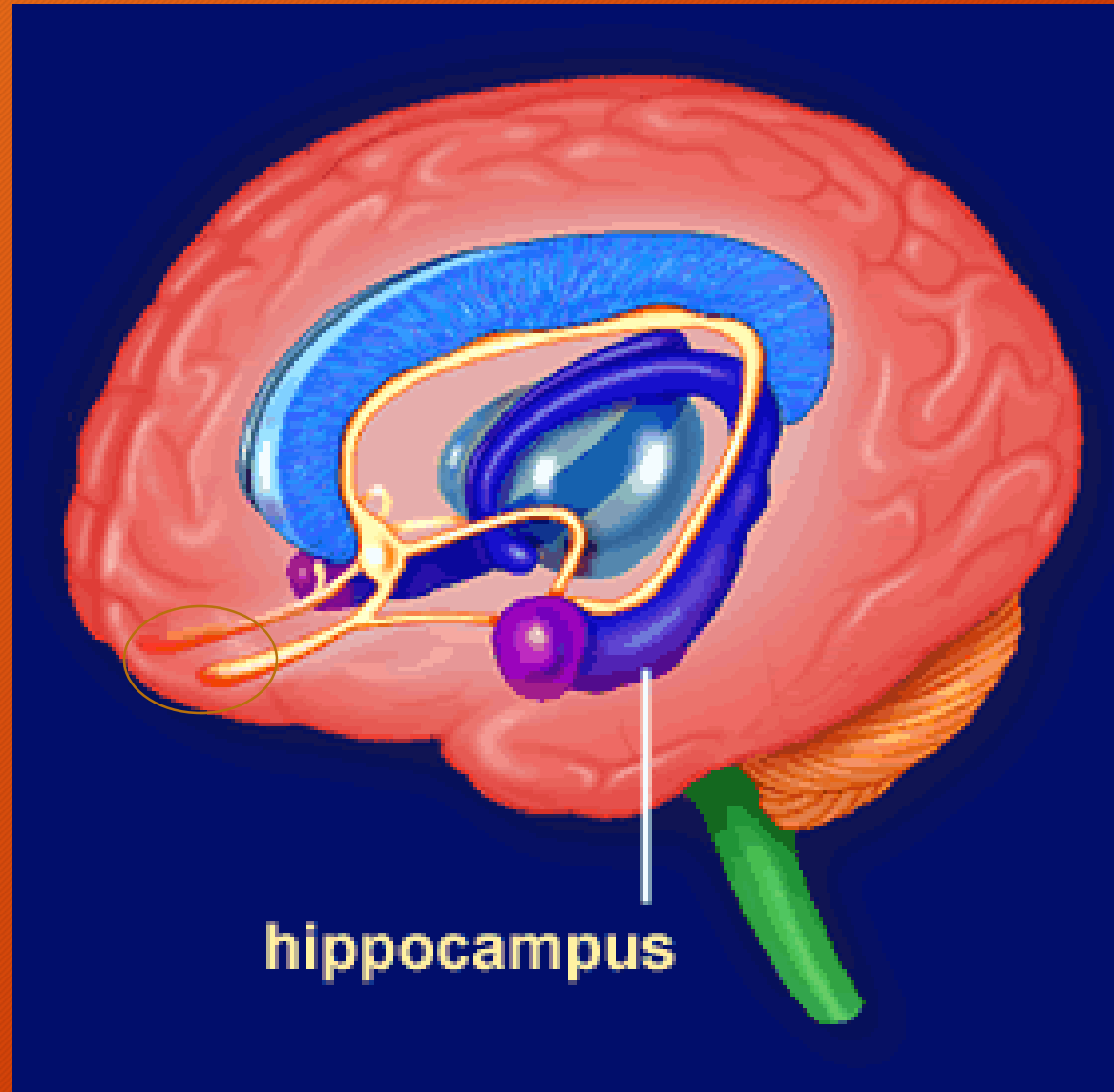
# Limbic System

- Mammals have this system
- Instinctual Memory
- Attention
- Motivation
- Level of arousal
- Emotional Memory
- Our Feeling and Reacting Brain

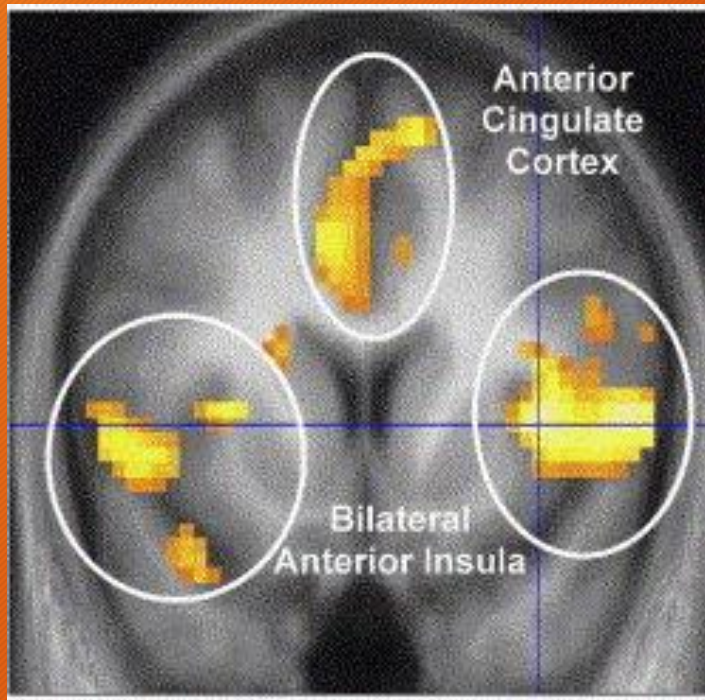
**Hippocampus:  
Greek for  
seahorse**



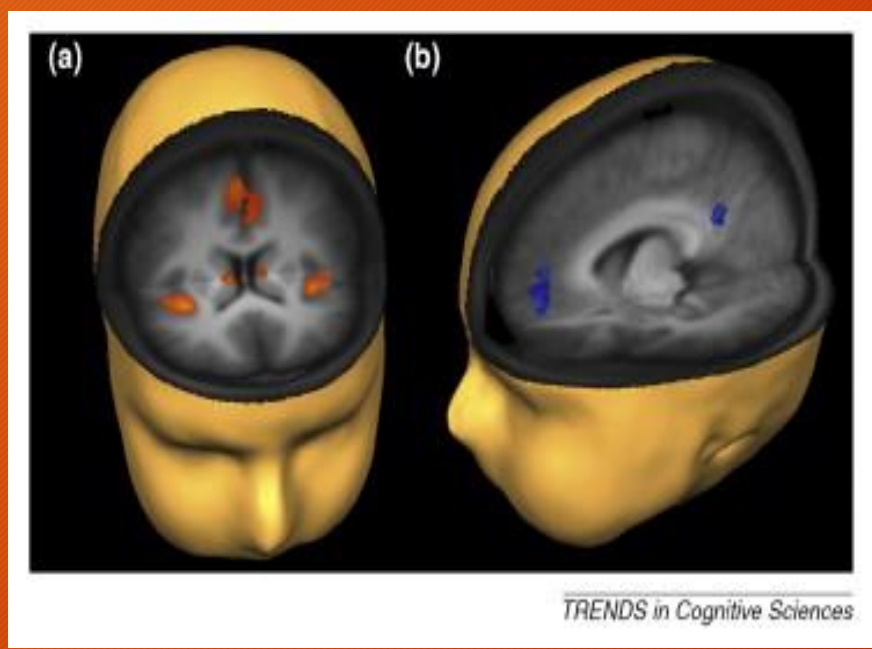
Olfactory  
Lobes







The insula also reads body states like hunger and craving and helps push people into reaching for the next sandwich, cigarette or line of cocaine. So insula research offers new ways to think about treating drug addiction, alcoholism, anxiety and eating disorders.



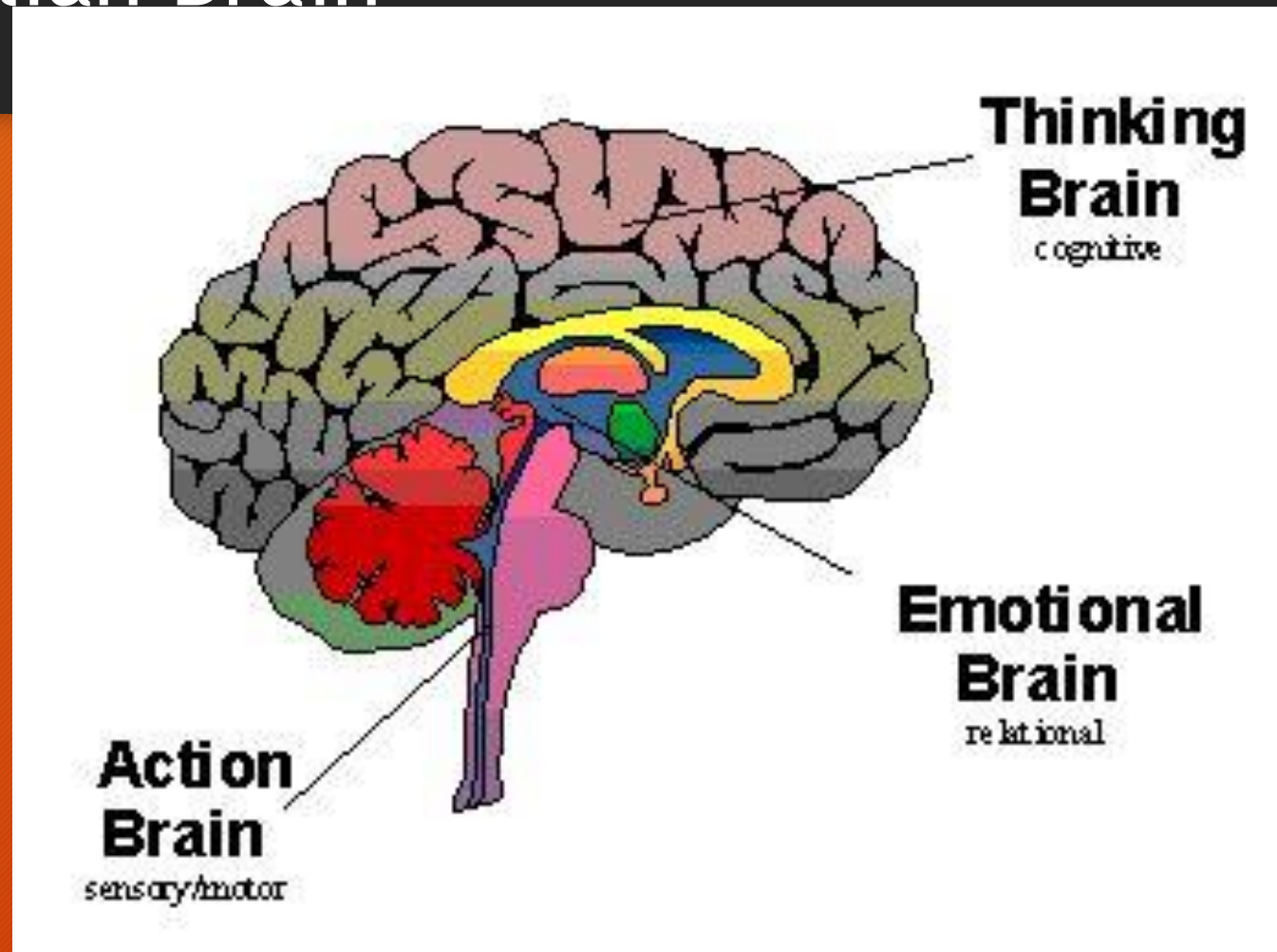
# Cingulate Gyrus



Fernando Da Cunha, BSID, 2014

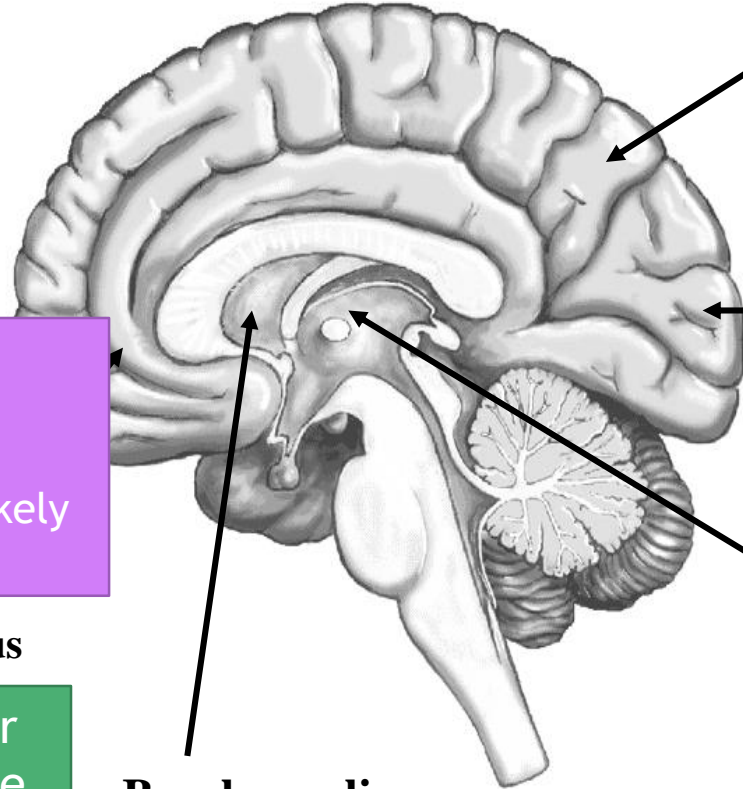


# Neomammalian Brain



Integration of Sensory Input, taste  
Smell, proprioception, vibration,  
sight, hearing, touch, heat, cold

**Parietal lobe**



**Prefrontal cortex**

CEO of the Brain  
When it works well you  
Can just say no....too little  
Activity makes you more likely  
To use

**Occipital lobe**

**Visual Processing**

**Anterior cingulate gyrus**

ACG = Brain's gear shifter  
Shift our attention and be  
flexible and adapt  
Too much activity become  
stuck in negative thoughts  
And actions, holds  
grudges, makes you worry

**Deep limbic system**

DLS= emotional tone  
When less active, then  
You are more positive  
and Hopeful  
Overly active Becomes  
negative, feels  
guilty and hopeless

**Basal ganglia**

BG= Integration of thoughts  
Feelings and movement  
Anxiety level is set here  
Too high=over react, anxious  
Too low=no motivation

# PreFrontal Cortex

- Executive Functions
- “the Cop in your head”
- Focus
- Impulse control
- Planning &  
    Organization
- Judgment
- Empathy
- Insight



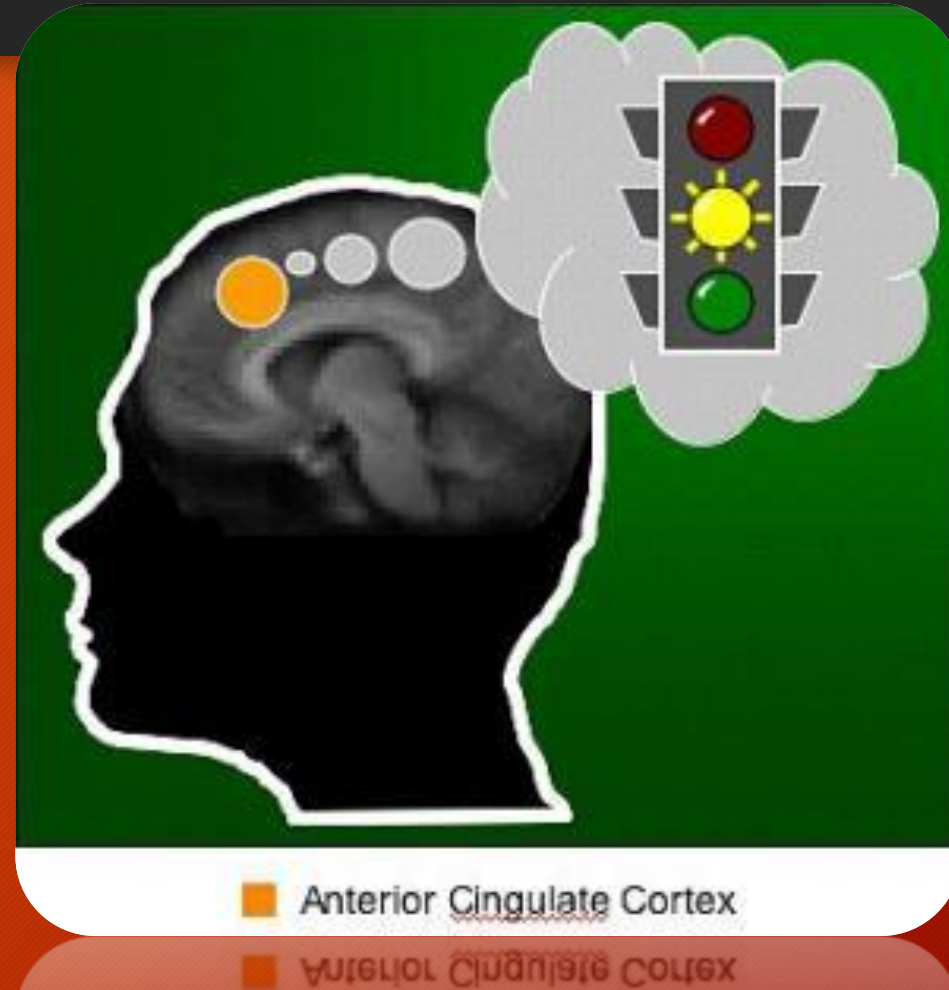
# PreFrontal Cortex Dysfunction

- Short Attention Span
- Impulsivity
- Disorganization
- Poor Judgment
- Procrastination
- Lack of Empathy and Insight



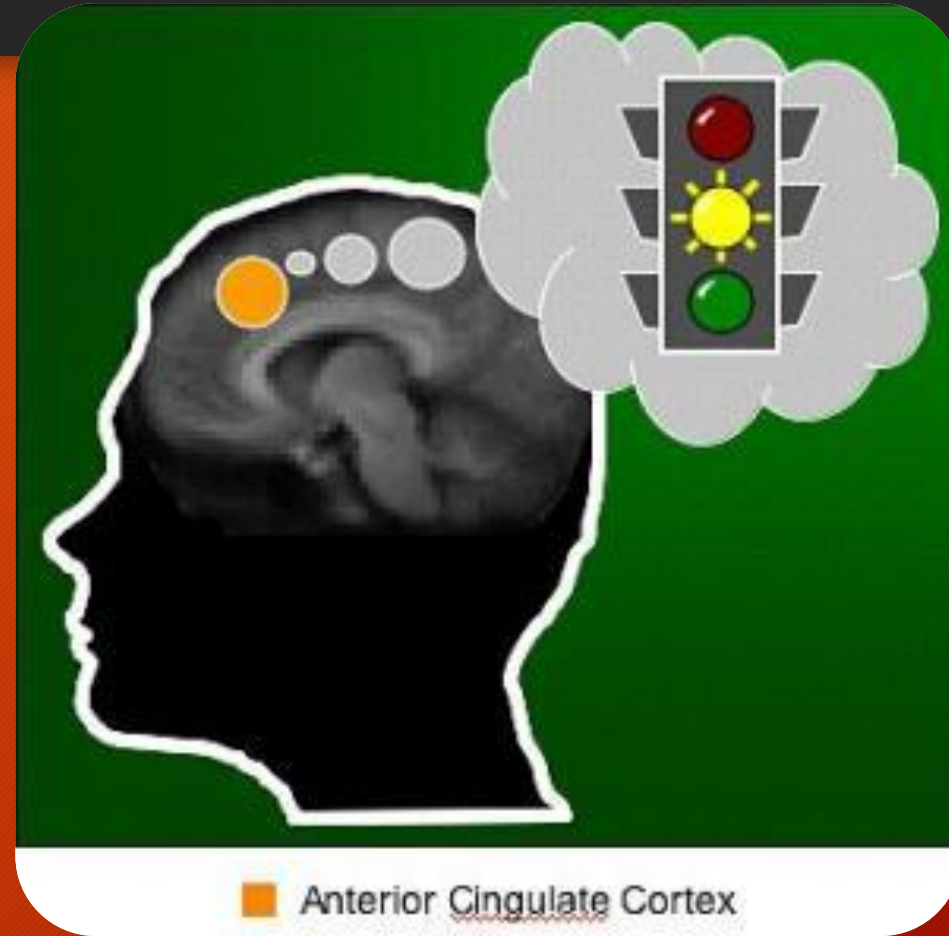
# Anterior Cingulate

- Gear Shifter of the Brain
- Shifts Attention
- Sees Options
- Cooperation
- “go with the flow”
- Error Detection



# Anterior Cingulate Dysfunction

- Gets Stuck
- Worries
- Holds grudges
- Obsesses
- Compulsions
- Addiction
- Eating Disorders
- Oppositional
- Argumentative
- Sees Too many Errors



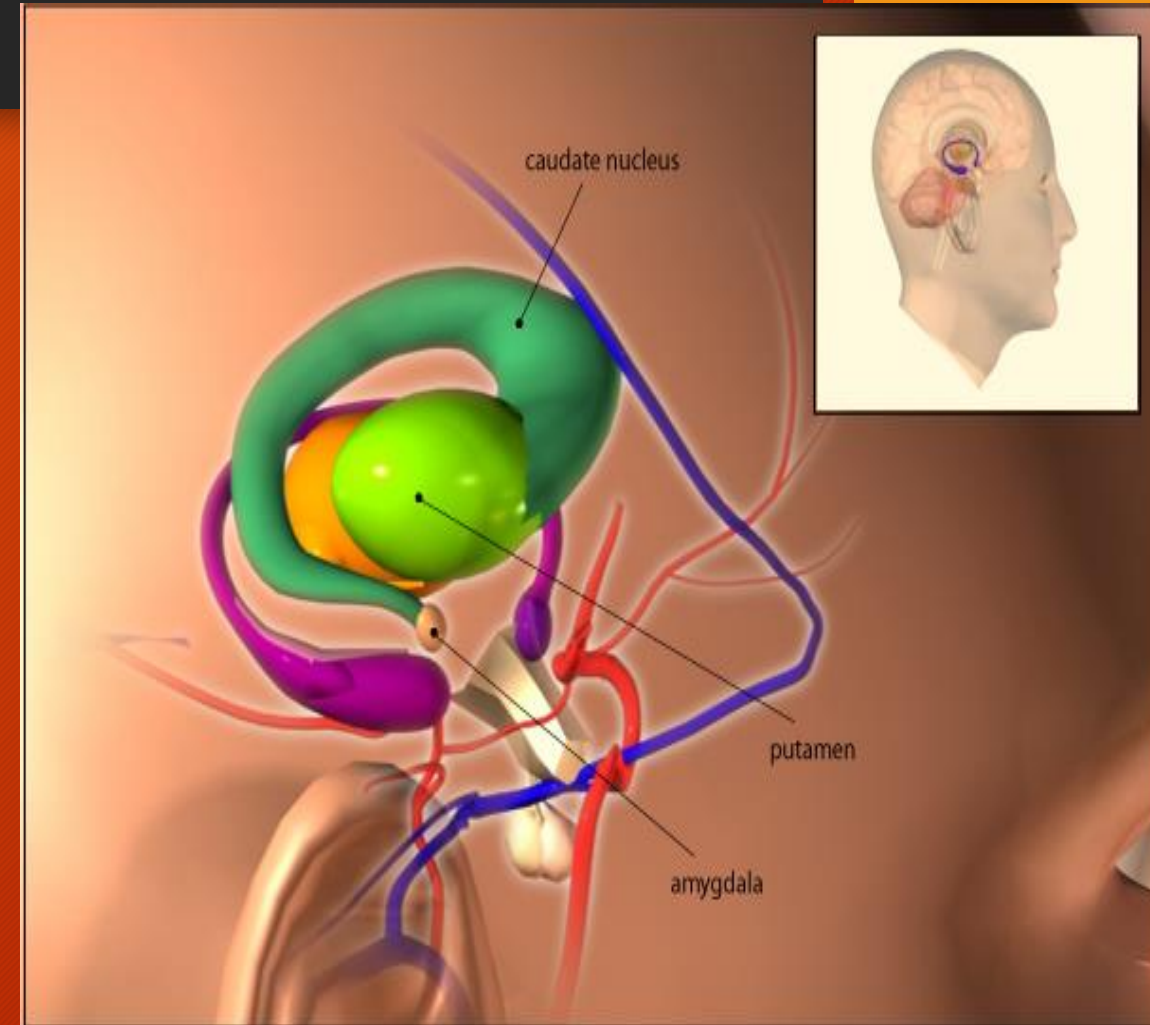
Anterior Cingulate Cortex

Anterior Cingulate Cortex



# Basal Ganglia: **Movement, Anxiety and Motivation**

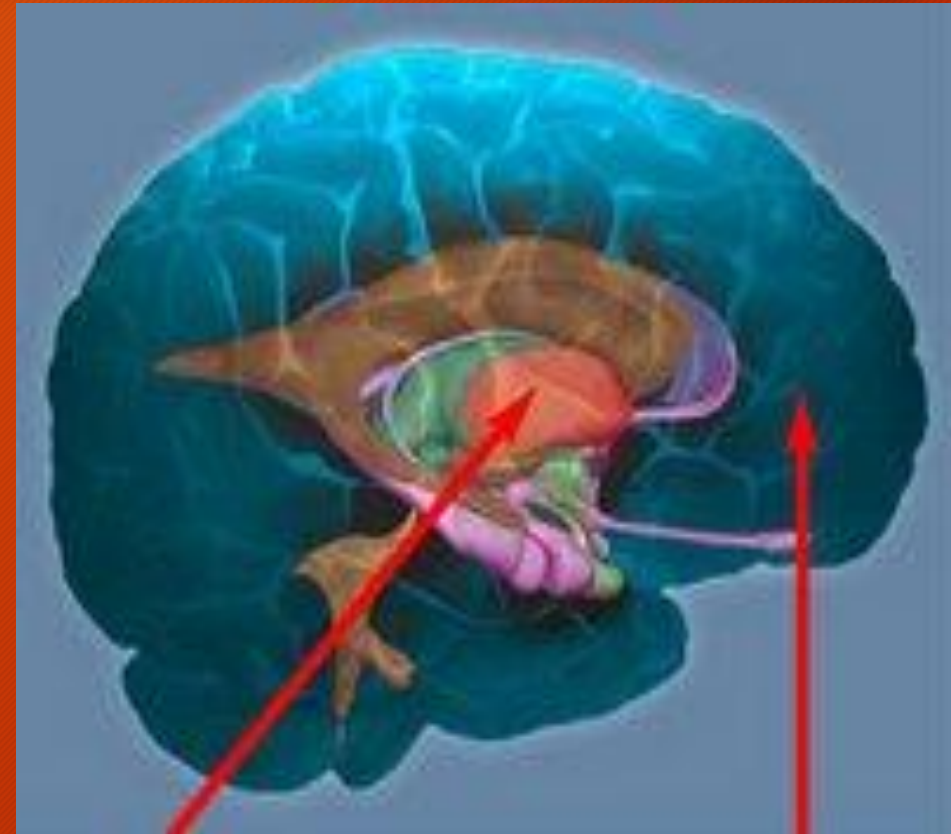
- Caudate
  - Thoughts
- Putamen
  - Motor
- Insula
  - Emotional Processing
  - Auditory/Visual processing
- Nucleus Accumbens
  - Pleasure
- **Amygdala=“am I safe????”**



Basal Ganglia

# Basal Ganglia

- Increased:
  - Anxiety/Panic Attacks
  - Conflict Avoidant
  - Excess motivation
  - Predicts the worst
- Decreased:
  - ADD Like Symptoms
  - Decreased Motivation
  - Movement Disorders  
(Parkinson's)

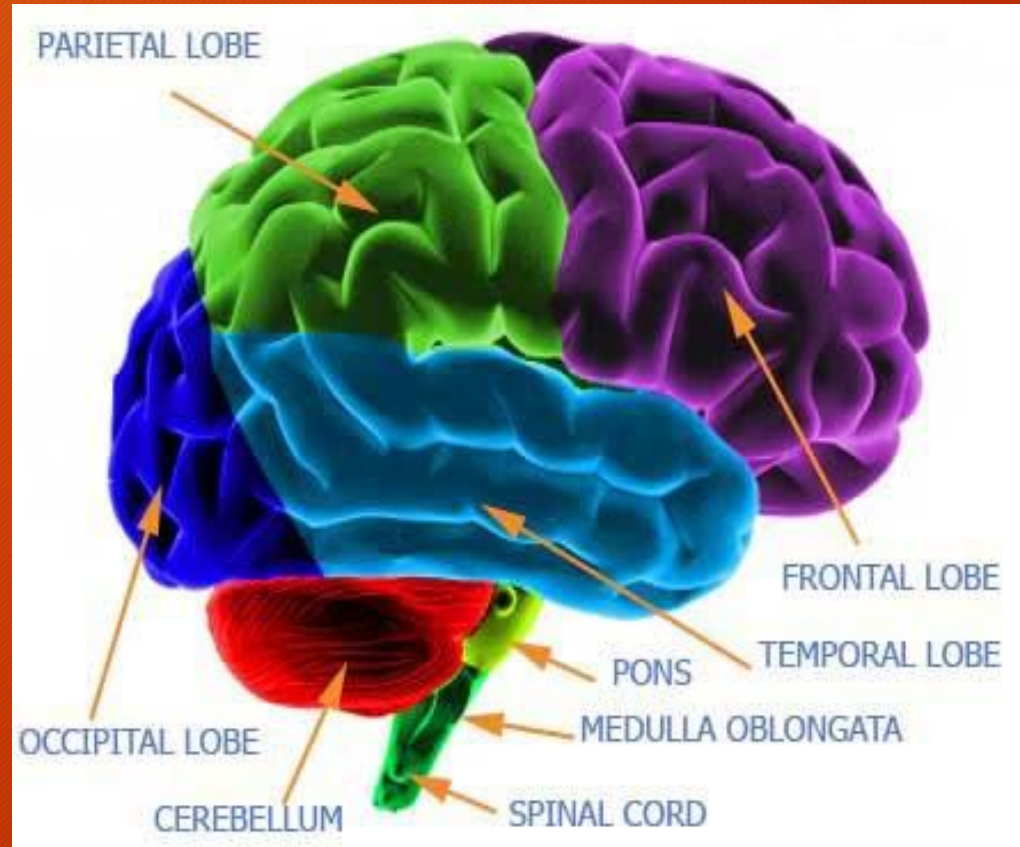


Basal Ganglia

PreFrontal Cortex

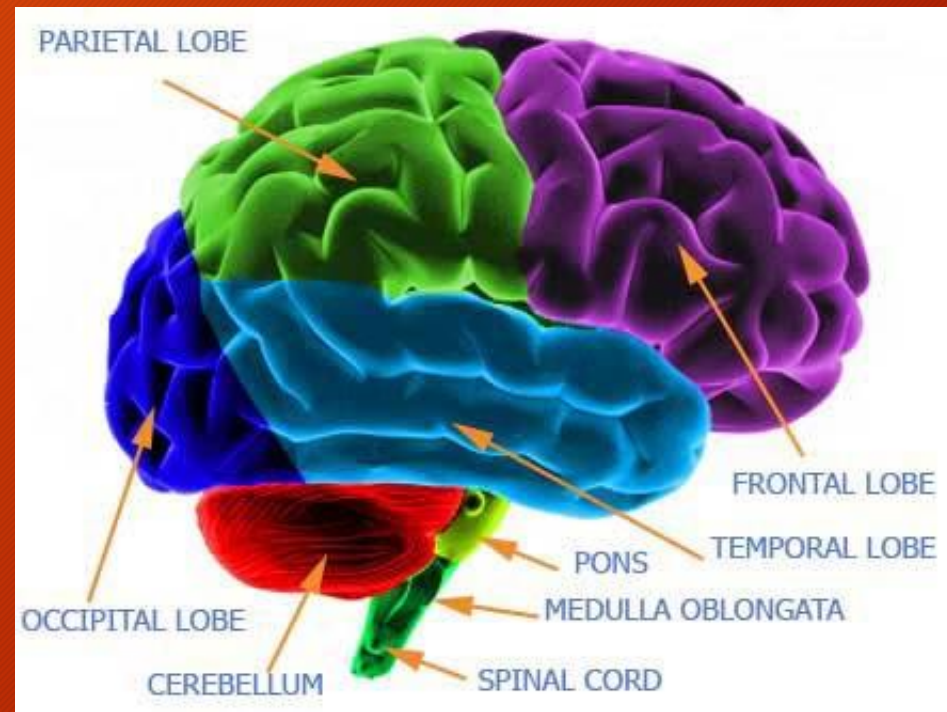
# Temporal Lobes

- Language
- Memory
- Retrieval of words
- Mood stability
- Read Social Cues
- Temper Control
- Spiritual Experience



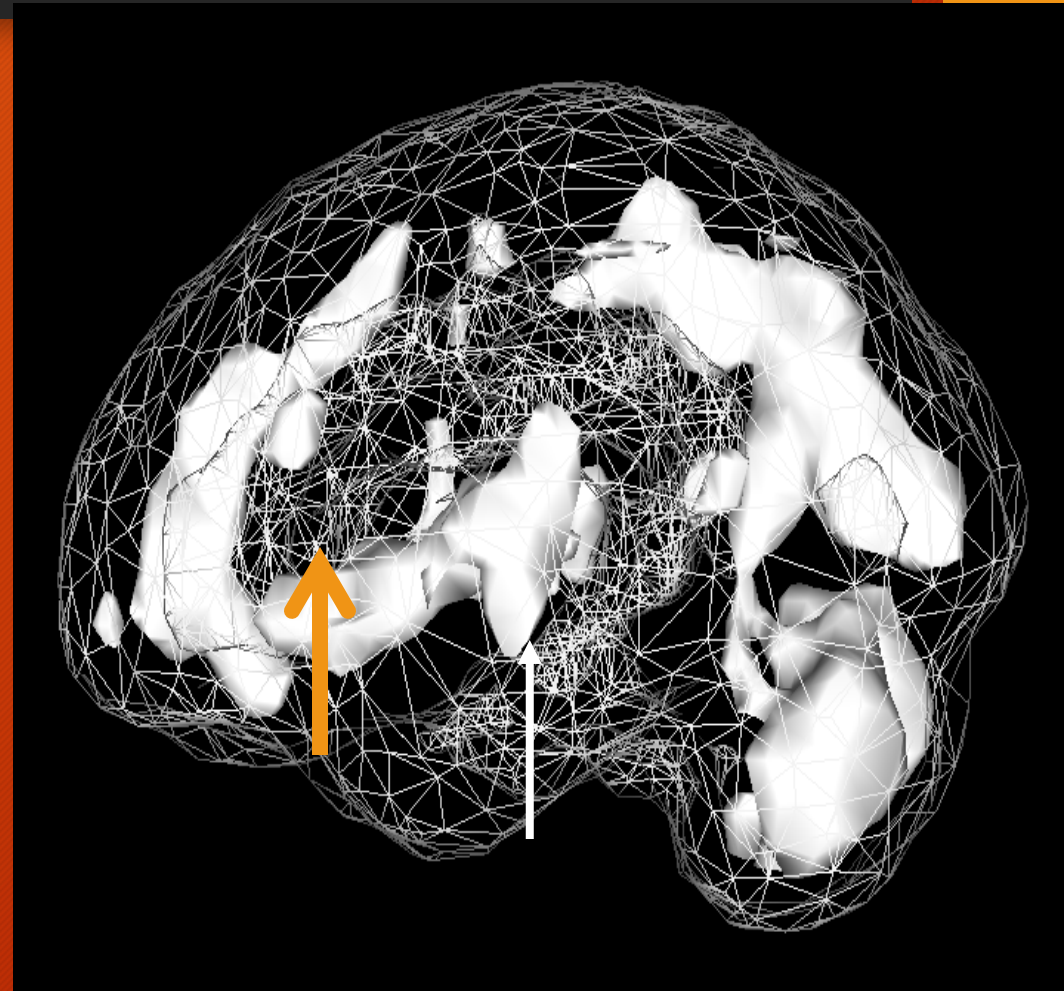
# Temporal Lobe Dysfunction

- The “what” Pathway
- Language Problems
- Memory Problems
- Dyslexia
- Word Finding Problems
- Panic/Anxiety
- Trouble with social cues
- Dark thoughts
- Aggression
- Illusions
- Hyper Religiosity



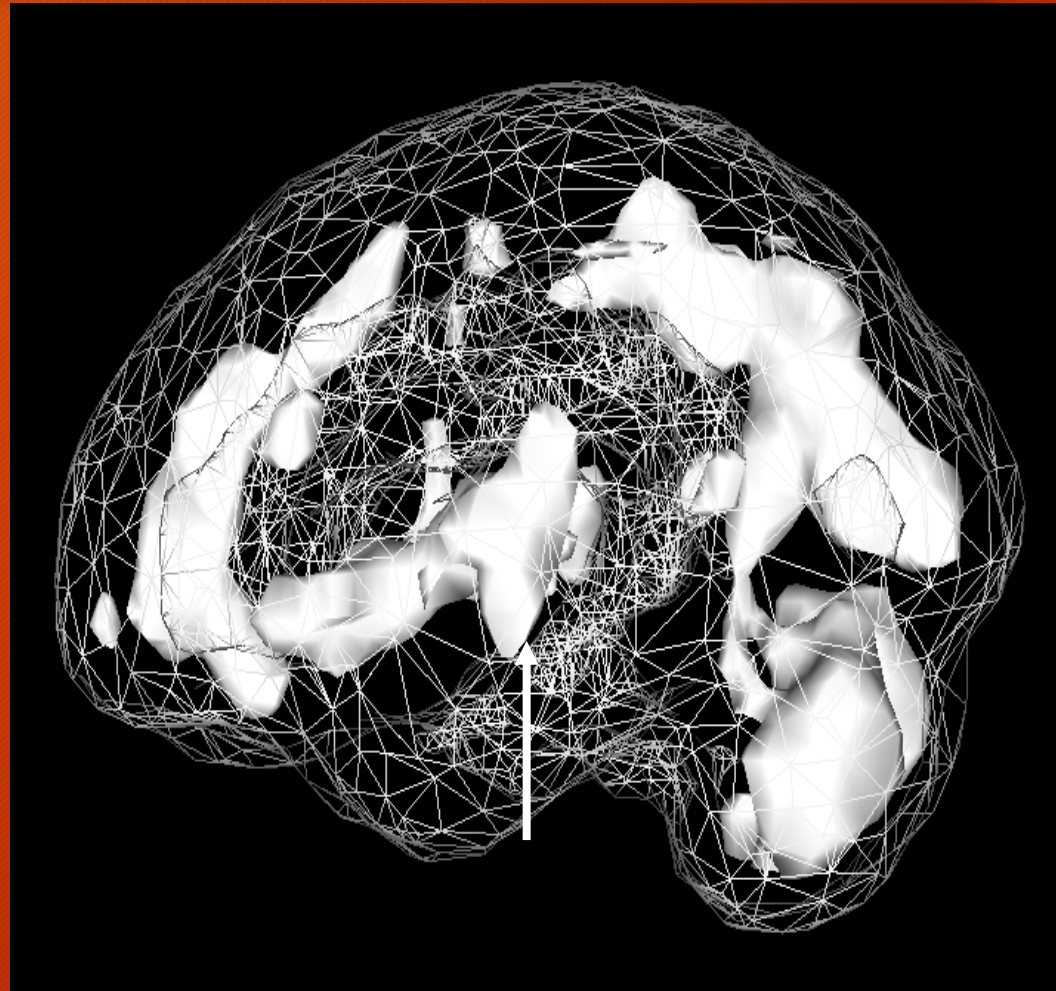
# Deep Limbic System

- Emotionally Charged memories
- Integration-
  - Sensory Info
- Sets emotional tone
- Bonding
- Sense of smell
- Libido
- Pain



# Deep Limbic System Dysfunction

- Depression, sadness
- Negative, irritability
- Low motivation
- Negativity, blame
- Guilt
- Social isolation
- Low self-esteem
- Low libido
- Low energy
- Decreased interest
- Worthlessness



# Cerebellum

- Motor control
- Posture, gait
- Executive function, connects to PFC
- Speed of cognitive integration (like clock speed of computer)
- Impulse Control



# Cerebellum Dysfunction

- Gait/coordination problems
- Disorganization
- Slowed thinking
- Slowed speech
- Impulsivity
- Poor conditioned learning
- Autism/ Aspergers
- ADD





# •QUESTIONS?????





Effects

Of Drugs

of

Addiction

On the Brain

# COGNITIVE DEFICITS IN PRENATAL EXPOSURE

- The consequences of prenatal alcohol exposure are well known: Fetal alcohol spectrum disorders are the leading cause of mental retardation in the United States (Centers for Disease Control and Prevention, 2009).
- In addition, fetal alcohol exposure increases susceptibility to later substance abuse problems (Yates et al., 1998).

# COGNITIVE DEFICITS IN PRENATAL EXPOSURE

5-year-olds whose mothers had used alcohol, cocaine, and/or opiates while pregnant ranked below unexposed controls in language skills, impulse control, and visual attention. (Pulsifer et al., 2008).

Another study documented memory deficits in 10-year-old children who had been exposed prenatally to alcohol or marijuana (Richardson et al., 2002).

# COGNITIVE DEFICITS IN PRENATAL EXPOSURE

The effects of prenatal tobacco exposure are particularly concerning because so many expectant mothers smoke—by one estimate, over 10 percent in the United States (Hamilton et al., 2007).

In utero exposure to tobacco byproducts has been linked to cognitive deficits in laboratory animals and human adolescents (Dwyer, Broide, and Leslie, 2008).

Some studies suggest that such exposure can lower general intelligence; for example, one found a 12-point gap in full-scale IQ between exposed and unexposed middle-class adolescents (e.g., Fried, Watkinson, and Gray, 2003).

# COGNITIVE DEFICITS IN PRENATAL EXPOSURE

In another study, the odds of having attention deficit hyperactivity disorder (ADHD) were more than three times as great for adolescents whose mothers smoked during pregnancy compared with children of nonsmoking mothers (Pauly and Slotkin, 2008).

The risk of developing ADHD is greatly increased in adolescents whose mothers smoked during pregnancy (Pauly and Slotkin, 2008).

1

Many drugs produce cognition-related withdrawal symptoms that may make abstinence more difficult. These include:

2

• cocaine—deficits in cognitive flexibility (Kelley et al., 2005);

3

• amphetamine—deficits in attention and impulse control (Dalley et al., 2005);

4

• opioids—deficits in cognitive flexibility (Lyvers and Yakimoff, 2003);

# COGNITIVE DEFICITS IN DRUG Withdrawal

- **Alcohol—deficits in working memory and attention** (Moriyama et al., 2006);
- **Cannabis—deficits in cognitive flexibility and attention** (Pope, Gruber, and Yurgelun-Todd, 2001);
- **Nicotine provides a familiar example of cognitive changes in withdrawal. In both chronic smokers and animal models of nicotine addiction, cessation of nicotine administration is associated with deficits in working memory, attention, associative learning, and serial addition and subtraction** (Bell et al., 1999; Blake and Smith, 1997; Davis et al., 2005; Hughes, Keenan, and Yellin, 1989; Jacobsen et al., 2006; Mendrek et al., 2006; Raybuck and Gould, 2009; Semenova, Stolerman, and Markou, 2007)

## COGNITIVE DEFICITS IN DRUG Withdrawal



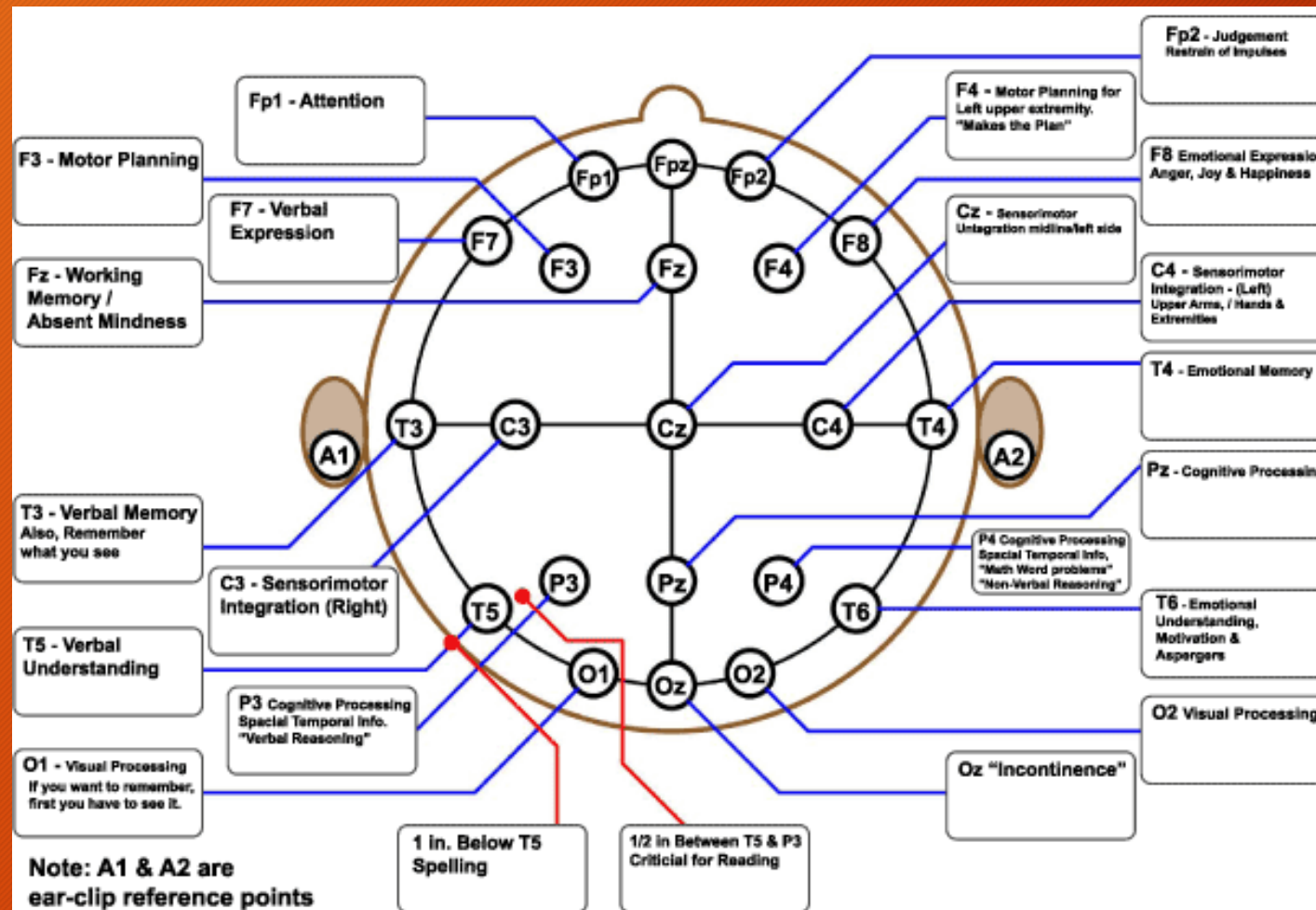
- Moreover, it has been shown that the severity of decreases in cognitive performance during periods of smoking abstinence predicts relapse (Patterson et al., 2010; Rukstalis et al., 2005).
- Although these deficits usually dissipate with time, a dose of nicotine will rapidly ameliorate them (Davis et al., 2005)—a situation that may contribute to some relapses.
- Thus, chronic substance abuse can lead to cognitive deficits that are particularly pronounced during early periods of abstinence.

## COGNITIVE DEFICITS IN DRUG RELAPSE



Director of the National Institutes of Health Dr. Francis Collins is a multiple-appearance guest on The Colbert Report and was on with the comedian last night to promote [Barack Obama's BRAIN initiative](#). April 5, 2013

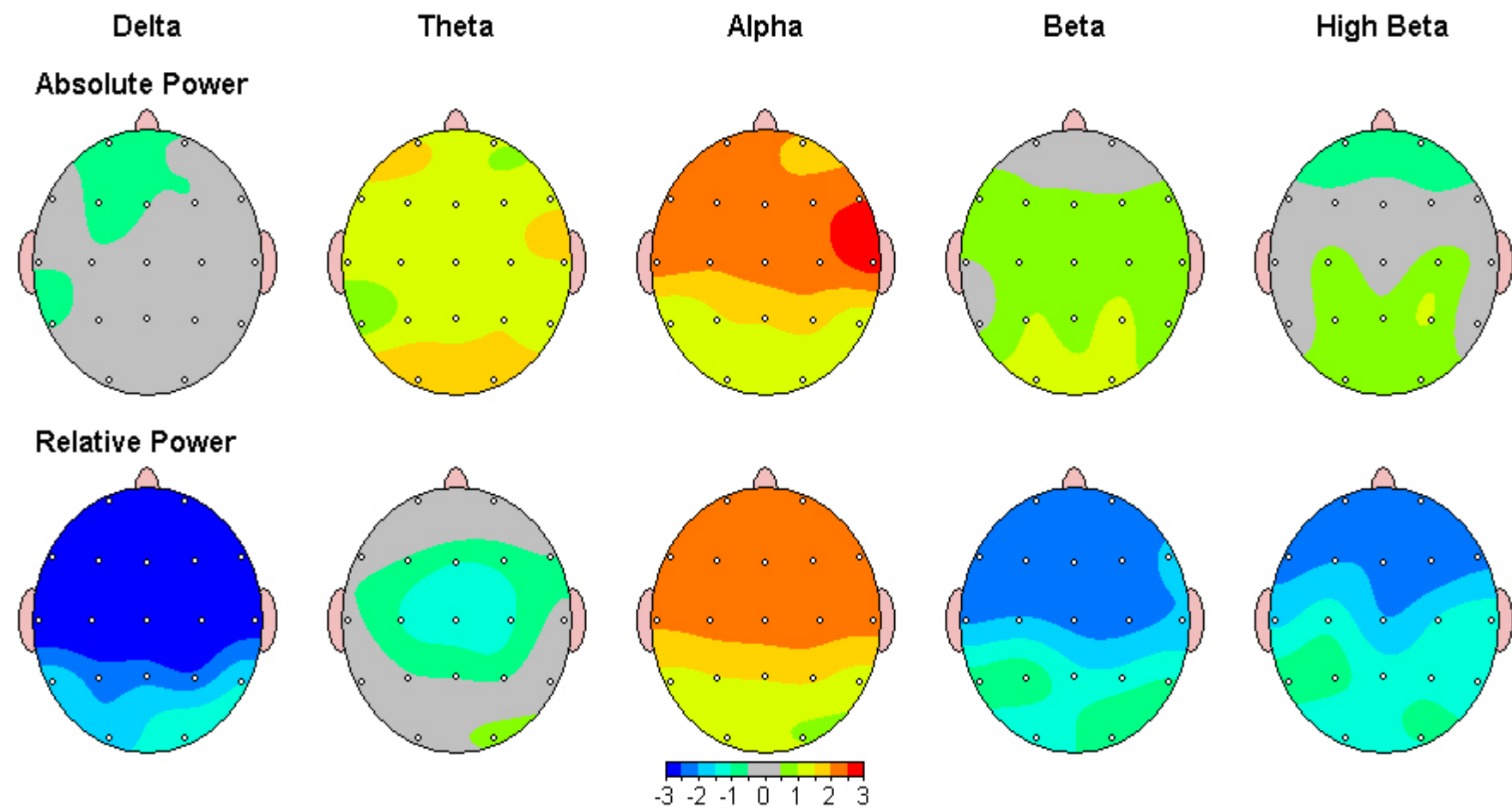
# 19 Channel Quantitative Electroencephalogram



Montage: LinkEars

EEG ID: ECa

### Z Scored FFT Summary Information



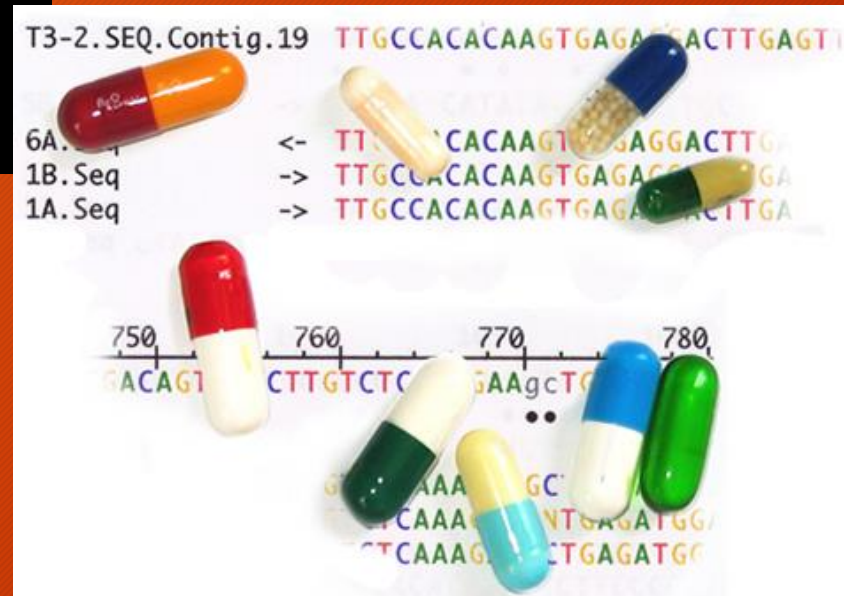
# Evaluation of Neurocognitive Function at AHC

Assess



My Brain Solutions  
Brain Health Report

Genetic Testing



QEEG

# Evaluation of Neurocognitive Function at AHC

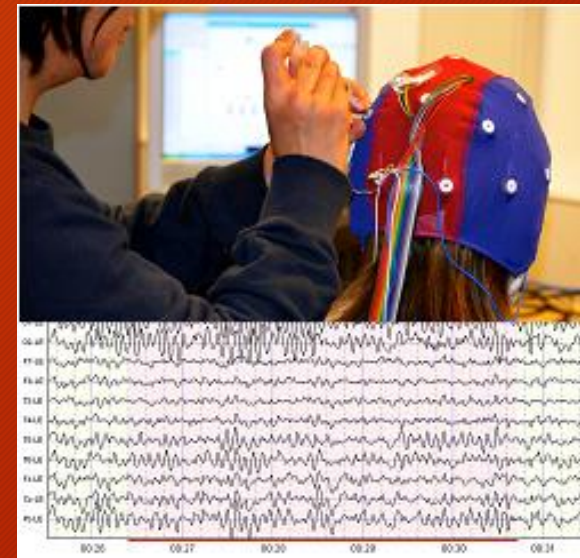
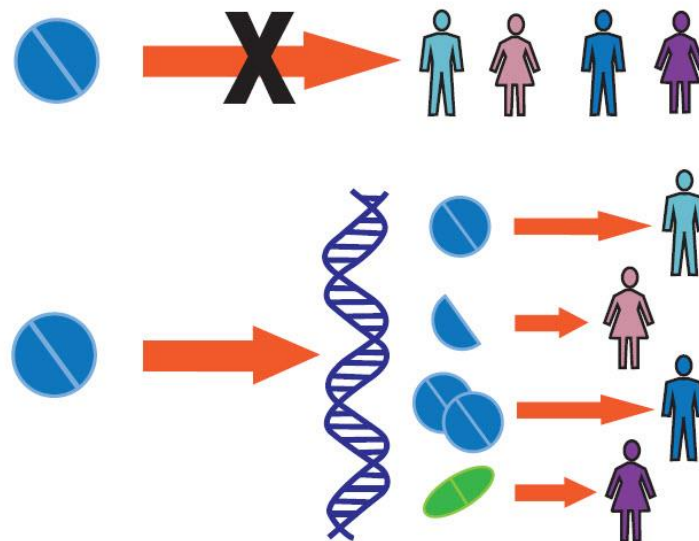
Train



Relaxation Room

Brain Games

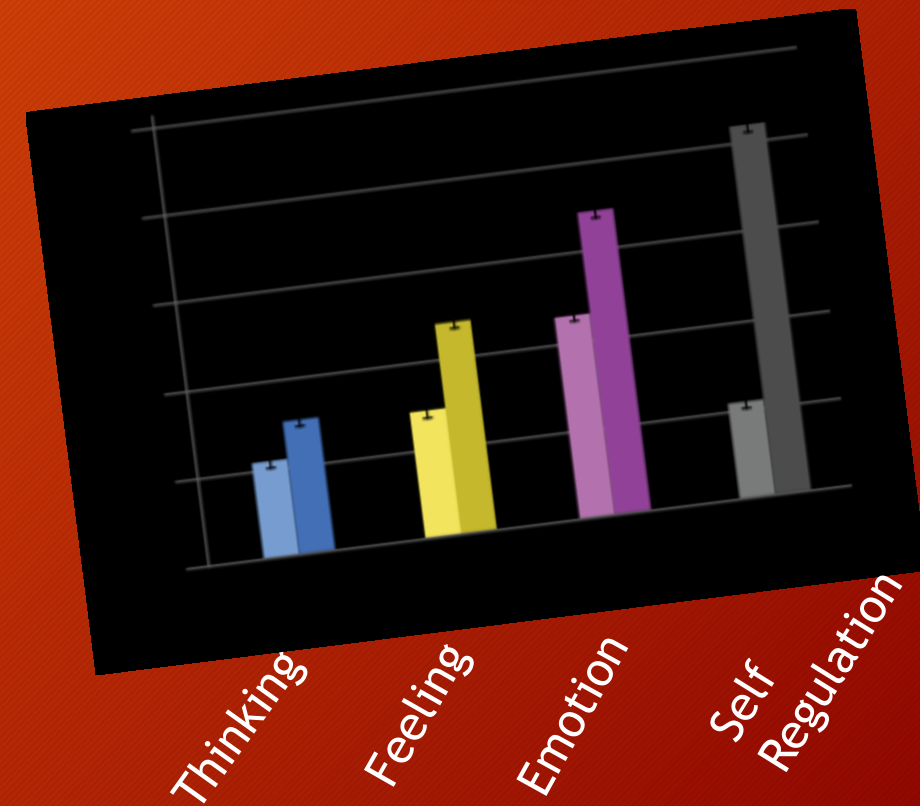
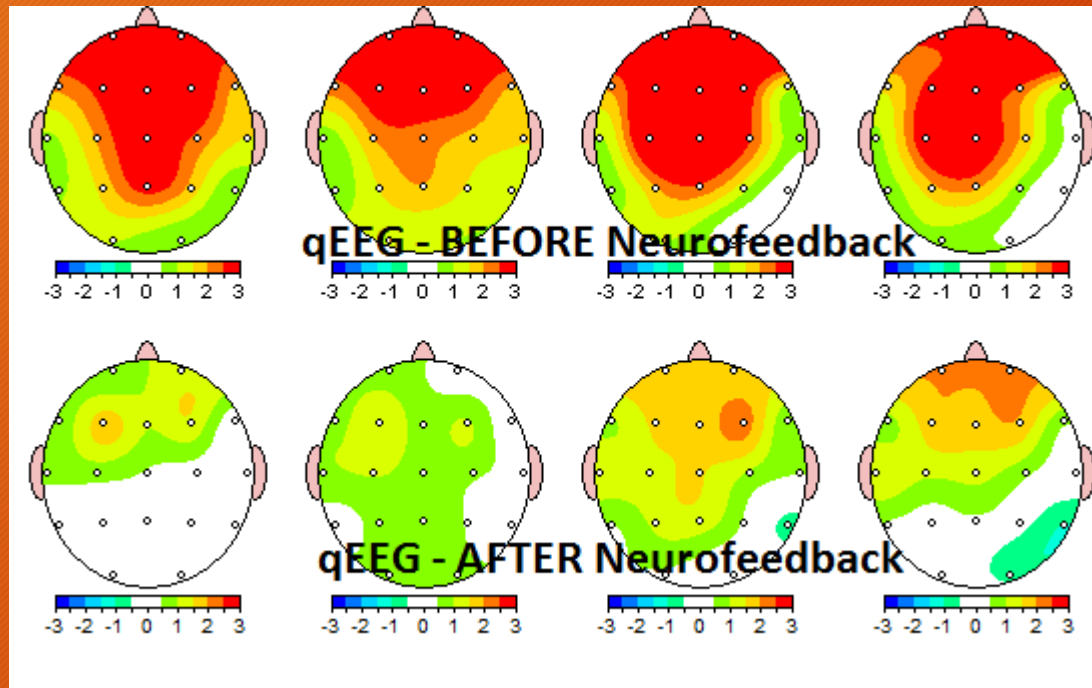
## Personalized Medicine



Neurofeedback Training

# Evaluation of Neurocognitive Function at AHC

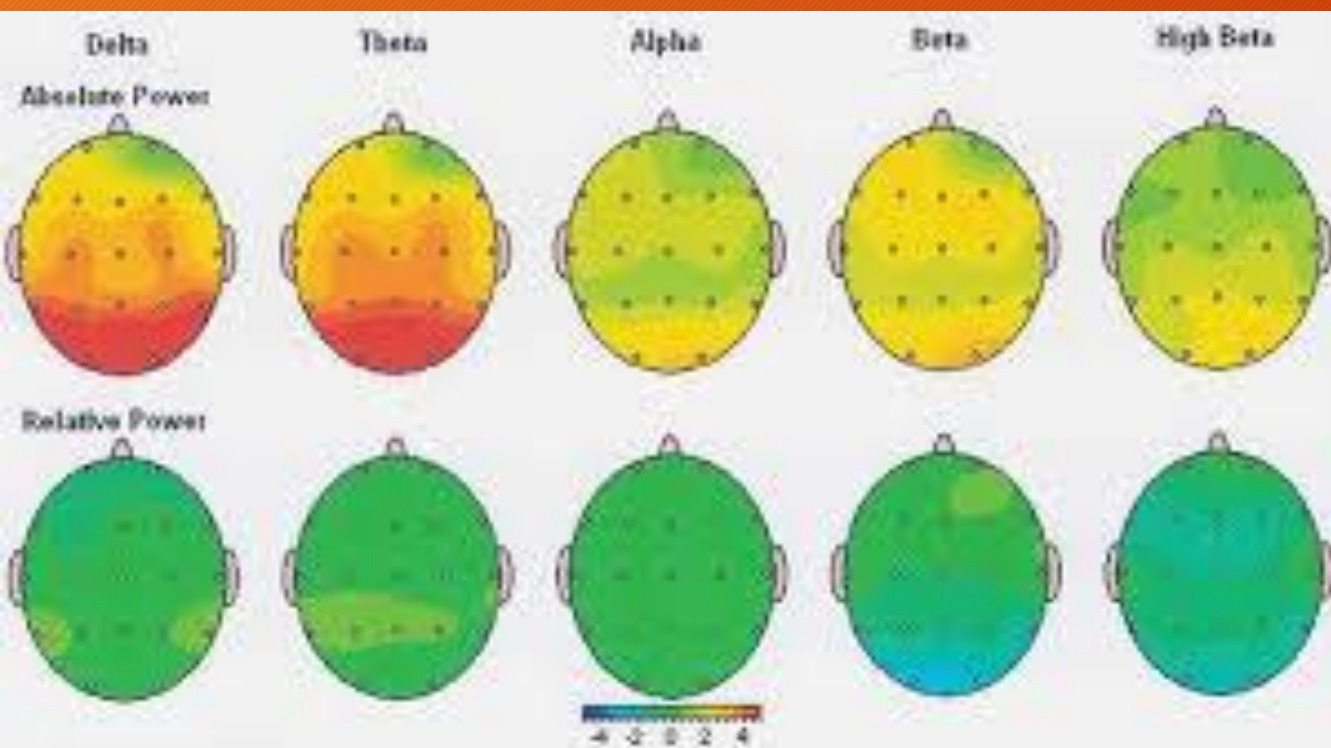
Track



# QEEG of Fetal Alcohol Syndrome-Cory Hammond

Journal of Neurotherapy, 16:47-52,

2012



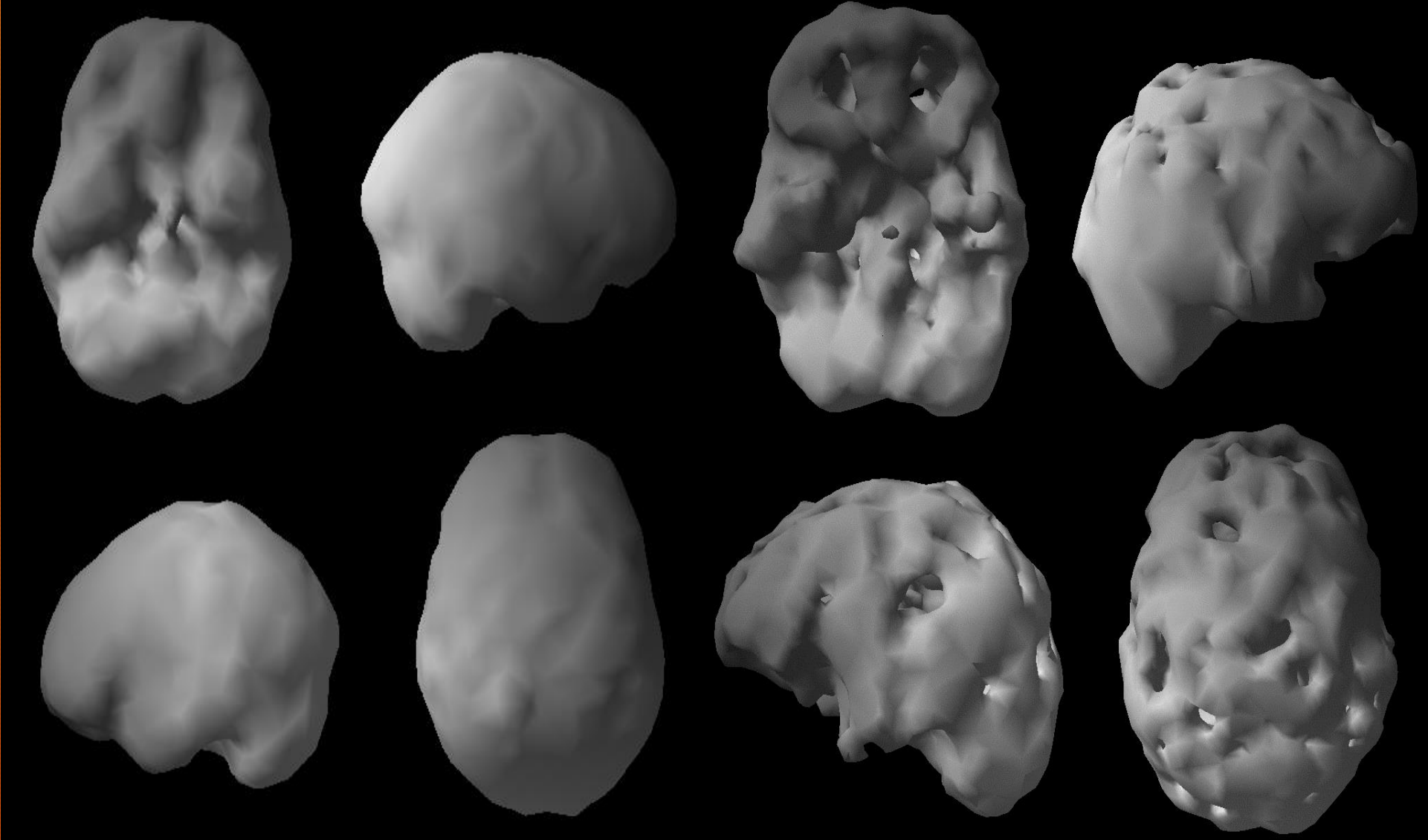


# Neurocognitive Effects of Alcohol

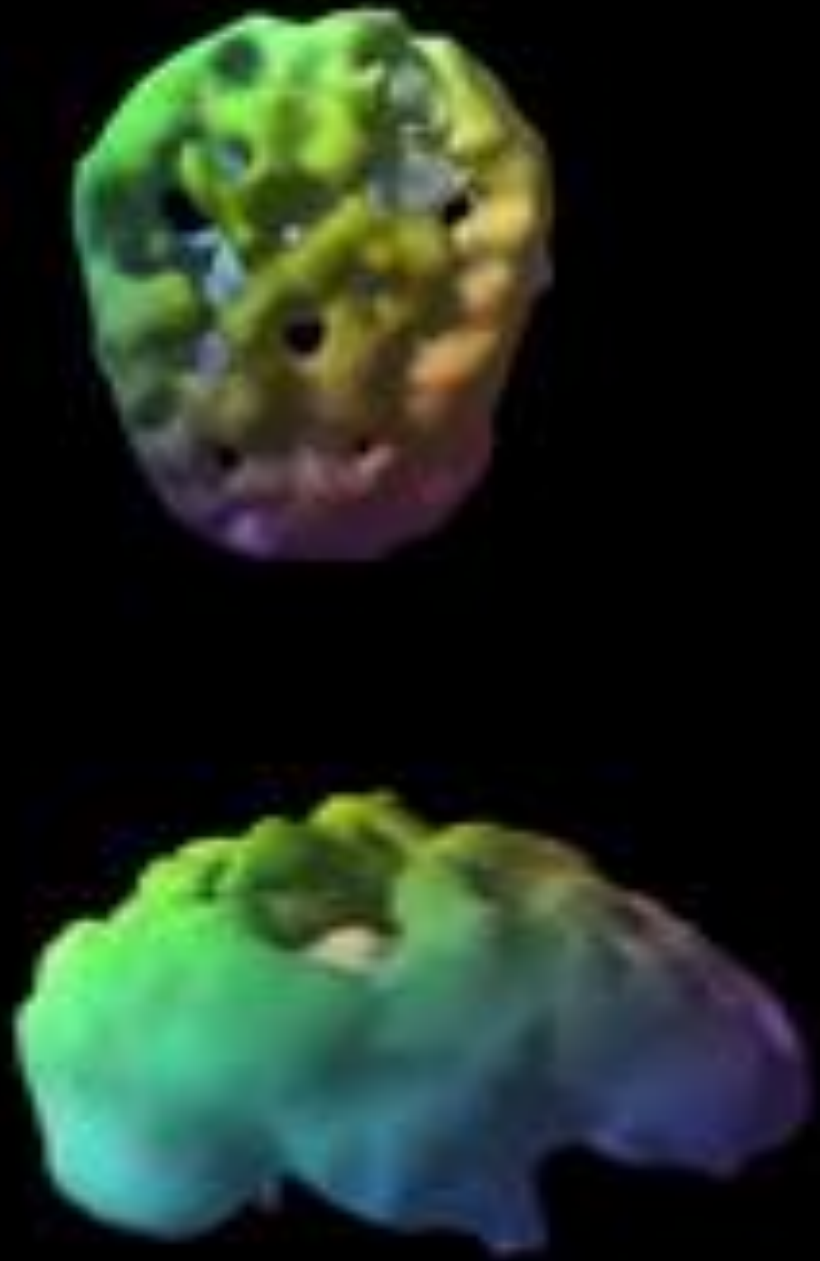


# Healthy Brain

# Alcohol Damaged Brain



*Unchain your brain, Amen, D and Smith D; 2010, Mindworks Press.*



38 y/o - 17 years of  
heavy alcohol  
weekend use  
(binge type drinking)

Table 2.

## Scores from the individual neuropsychological tasks from which outcome scores were derived

	Controls ( <i>n</i> = 58)	Alcohol-dependent ( <i>n</i> =43)	Uncorr. <i>P</i> -value
<b>WAIS-R tests</b>			
Vocabulary: age scaled scores	14.1 ± 2.7	12.5 ± 3.3	0.006
Arithmetic: age scaled scores	12.0 ± 2.7	11.9 ± 3.1	NS
Picture arrangement: age, scaled scores	13.7 ± 2.8	12.6 ± 3.4	NS
Block design: age scaled scores	12.7 ± 3.3	12.1 ± 2.9	NS
Digit symbol: age scaled scores	10.9 ± 2.5	<b>9.3 ± 2.7</b>	0.002*
Pro-rated verbal IQ	114.6 ± 12.2	109.7 ± 15	NS
Pro-rated performance IQ	114.5 ± 11.4	109.8 ± 13.3	NS
Pro-rated full scale IQ	117.0 ± 12.0	110.9 ± 14.7	0.024
<b>Trail-Making Tests</b>			
Trail A (s)	33.0 ± 10	36.9 ± 12.8	NS
Trail B (s)	66.1 ± 23.9	<b>84.4 ± 42.9</b>	0.007
Total: Trail A ± B (s)	99 ± 28	121 ± 51	0.007
<b>WMS: logical memory test</b>			
Immediate recall	13.3 ± 3.0	12.0 ± 3.5	0.05
30-min recall	11.7 ± 3.2	10.1 ± 3.9	0.03
Total Wechsler memory score: (immediate + recall).	25.0 ± 6.0	22.2 ± 7.1	0.033

# Cognitive Effects of Chronic Alcohol Use

- Both **smoking and alcoholism** were related to impaired executive function.
- However, the effect of **alcoholism** was not independent of IQ
- Suggesting a generalized effect, perhaps affecting **a wide range of cognitive abilities** of which executive function is a component.

Glass, J, et al. *Addiction*. 2009 Jan;104(1):38-48. *Effects of alcoholism severity and smoking on executive neurocognitive function.*

SIMON J. C. DAVIES, et al..University of Bristol London, recommend:

- Trail A and B test, in particular the **Trail B** section, and **the digit symbol test** should be considered for routine clinical use in the assessment and treatment of alcohol dependence, even in apparently cognitively, mentally, and physically healthy patients.
- The Trails test requires minimal training, can be easily used by a range of workers, takes about **5 min** to complete, and requires no special equipment

# Trails: Part A

## Trail A

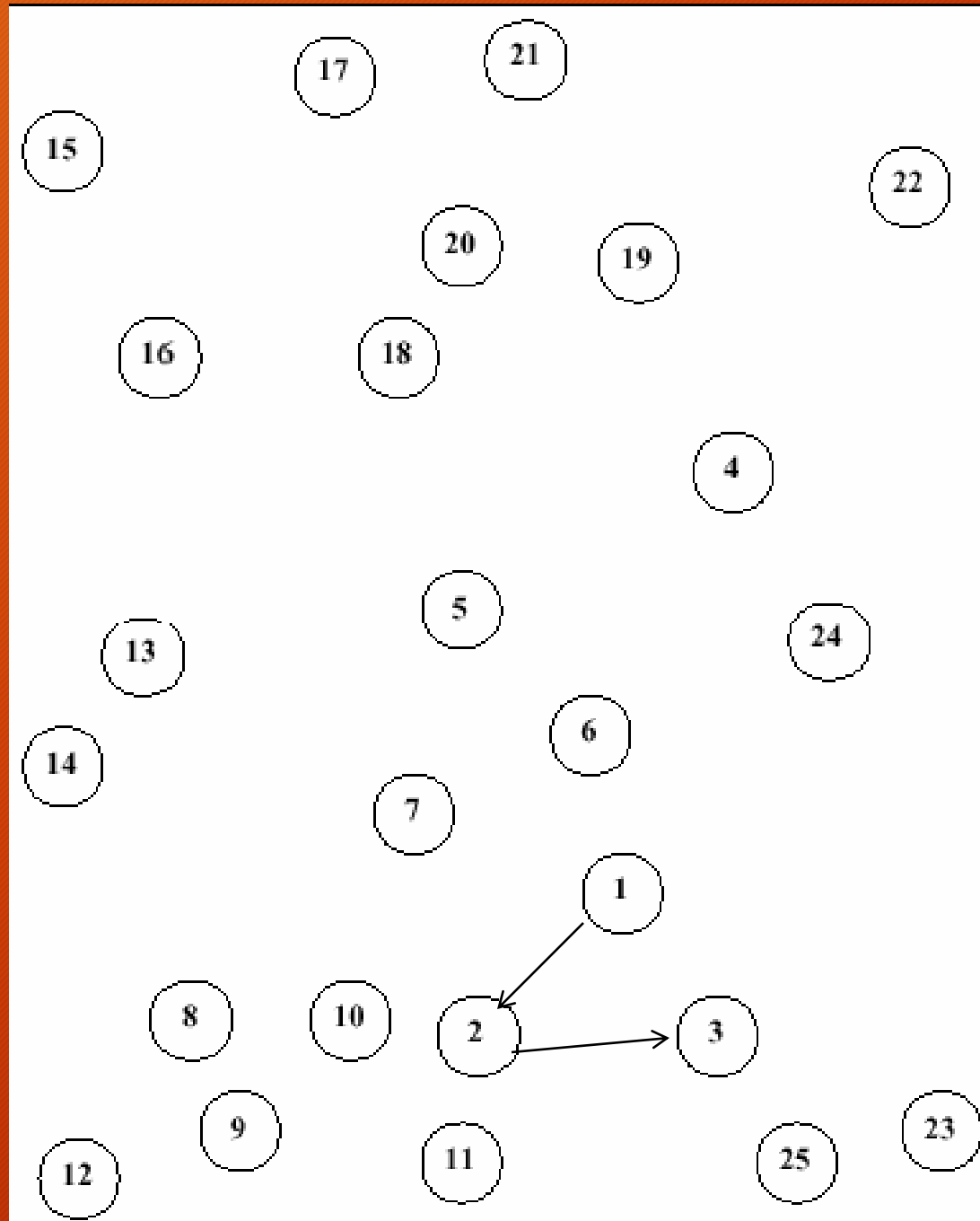
Controls  $33 \pm 10$  seconds

Average: 29

## Alcoholics

>78 seconds

Most in 90 seconds



# Trails: Part B

Trail B

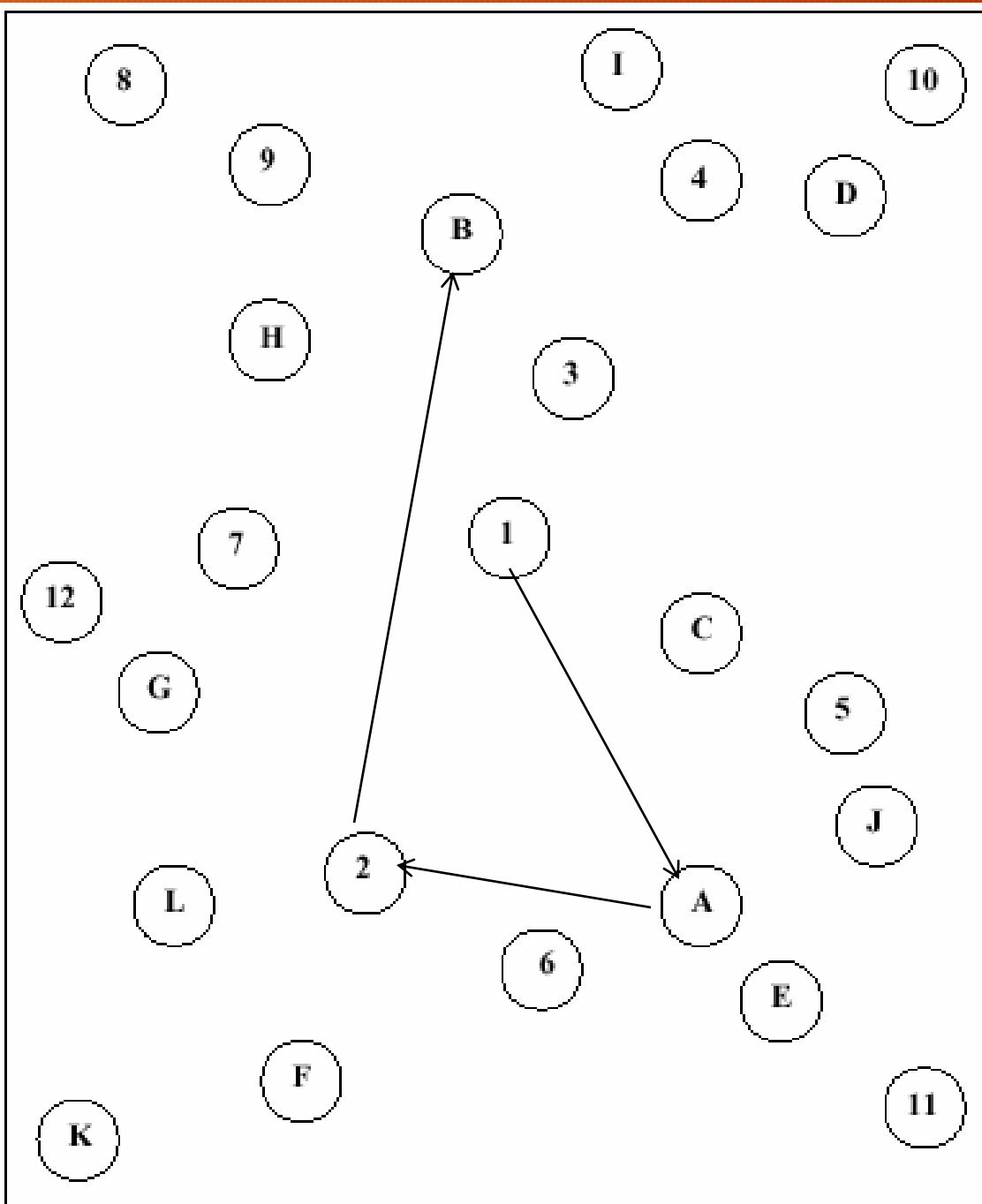
Controls  $66.1 \pm 23.0$

Average: 75 seconds

Alcoholics

$84.4 \pm 42.9$

Most in 3 minutes





# DIGIT SPAN TEST

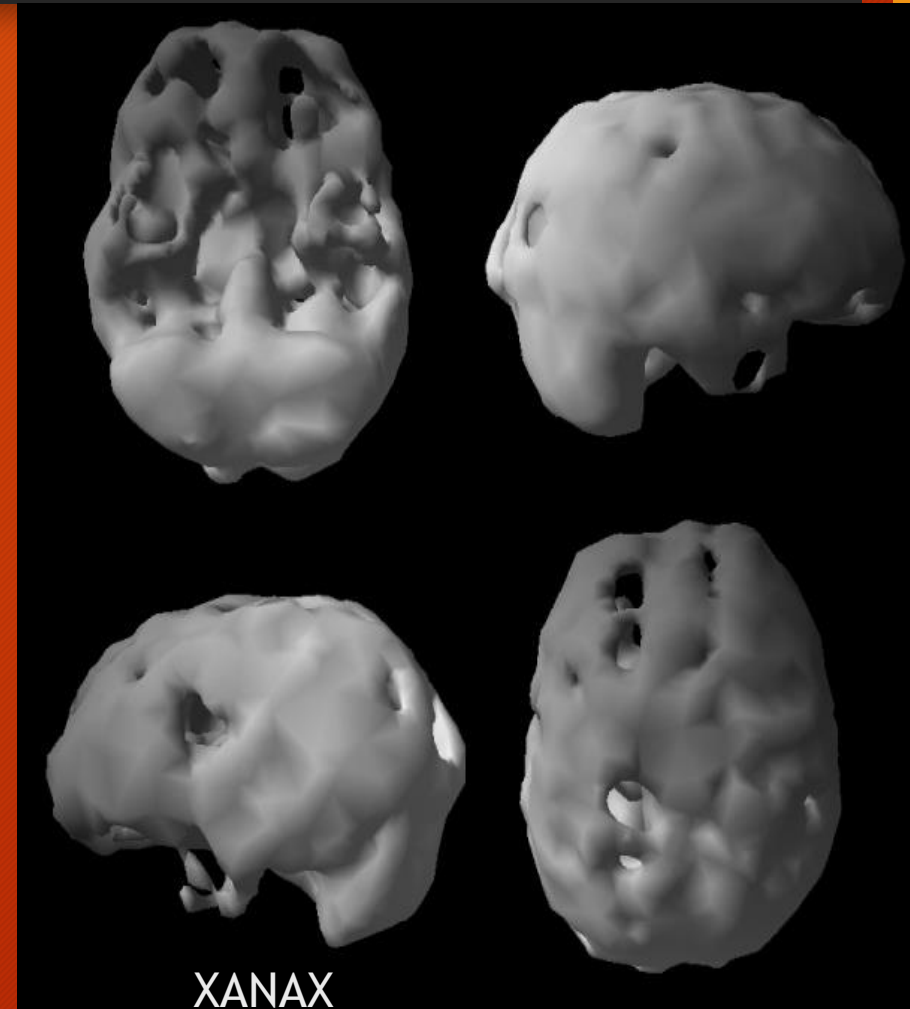
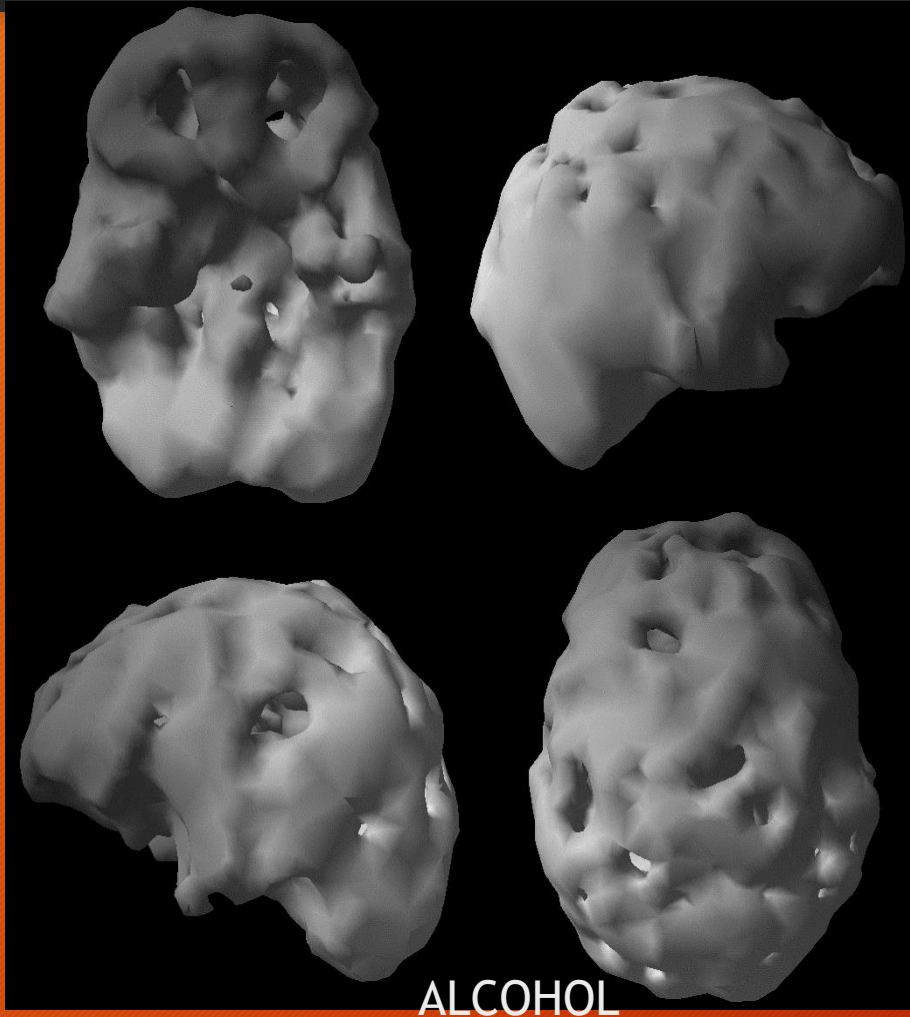
- A common test of short term memory
- Say the digits slowly in a monotone at one second intervals
- Patient must say the digit back 75% correct on the first try to be considered as having a digit span of X
- A 2 year old will have a digit span of 2, a 3 year old-3, 4year old-4
- Average for 7 year old-7 thru adult

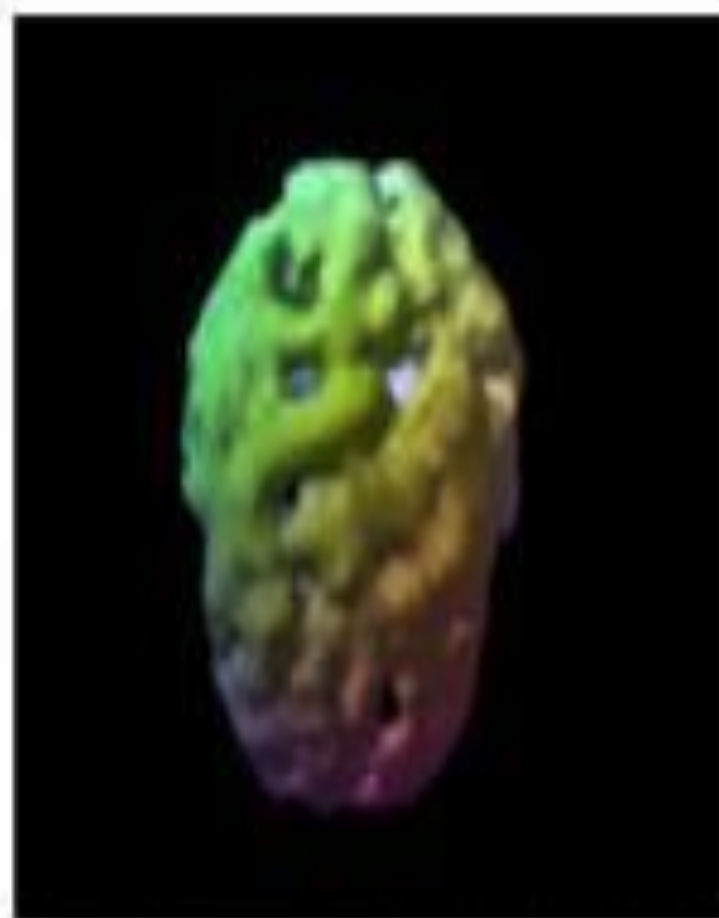
71504  
284936  
8351609  
25736184  
940627135  
2753180649

Controls  
11  $\pm$  2.5

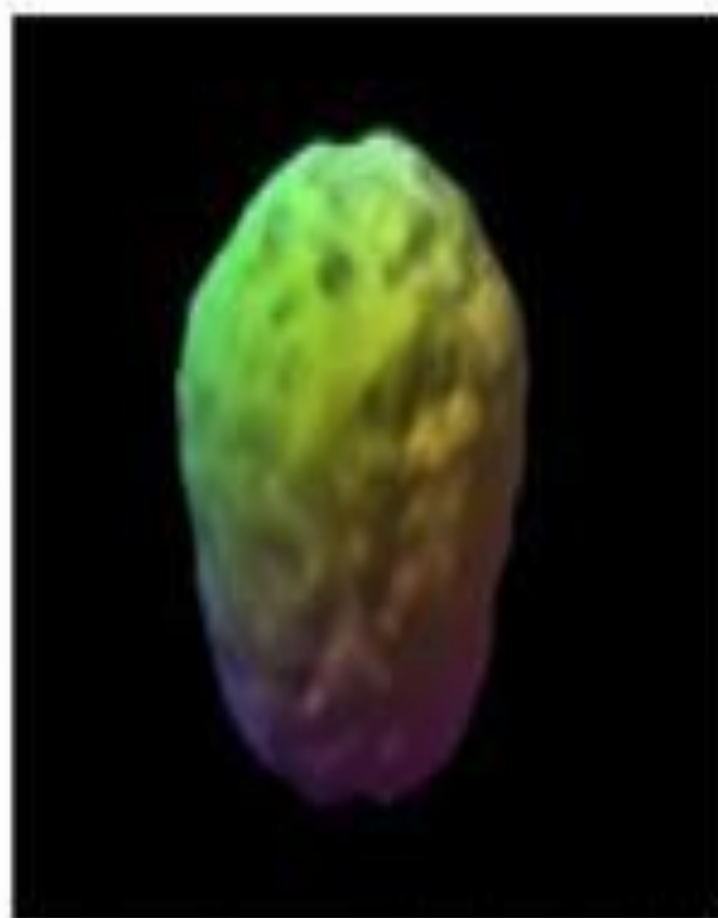
Alcoholics  
9.2  $\pm$  2.7

# XANAX and Alcohol

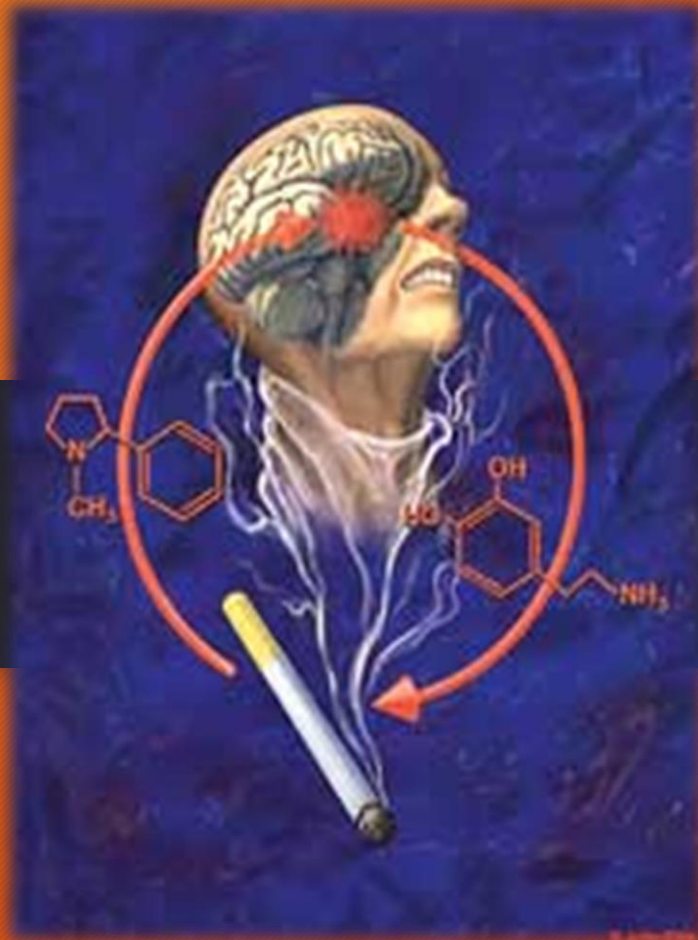




Active drug and alcohol abuse



A year drug and alcohol free



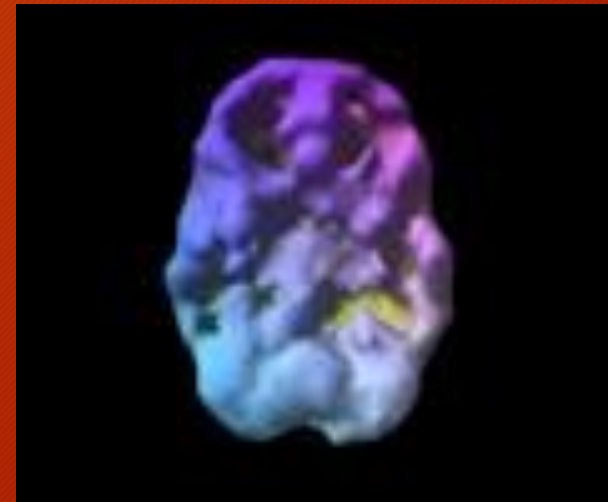
# Smoking

The worst addiction

# Cognitive Effects of Chronic Smoking

- The effect of smoking on measures relying on response speed were independent of IQ
- Suggesting a more specific processing speed deficit associated with chronic smoking

45 y/o – 27 year history of Smoking 3 packs of cigarettes and drinking 3 pots of coffee daily



Glass, J, et al. *Addiction*. 2009 Jan;104(1):38-48. *Effects of alcoholism severity and smoking on executive neurocognitive function.*

# The Whitehall II study is based on employees of the British Civil Service

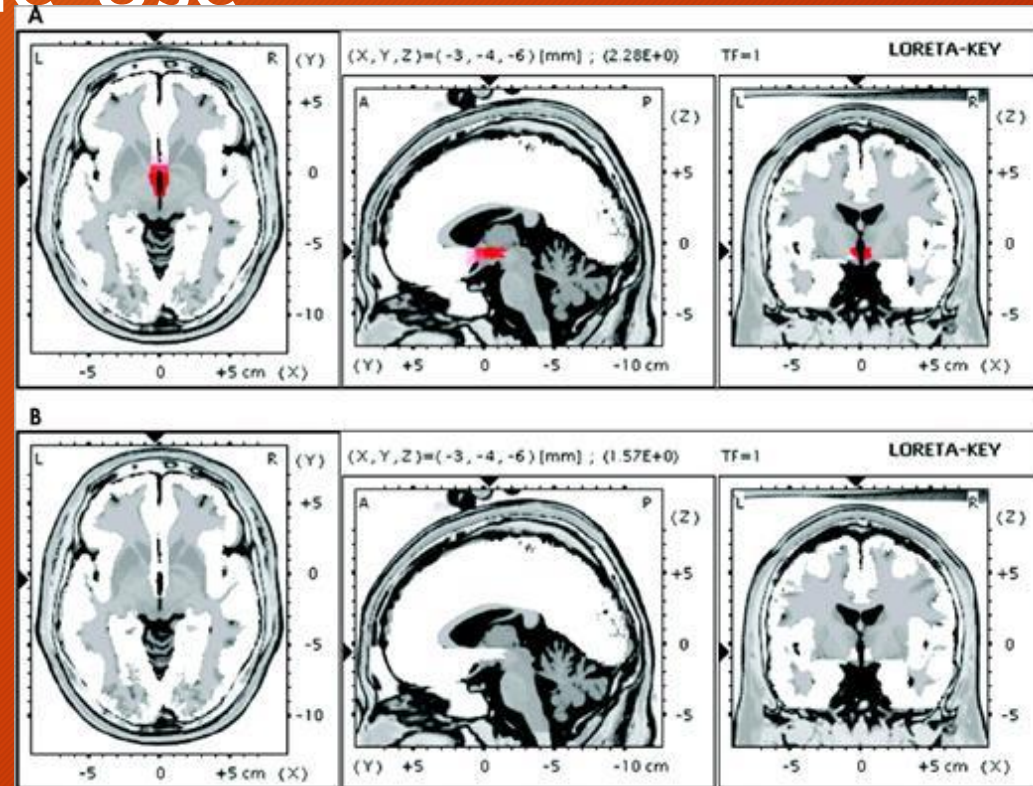
- Analysis of data of over **7,000** using 6 assessments of smoking status over **25 years** and 3 cognitive assessments over 10 years.
- 1. Men: smoking was associated with faster cognitive decline; analyses using pack-years of smoking suggested a dose-response relation.
- 2. Men: who continued smoking over the follow-up experienced greater decline in all cognitive tests.

## The Whitehall II study is based on employees of the British Civil Service

- 3. Men who quit smoking in the 10 years preceding the first cognitive measure **were still at risk** of greater cognitive decline, particularly in executive function. However, long-term ex-smokers did not show faster cognitive decline.
- 4. Association between smoking and cognition, particularly at older ages, is likely to be **underestimated** owing to higher risk of death and dropout among smokers.

# QEEG and Nicotine Use

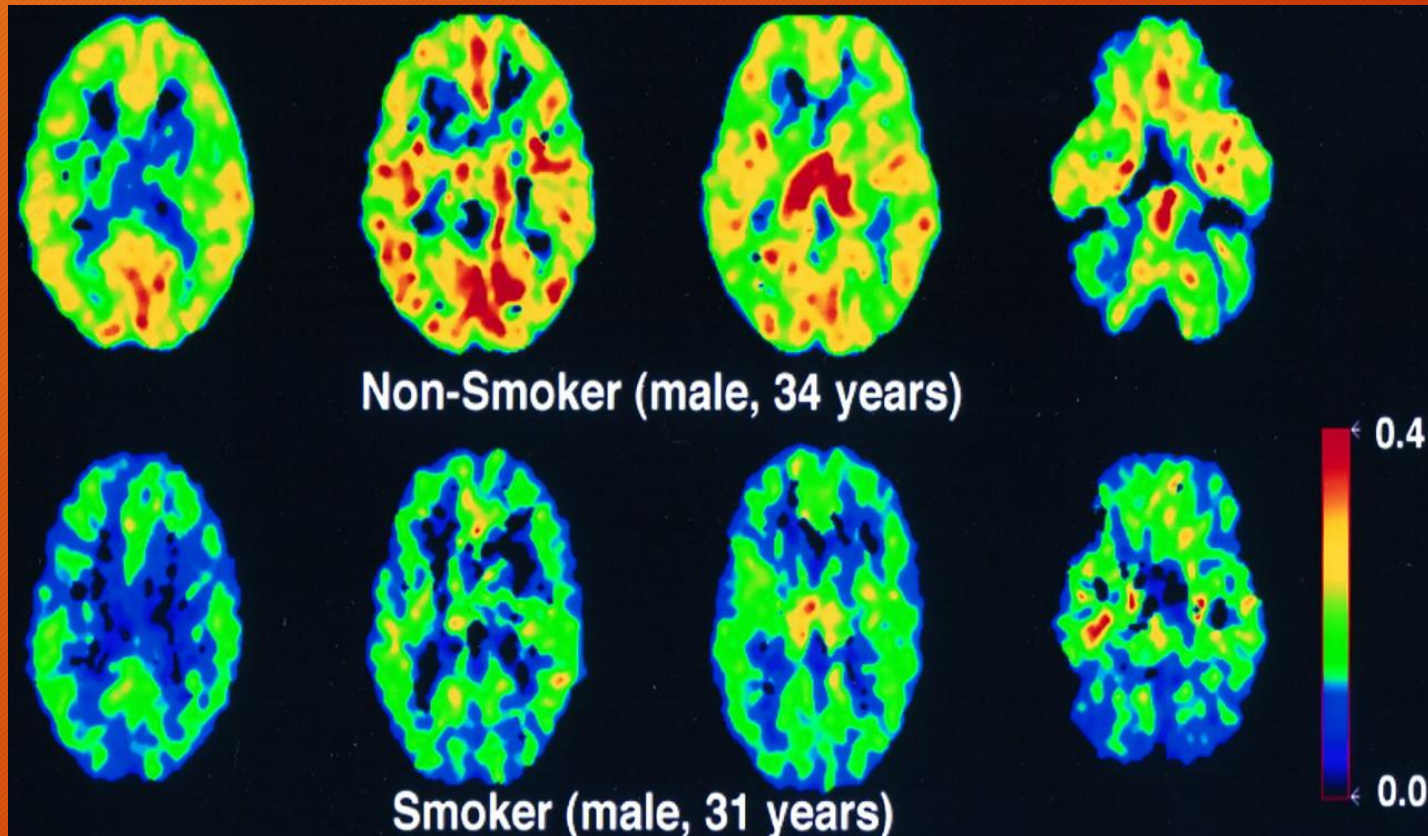
- Neuroelectric source analysis [LORETA] revealed hypoactivation of
- anterior cingulate,
- orbitofrontal cortex
- prefrontal cortex
- of smokers and former smokers, as compared to never-smokers.



Neuhaus A, et al; Persistent dysfunctional frontal lobe activation in former smokers. *Psychopharmacology*. 2006;186:191-200



# Loss of MAO in brains Of smokers



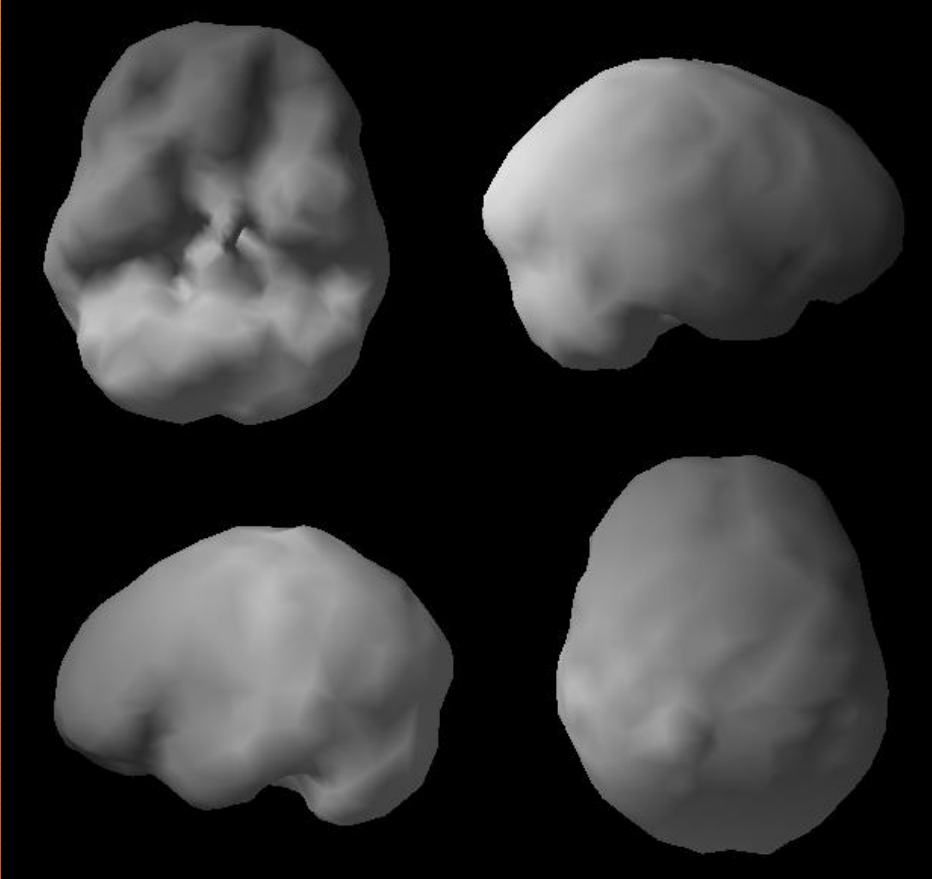
MAO's are important Enzymes in the break down of Neurotransmitters Like **Serotonin**, **Norepinephrine** and **Dopamine**



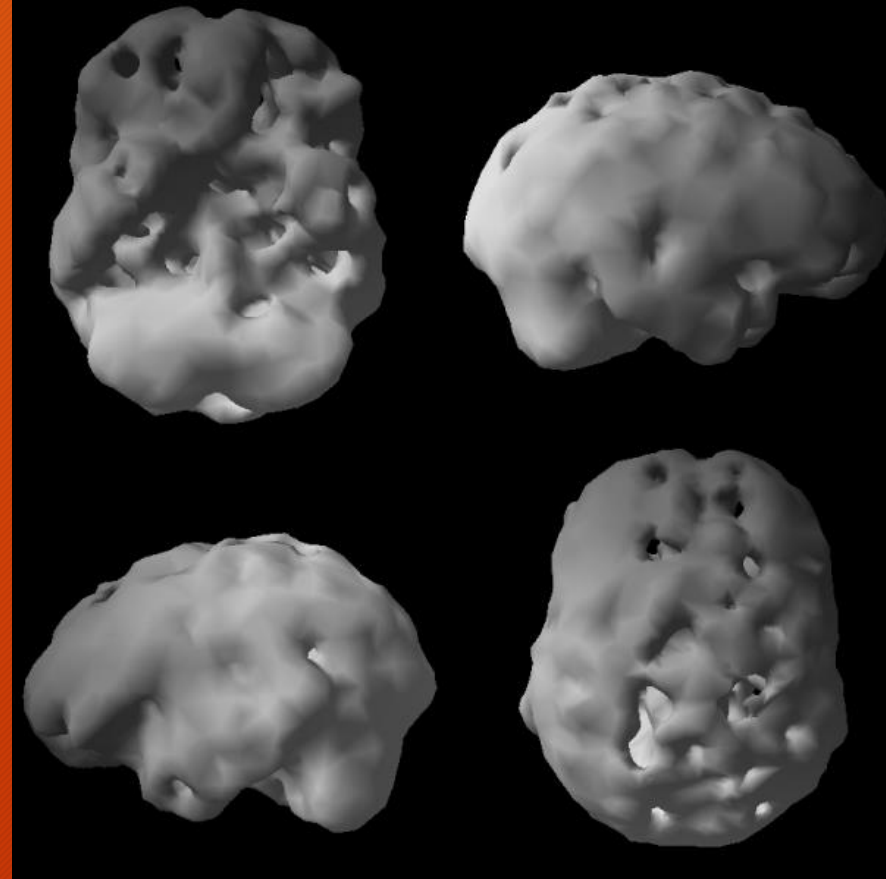
COCAINE

? Our next epidemic?

Healthy Brain



Cocaine Damaged Brain



*Unchain your brain*, Amen, D and Smith D;  
2010, Mindworks Press.

# Cognitive Impairment: Cocaine

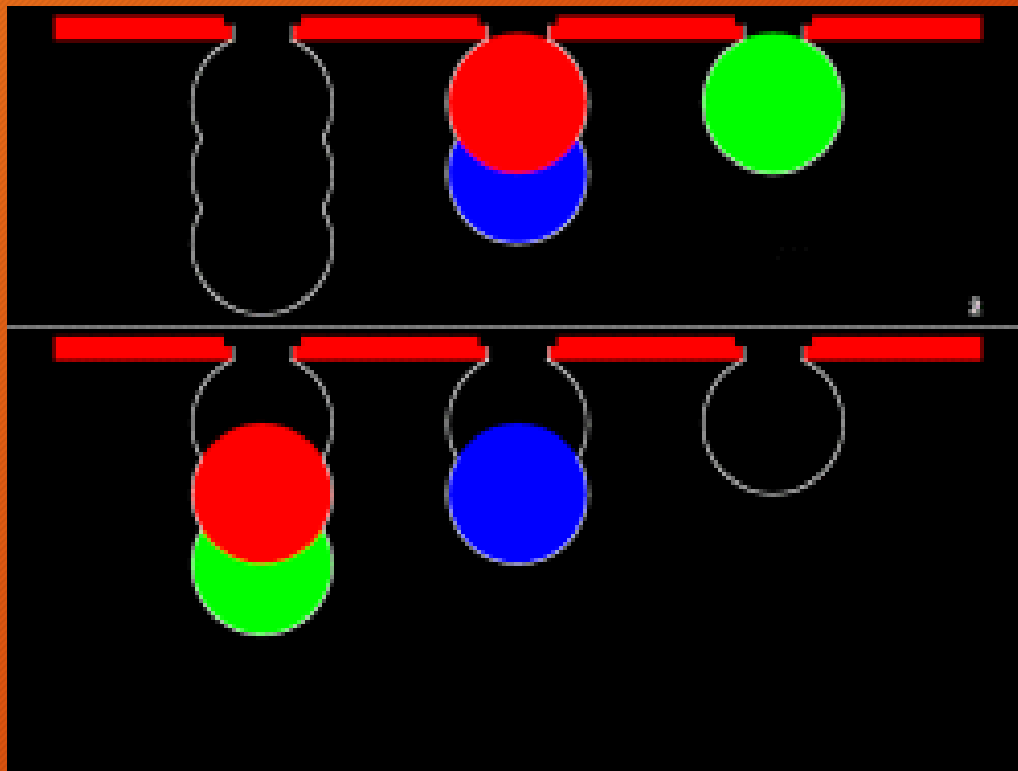
- Compared with healthy subjects, cocaine abusers had deficits on tasks that tested attention, executive function, and verbal memory.
- The deficits were most obvious in the cocaine-addicted individuals who had been abstinent from cocaine longer than 72 hours. “and **this effect was not due to withdrawal-related depressive symptoms.**”
- Surprisingly, the subjects with the **most cognitive impairment reported the least depression** and vice versa.

# Neuropsychological Testing in COCAINE USE

- Chronic cocaine users show performance declines over time in:
- Vigilance
- Reaction time
- Recognition memory
- From binge to abstinence days and during abstinence itself.

Cognitive performance by humans during a smoked cocaine binge-abstinence cycle. [\*American Journal of Drug and Alcohol Abuse\*, Nov, 2005](#) by [Edward F. Pace-Schott](#),

SOC is a spatial planning test which gives a measure of frontal lobe function.



The subject must use the balls in the lower display to copy the pattern shown in the upper display.

The balls may be moved one at a time by touching the required ball, then touching the position to which it should be moved.

The time taken to complete the pattern and the number of moves required are taken as measures of the subject's planning ability.

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**HEROIN**

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**HEROIN HYDROCHLORIDE**

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Write for literature to

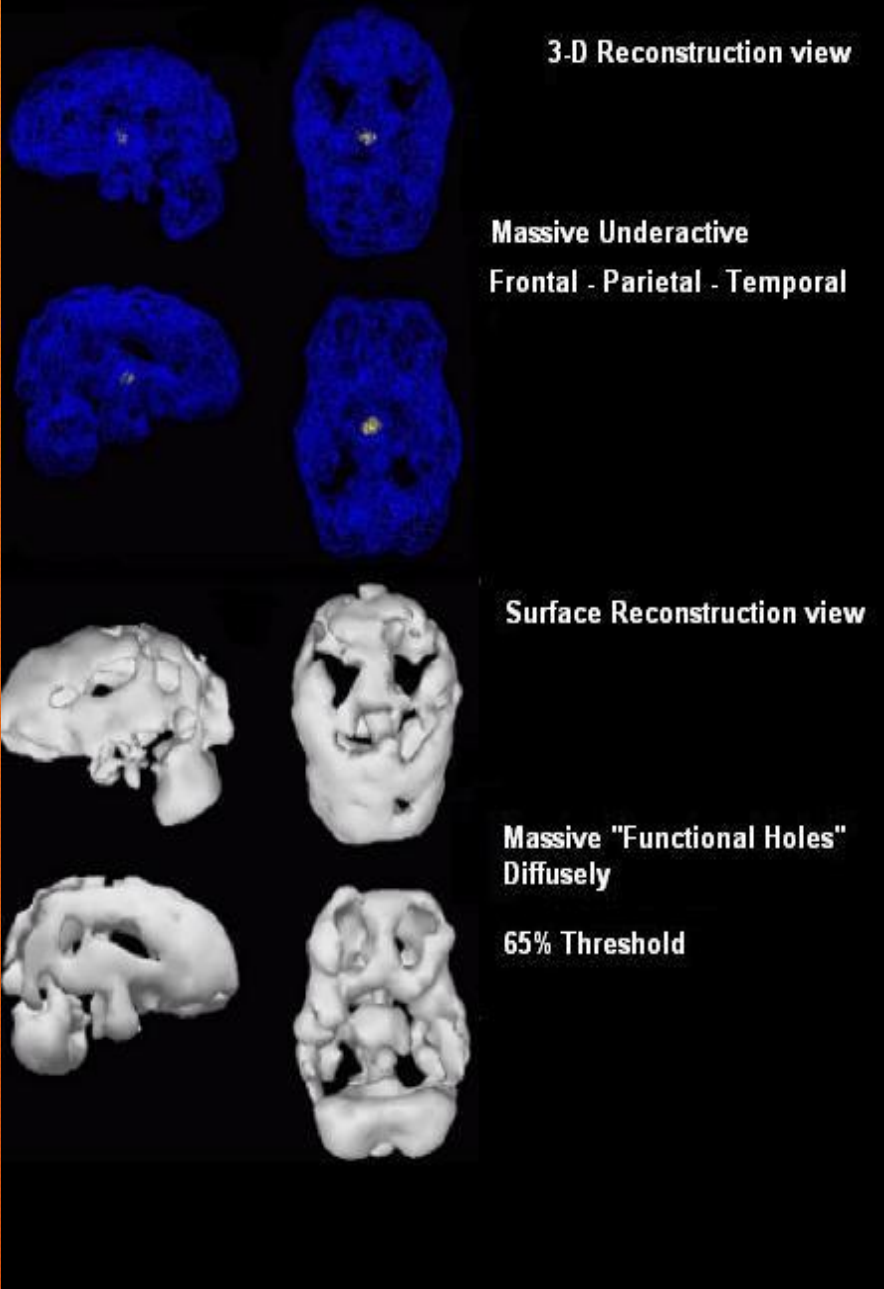
**FARBENFABRIKEN OF ELBERFELD CO.**

40 Stone Street, New York,

SOLE U.S. AGENTS

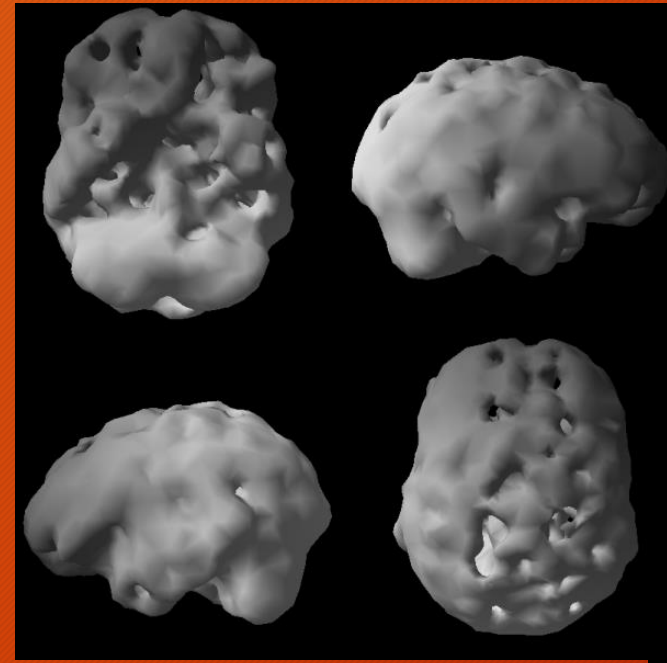
# OPIATES

Brain Effects with:

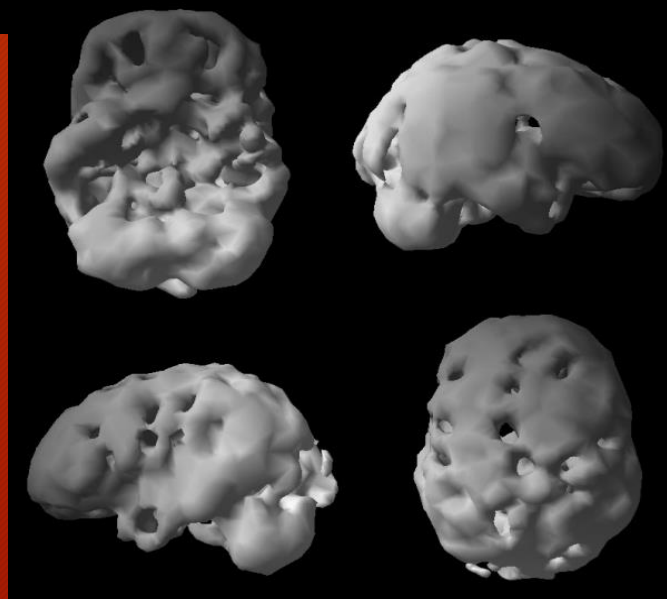


Heroin Damaged Scan

OxyContin Damaged Scan

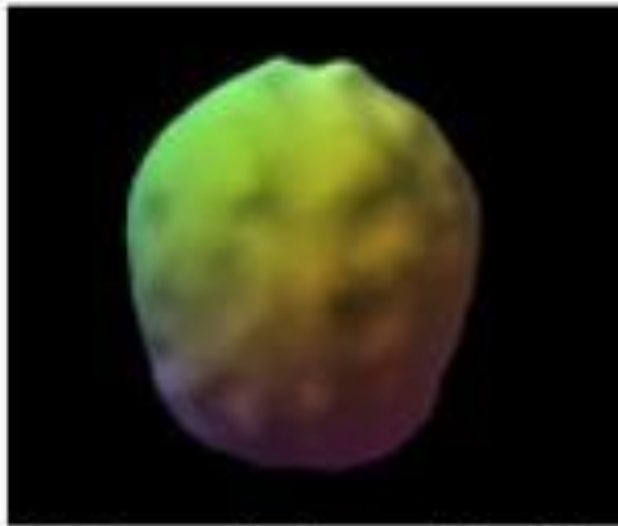
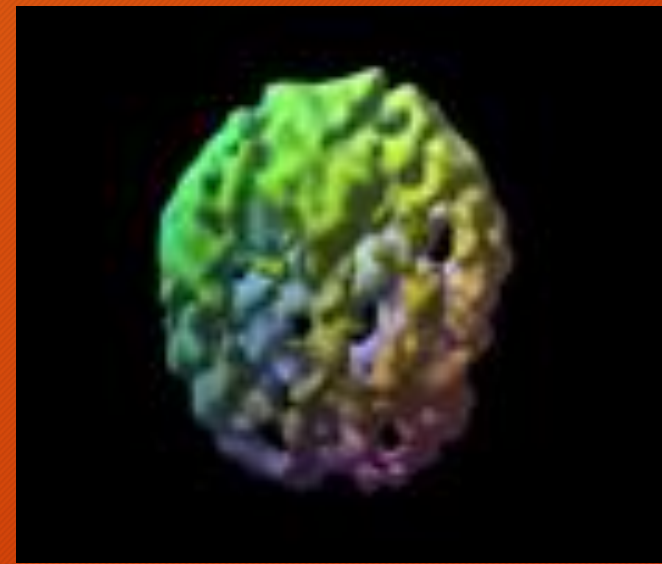


Vicodin Damaged Brain

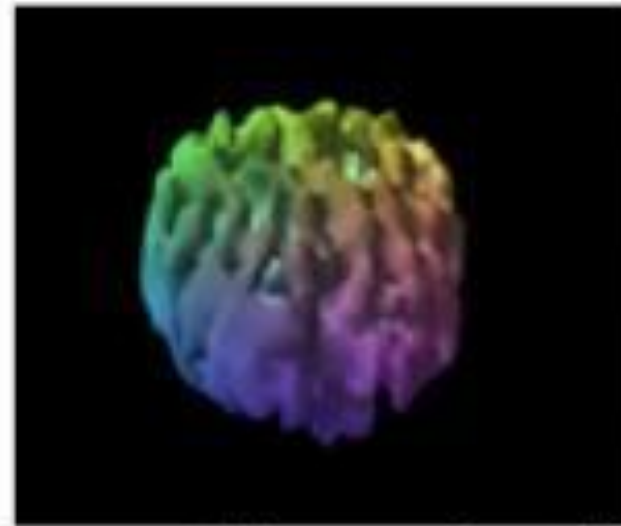




40 y/o, 7 yrs on methadone  
heroin 10 yrs prior



Normal view of brain



25 years of frequent heroin use

# Stroop Effect

YELLOW BLUE ORANGE

BLACK RED GREEN

PURPLE YELLOW RED

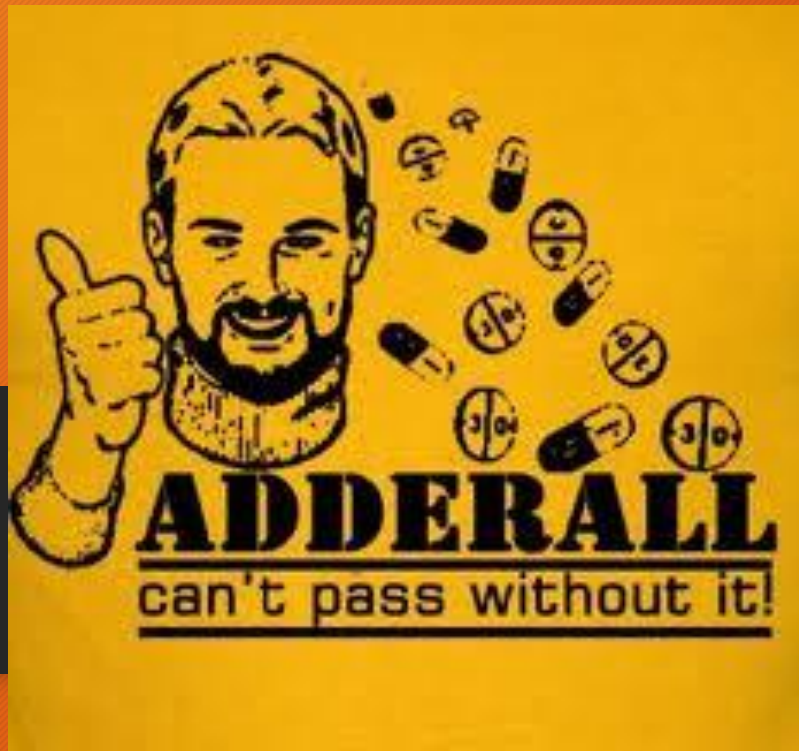
ORANGE GREEN BLUE

BLUE RED PURPLE

YELLOW RED GREEN

# Long Term Opiate User's Cognitive Impairment

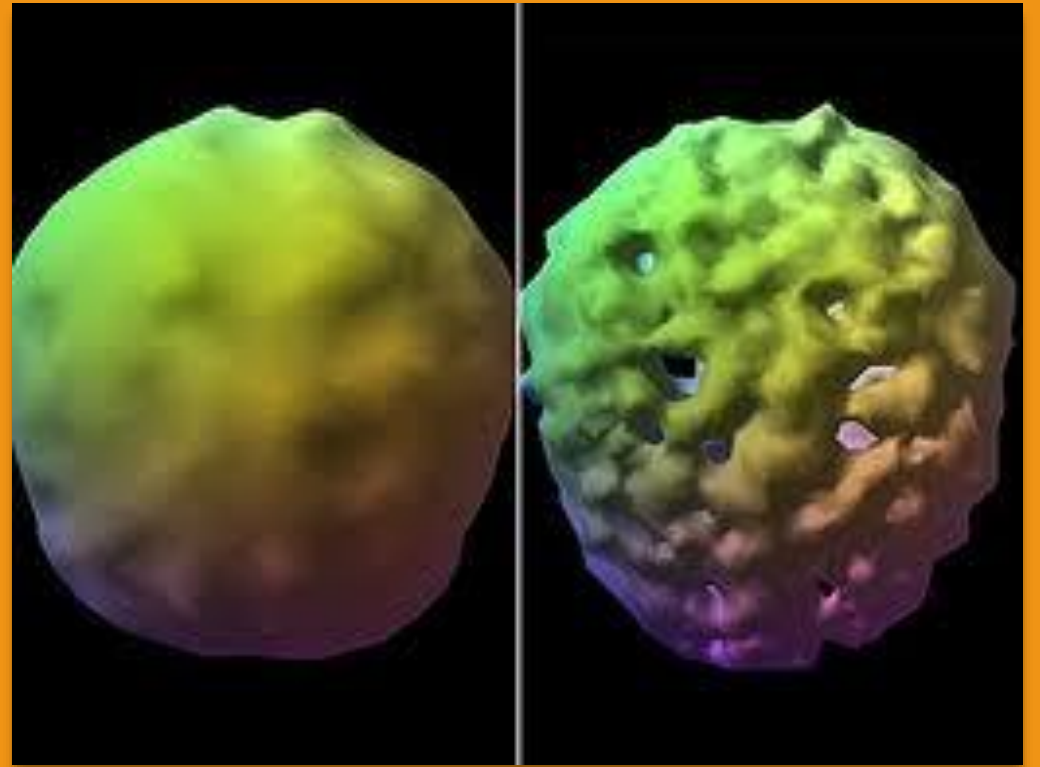
- The results of this study have important clinical implications.
- It seems likely that participants in opiate abuse treatment programs will have **difficulty with attention and memory, and these deficits may persist for months and years past detoxification.**
- Recent studies have suggested that cognitive status may play a role in treatment efficacy



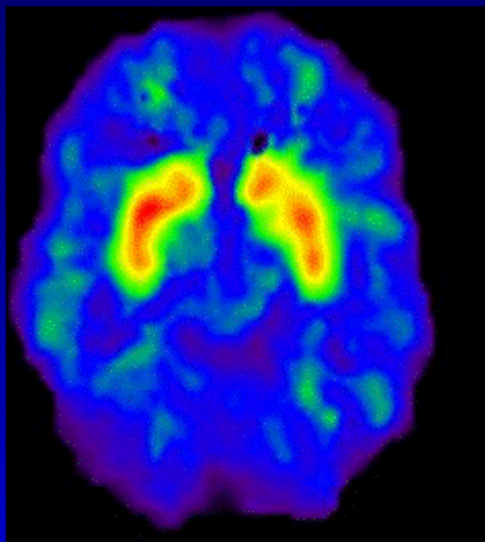
Brain Effects with:

**AMPHETAMINES**

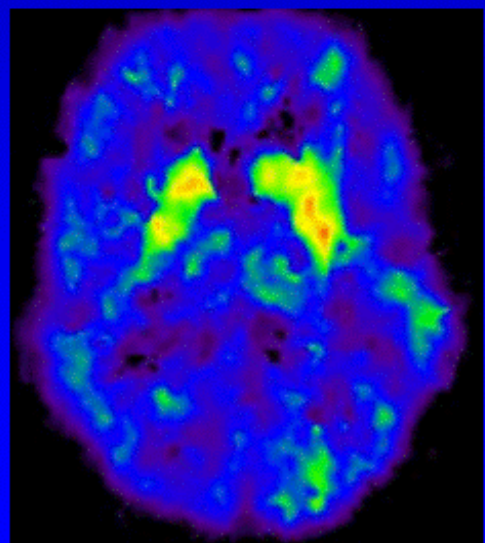
# NORMAL Methamphetamine



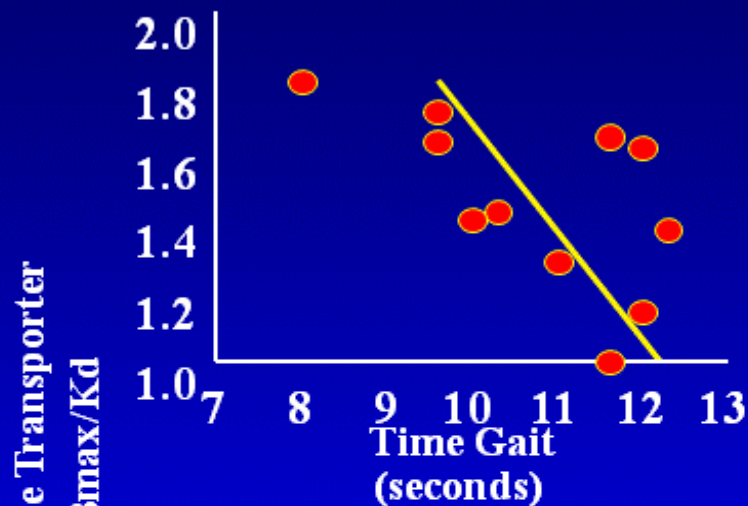
# Dopamine Transporters in Methamphetamine Abusers



Normal Control

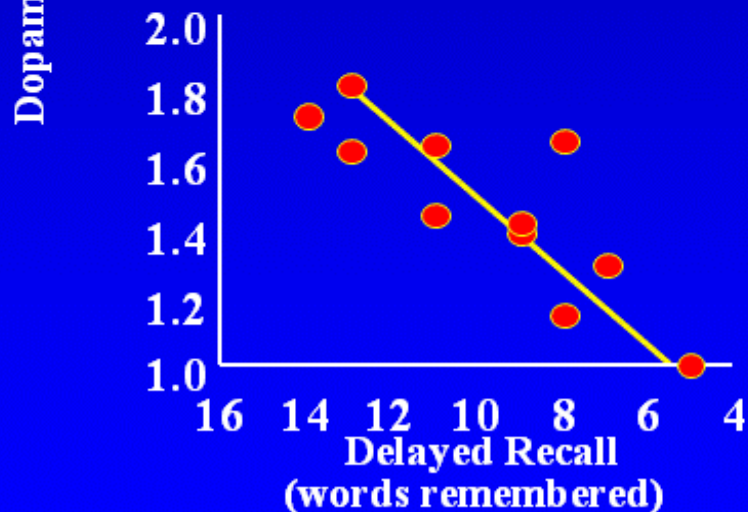


Methamphetamine Abuser



## Motor Task

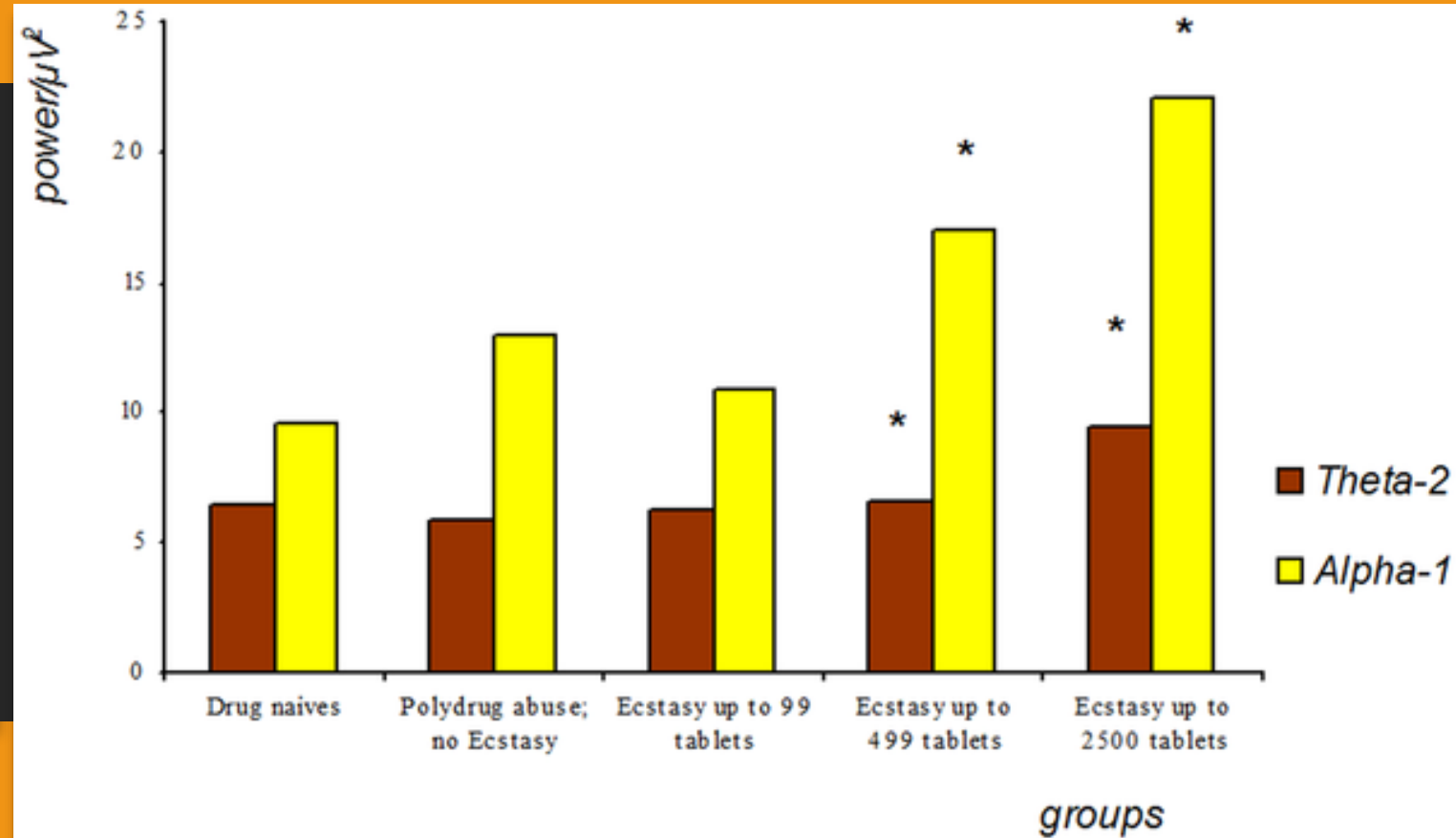
Loss of dopamine transporters in methamphetamine abusers may result in slowing of motor reactions.



## Memory Task

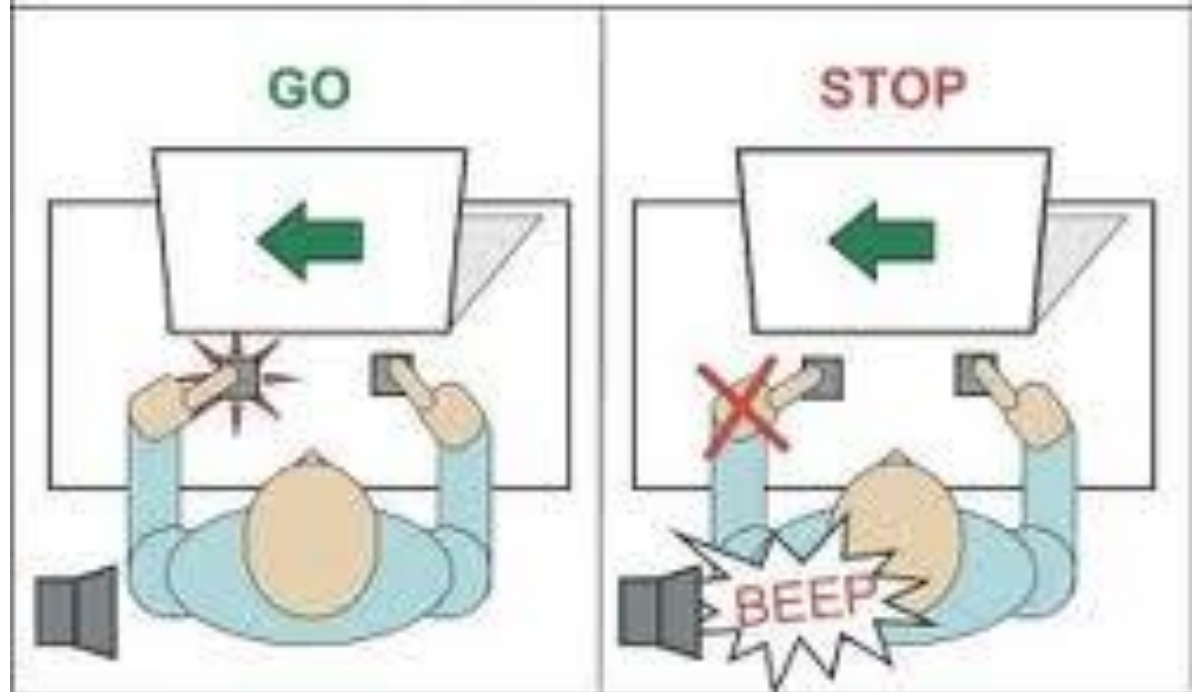
Loss of dopamine transporters in methamphetamine abusers may result in memory impairment.

# QEEG changes in Amphetamine Useage



# STOP SIGNAL TASK

*"press left if the arrow points left  
press right if the arrow points right  
do not press (stop) if you hear the stop tone"*







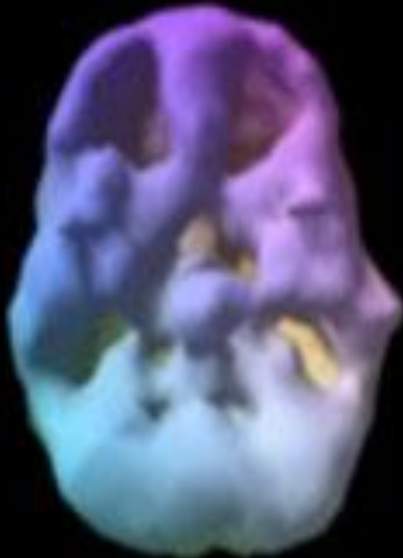
Wow, you ever just like, stare at your foot?



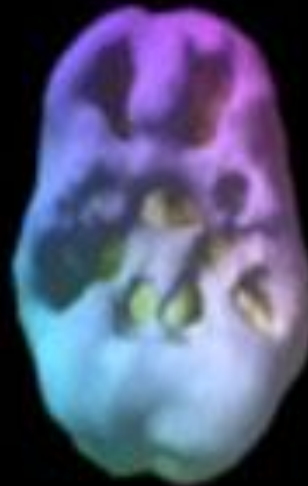
# Marijuana Effects



**Brain Activity:**  
Normal, Healthy Brain  
*(Underside surface)*

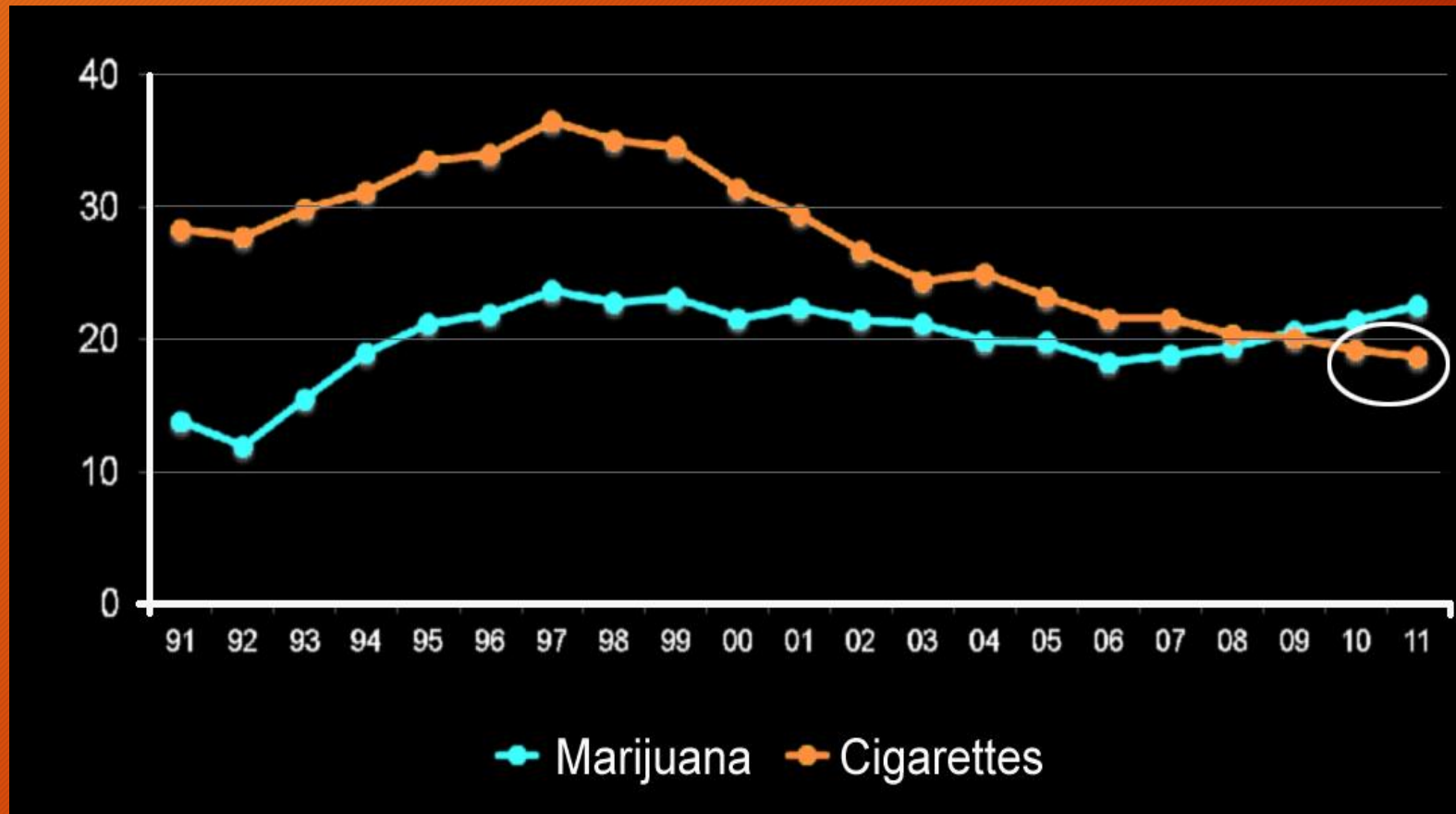


**Brain Activity:**  
18 year old  
3 years of  
4x week  
marijuana use  
*(underside surface)*

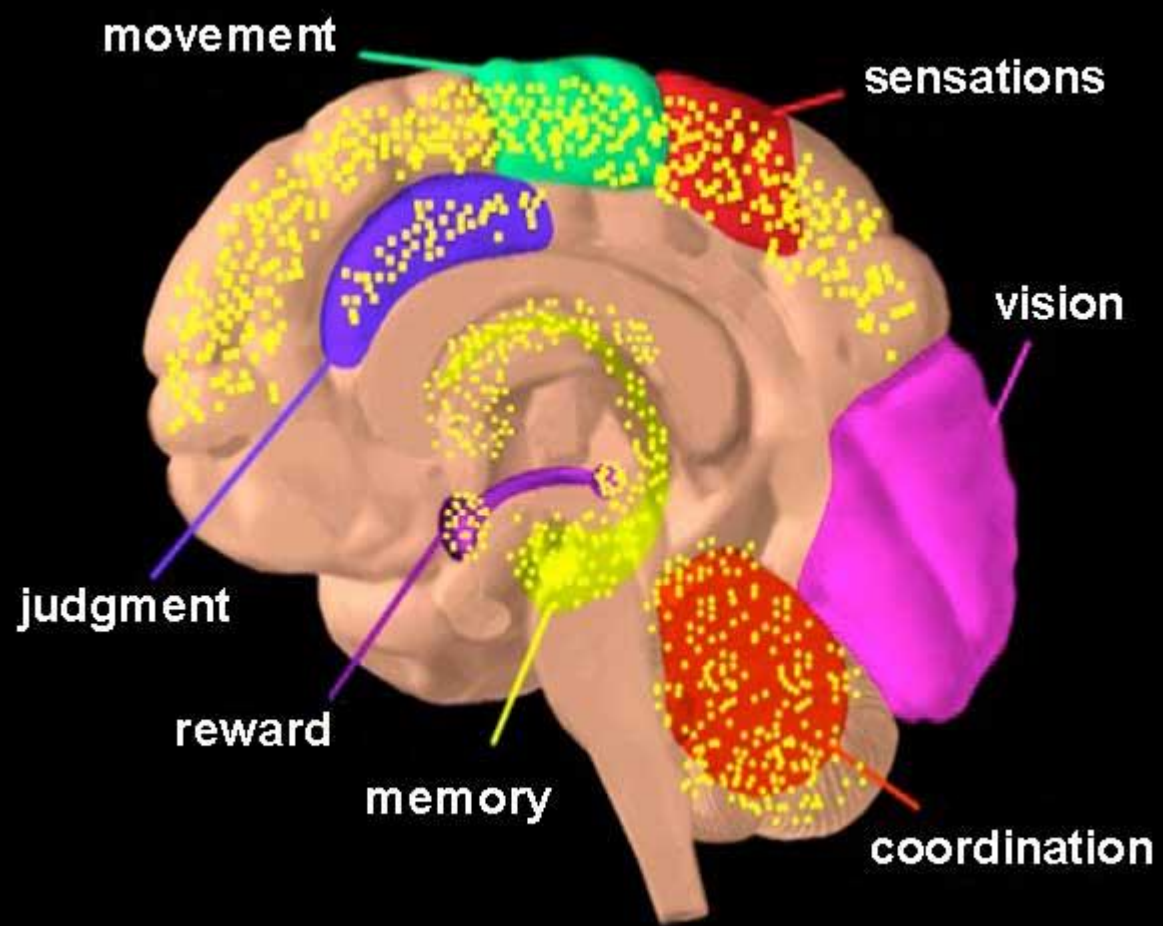
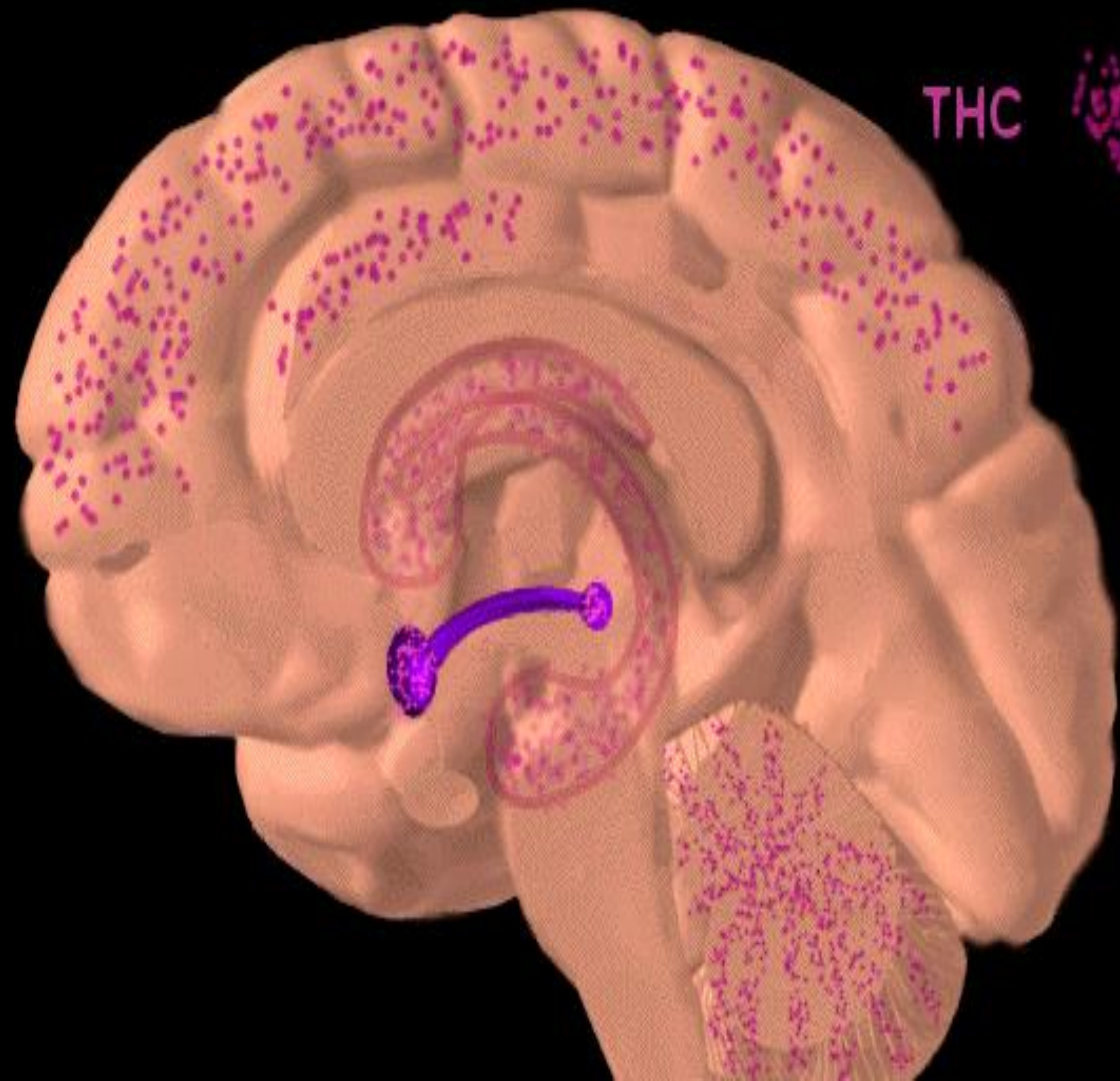


**Brain Activity:**  
16 year old  
2 years of  
daily marijuana use  
*(underside surface)*

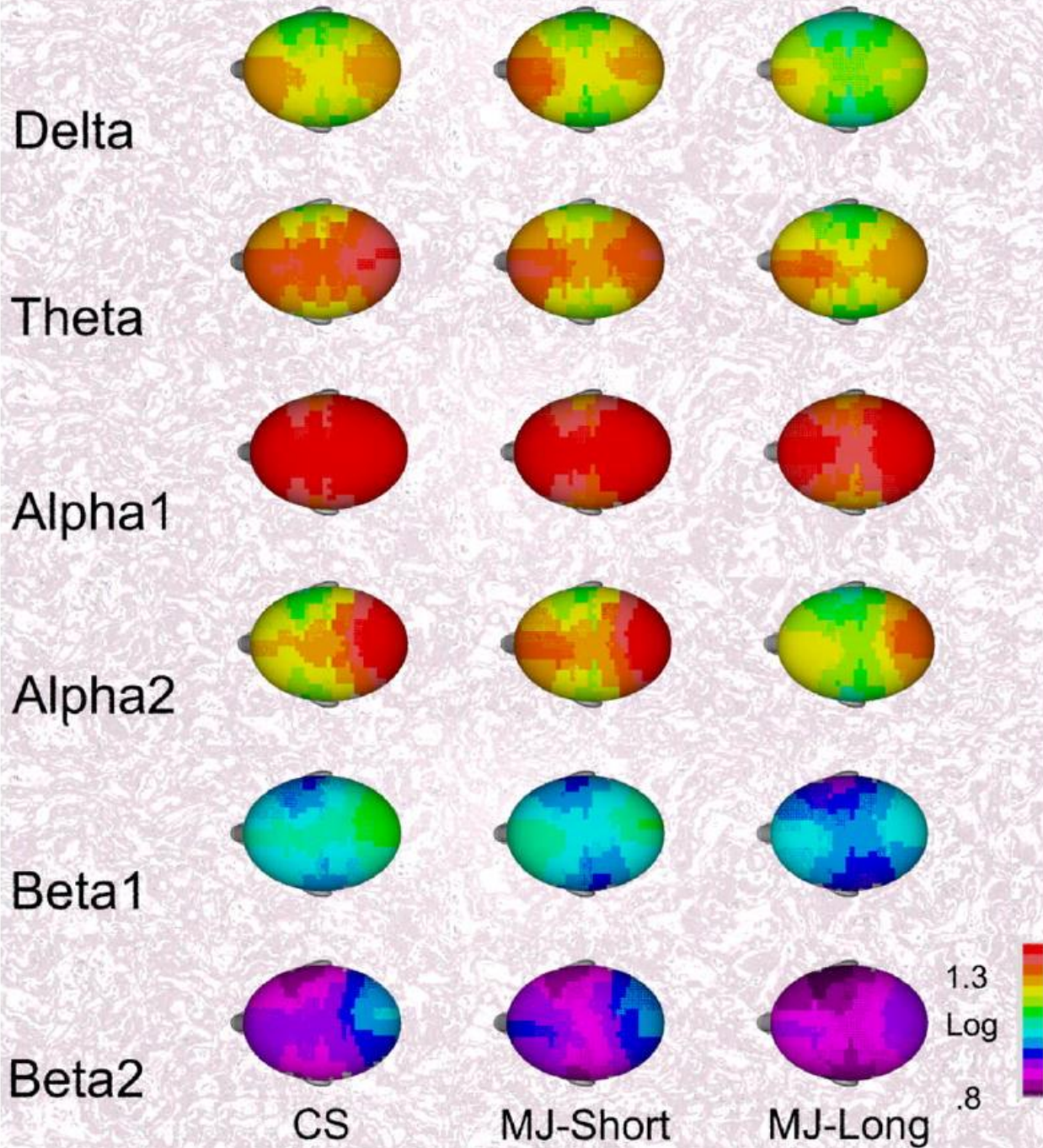
## In 2009, Reports of Past Month Use of Marijuana Among 12<sup>th</sup> Graders Exceeded that of Cigarette for the First Time in the Survey's History



SOURCE: University of Michigan, 2011 Monitoring the Future Study



## Log Power



The mean topographical maps of log power for the six EEG bands are shown for the three groups.

The mean maps for the control subjects (CS) and marijuana subjects using for less than eight years (MJ-Short) appear similar

The maps of the marijuana subjects using more than eight years appear to have less EEG power.

Herning, R. I., Better, W., & Cadet, J. L. (2008). EEG of Chronic Marijuana Users during Abstinence: Relationship to Years of Marijuana Use, Cerebral Blood Flow and Thyroid Function. *Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology*, 119(2), 321-331. <http://doi.org/10.1016/j.clinph.2007.09.140>

# Cognitive Impairment: Marijuana

- NIDA study at McLean Hospital revealed that college students who used THC had impaired skills related to
  - Attention
  - Memory
  - Learning
  - 24 hours after they last used the drug

Pope, H G, Yurelun-Todd, D. The residual cognitive effects of heavy marijuana Use in college students. *Journal of American Medical Association*, 275 (7): 521-527, 1996

# Cognitive Impairment: Marijuana

- Study at University of Iowa College of Medicine
- Frequent Marijuana users (7 or more times weekly)
- Deficits in Mathematical skills
- Verbal expressions
- Memory -retrieval processes
- Youths with a GPA of D or below were 4 times more likely to have used THC than those with a GPA of A

# Cognitive Impairment: Marijuana

- Other Impairments:
- Sensory and time perception
- Problems with driving
- Difficulty with sports performance
- Effects may be especially problematic during teen's peak learning years when brain is still developing.



# September 2012 NIH Study Results

- NIH-funded research shows that long-term marijuana is associated with impaired intellectual functioning, especially if usage starts during the teen years.
- Over **1,000** study participants were given neuropsychological tests in early adolescence, prior to initiation of marijuana use, and then re-tested in mid adulthood after **20 + Years**.



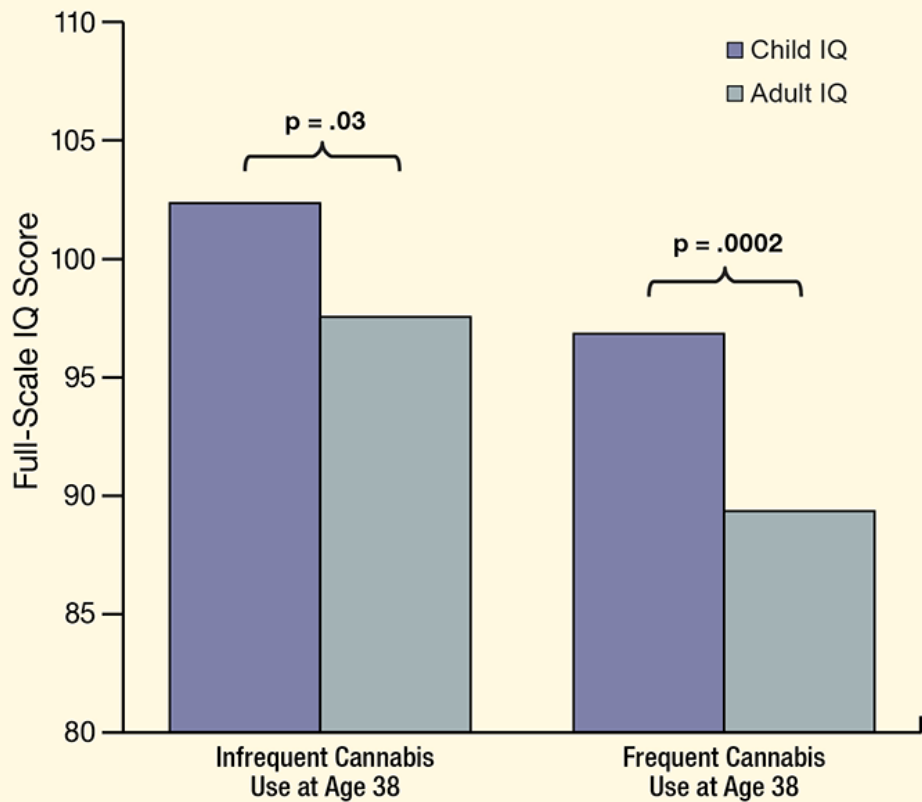
[Meter, et al Long-term effects of adolescent-onset and persistent use of cannabis. \[Proc Natl Acad Sci U S A. 2012\]](#)

# September 2012 NIH Study Results

- Study members with more persistent marijuana dependence showed greater IQ decline and greater impairment across five different cognitive domains, especially executive function and processing speed.
- The study was thus able to rule out pre-existing differences in IQ between heavy marijuana users and others; it is also significant for including degree of cannabis exposure and age of onset as factors.

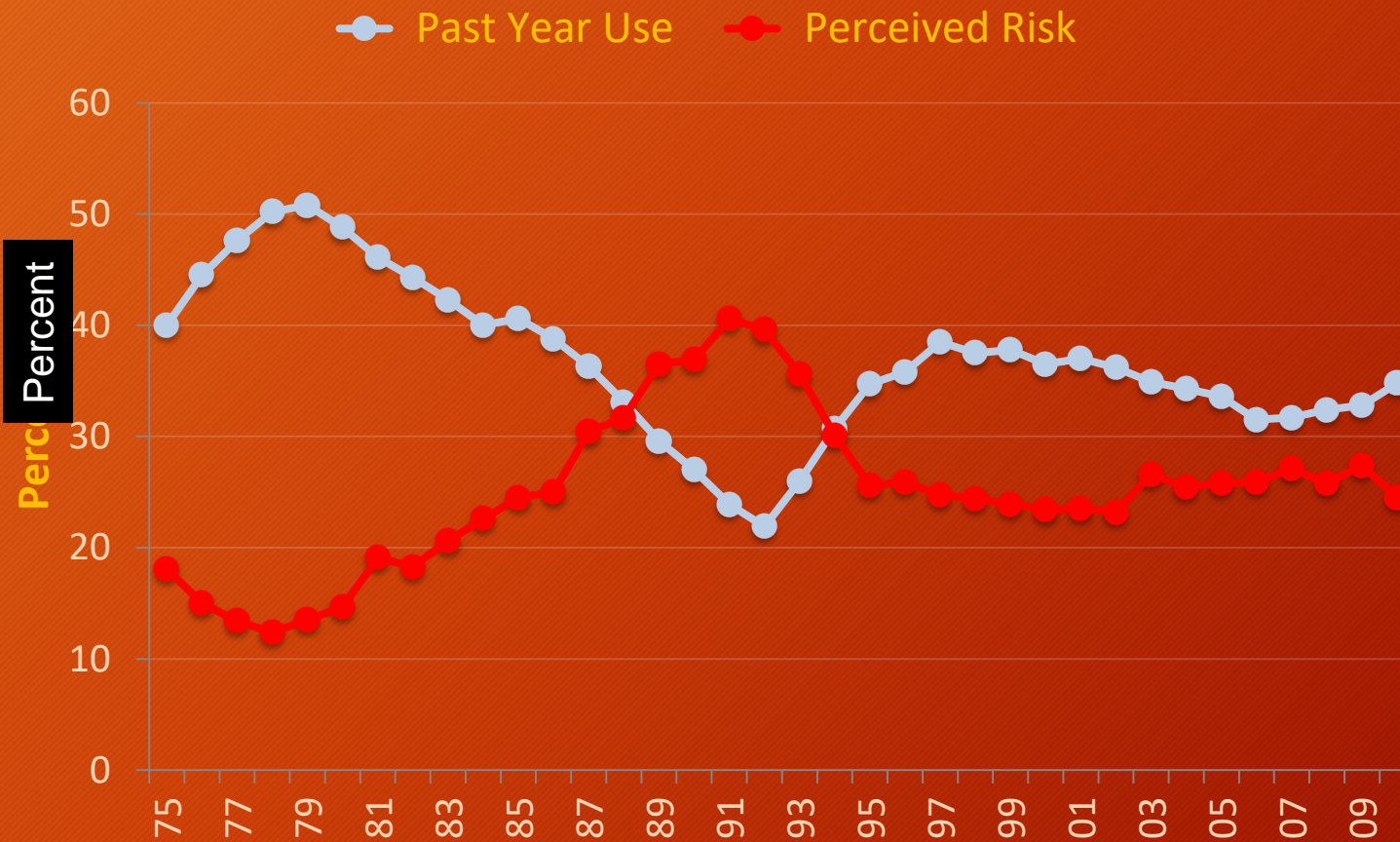


# September 2012 NIH Study Results



- Those who started use during the teen years showed greater IQ decline than those who began use as adults.
- These latter results are especially troubling, given recent data showing **increased marijuana use** among teens over the last five years, along with declines in perceived risk of harm associated with use.

# Changes in Attitude Lead to Changes in Use: Marijuana Use and Perceived Risk in 12<sup>th</sup> Graders, (1975 to 2010)



Source: The Monitoring the Future study, the University of Michigan



# Bath Salts

# Bath Salts Overview

- Not the bath salts you use in your tub!
- Designer drug that contains substituted cathinones
- Methylenedioxypyrovalerone (MDPV), mephedrone & methylone most commonly used
- Classified as Schedule I substance in October 2011

# History

- Cathinone: found naturally in the plant *Catha edulis* (**khat**)
  - Beta-keto analog of **amphetamine**
- 1<sup>st</sup> synthetic cathinones synthesized in late 1920s
- Limited therapeutic use due to serious side effects
- Emerged as popular designer drugs of abuse in 2000's
- Permanent Psychosis is real risk

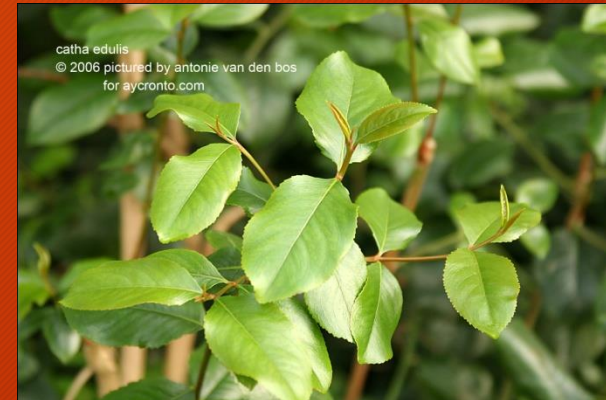


Photo From:  
<http://www.botanypictures.com/plantimages/catha%20edulis%204%20NL%20uithof%20grethouse.jpg>

# Snorted, Smoked or Injected

- Extreme Agitation
- Hallucinations & Delusions
- Chest Pain
- Suicidal Thoughts
- High Blood Pressure
- Acute Toxicity
- Hyperthermia
- Delirium
- Violent Behavior
- Foaming at the Mouth
- Extreme Paranoia
- Delusional Paracitosis
- Parkinson-Type Limb Twitching
- Paranoia
- Severe Insomnia





# Common Names<sup>3,4</sup>

- Ivory Wave
- Purple Wave
- Red Dove
- Blue Silk
- Zoom
- Bloom
- Cloud Nine
- Drone
- Meow Meow
- Plant Fertilizer
- Ocean Snow
- Lunar Wave
- Vanilla Sky
- White Lightning
- Scarface
- Hurricane Charlie
- Bliss
- Energy-1
- Stardust
- Insect Repellent

# Neurocognitive Effects: Few Studies

- Only few studies have investigated cognitive deficits associated to mephedrone exposure in humans.
- Freeman and colleagues found that mephedrone users showed significant deficits in working memory performance compared to controls.
- Herzig and colleagues instead speculated that “mephedrone consumption does not necessarily exert a negative impact on cognitive functioning by itself. Instead, mephedrone users are likely those individuals who are prone to consuming other psychoactive drugs in conjunction with mephedrone.”

Hallucinogens

Hallucinogens

# Hallucinogenic Drug effects related to neurotransmitters:

- **Serotonin:**

LSD, psilocybin, DMT

- **Norepinephrine:**

amphetamine related,  
mescaline, MDMA

- **Acetylcholine:**

atropine, scopolamine

- **Dissociative anesthetics:**

PCP, ketamine



# Impairment related to Hallucinogens

- Persistent palinopsia:  
Visual changes,  
afterimages
- Visual Snow
- Can last for months to years,  
causing significant depression



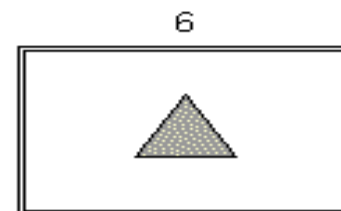
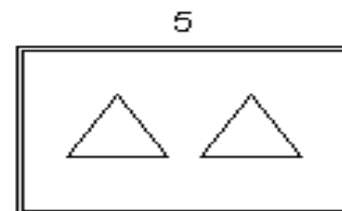
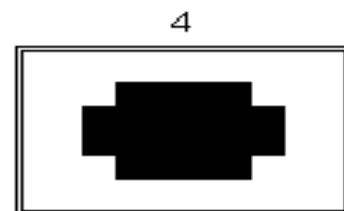
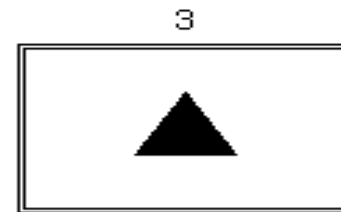
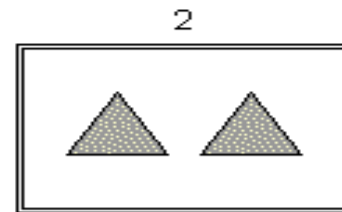
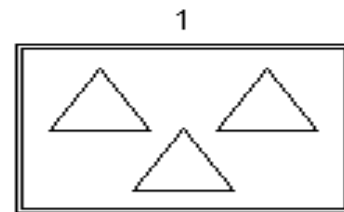
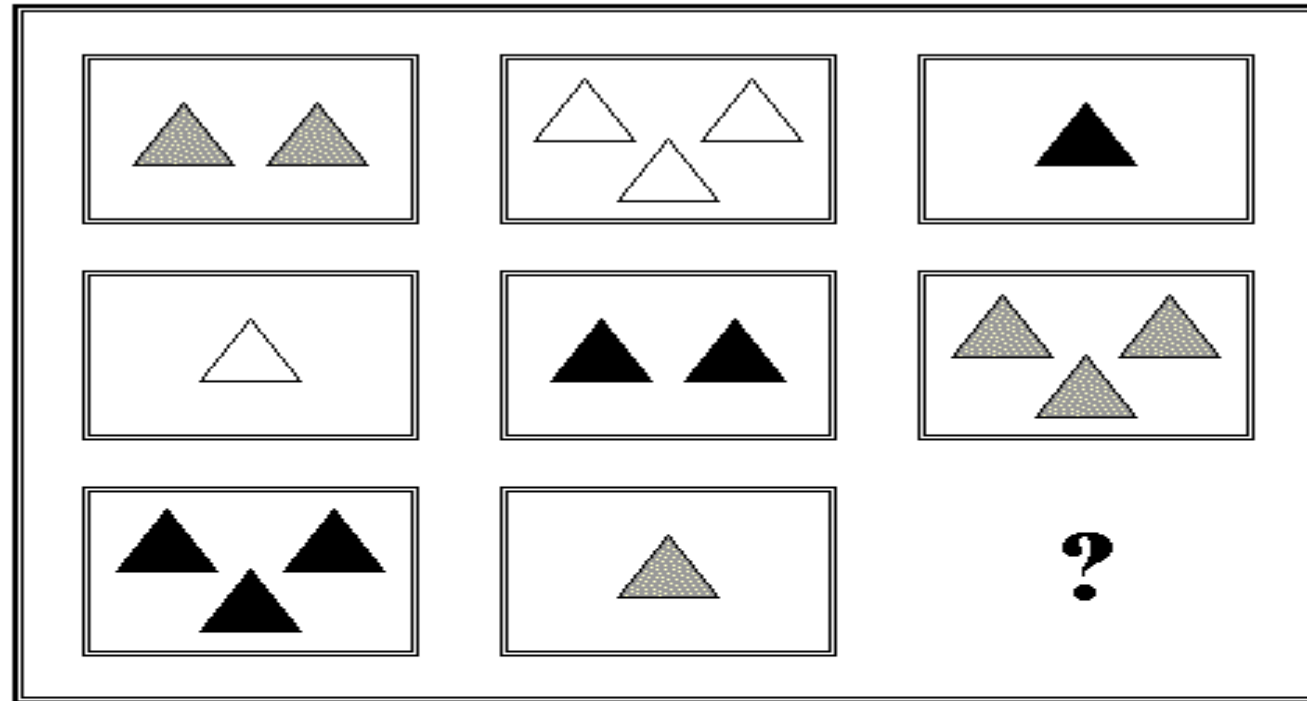
- Flash backs
- Psychosis- which may be permanent

# Neuropsych Testing

- Cohen and Edwards reported impaired **visuospatial orientation** among 30 LSD users in contrast to 30 controls
- The authors also found that performance on the **Reitan Trail Making Test A and B** and the **Ravens Matrices** correlated negatively with extent of LSD use.

# Ravens Matrices

Which answer fits in the missing space to complete the pattern?



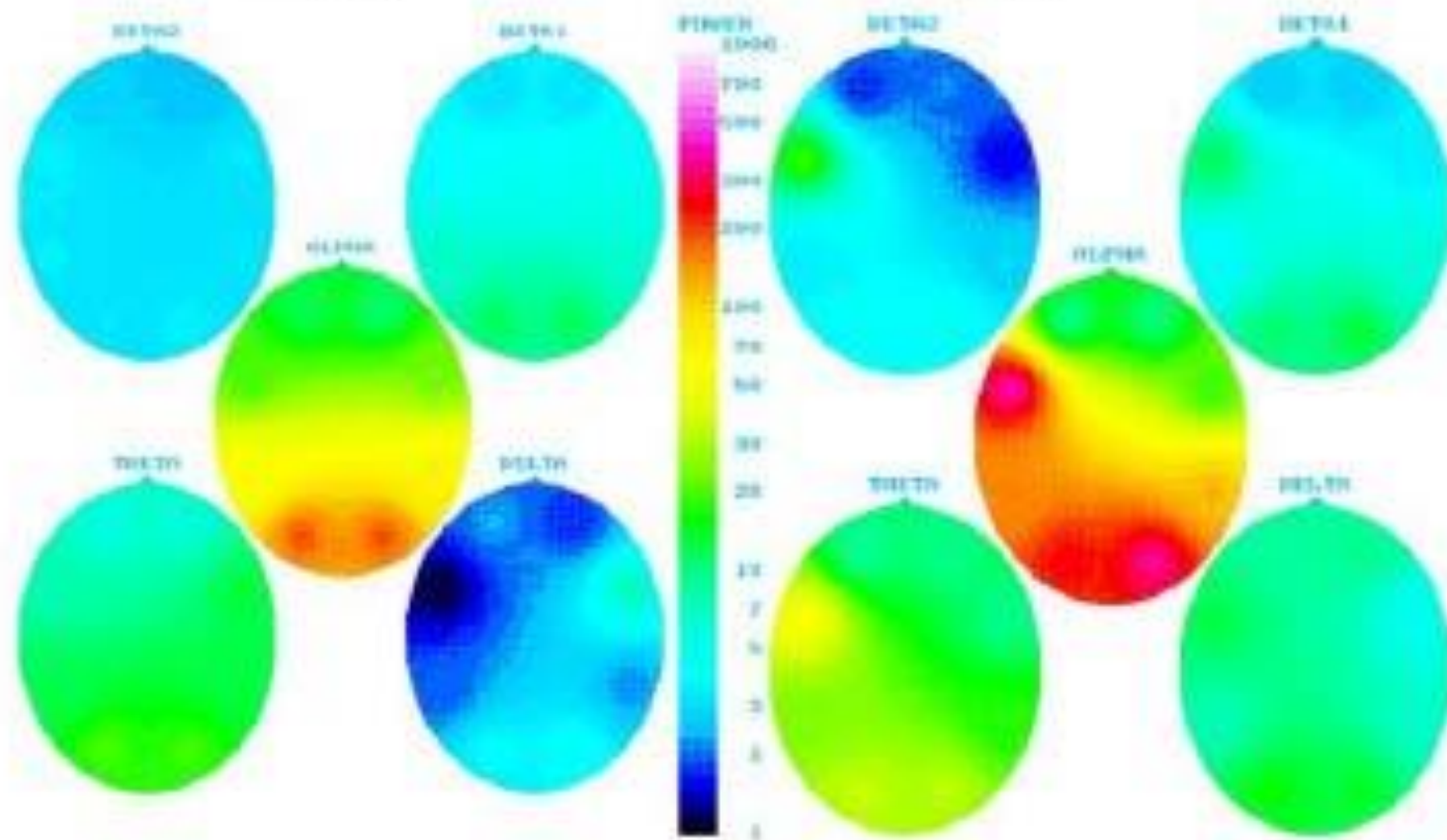
# EEG and LSD

- Blacker et al. (1968) compared 21 LSD users (whom the authors referred to as 'acidheads') with unmatched controls
- The investigators found subtle electroencephalographic (EEG) changes in the LSD group in comparison to controls, with **increased alpha, beta, delta, and theta activity** and increased visual evoked response amplitudes at the dimmer intensities.



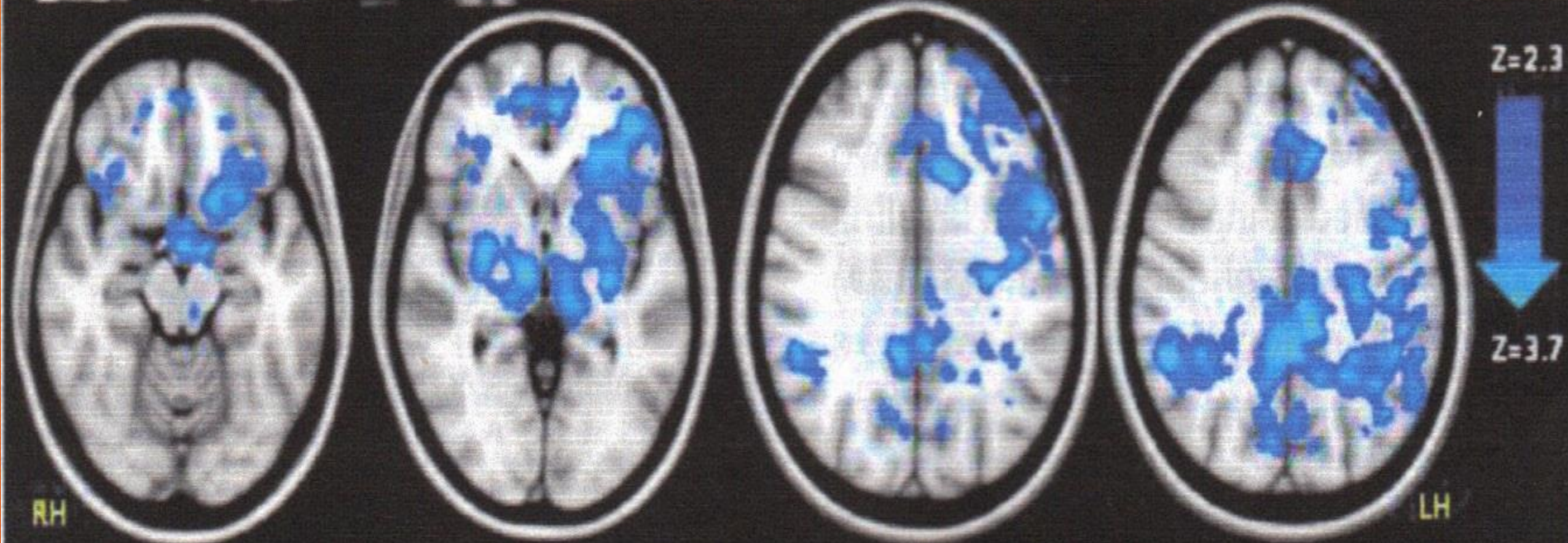
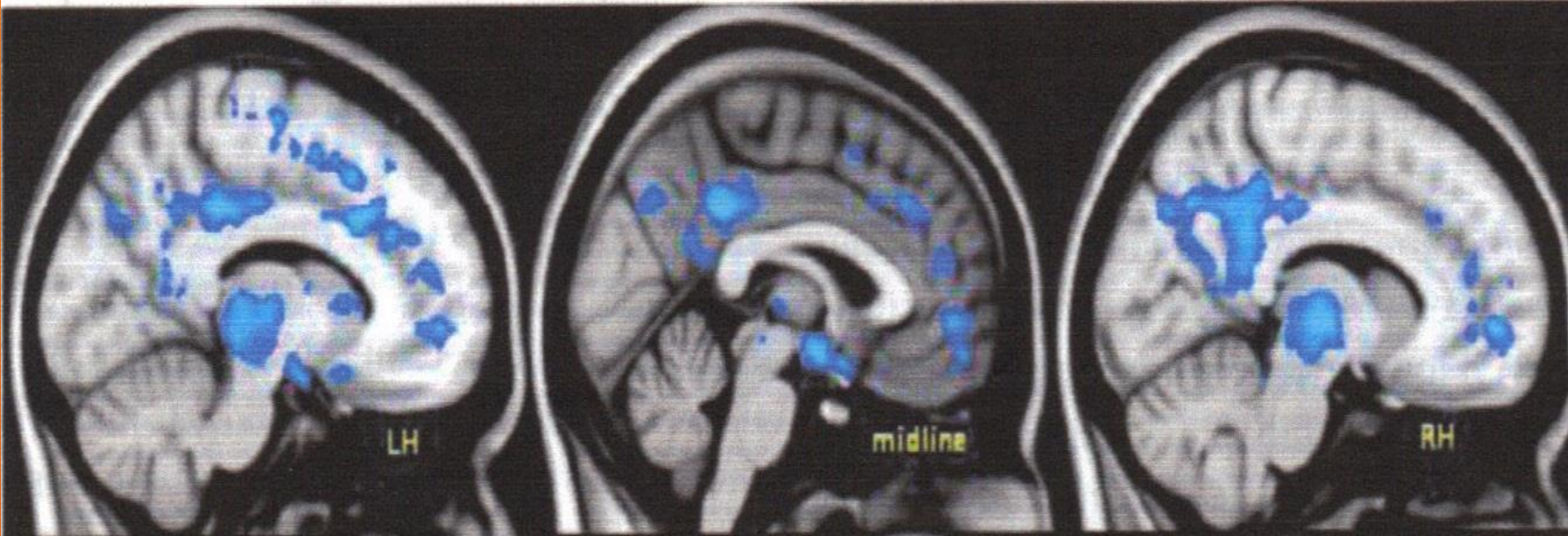
Before drinking Ayahuasca

After drinking Ayahuasca



Brainmaps showing strongly increased alpha and theta activity following the intake of Ayahuasca

A current paper in the prestigious Proceedings of the National Academy of Science, "Neural Correlates of the Psychedelic State As Determined By fMRI Studies with Psilocybin" by Carhart-Harris, et.al from Oxford, Imperial College London, University of Bristol, Cardiff University and University of Copenhagen, is the first to examine how the active material in mushrooms, psilocybin, works in the brain.



Decreased CBF after psilocybin v after placebo

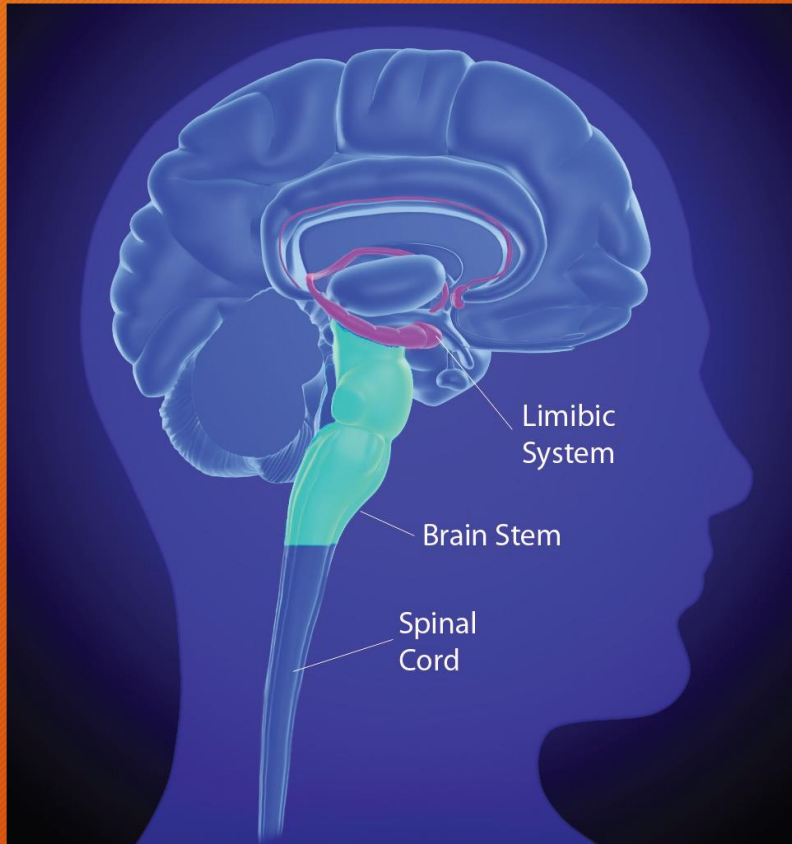
# Adverse Effects

- Prolonged Panic Attack
- Tremor
- Agitation
- Insomnia
- Nausea
- Headache
- Tinnitus
- Vertigo
- Muscle Twitching
- Dizziness
- Elevated Heart Rate
- Altered Vision
- Confusion
- Short-term Memory Loss
- Anhedonia
- Depression
- Suicidal Thoughts
- **Psychosis**

# Neuroendocrine Dysfunction

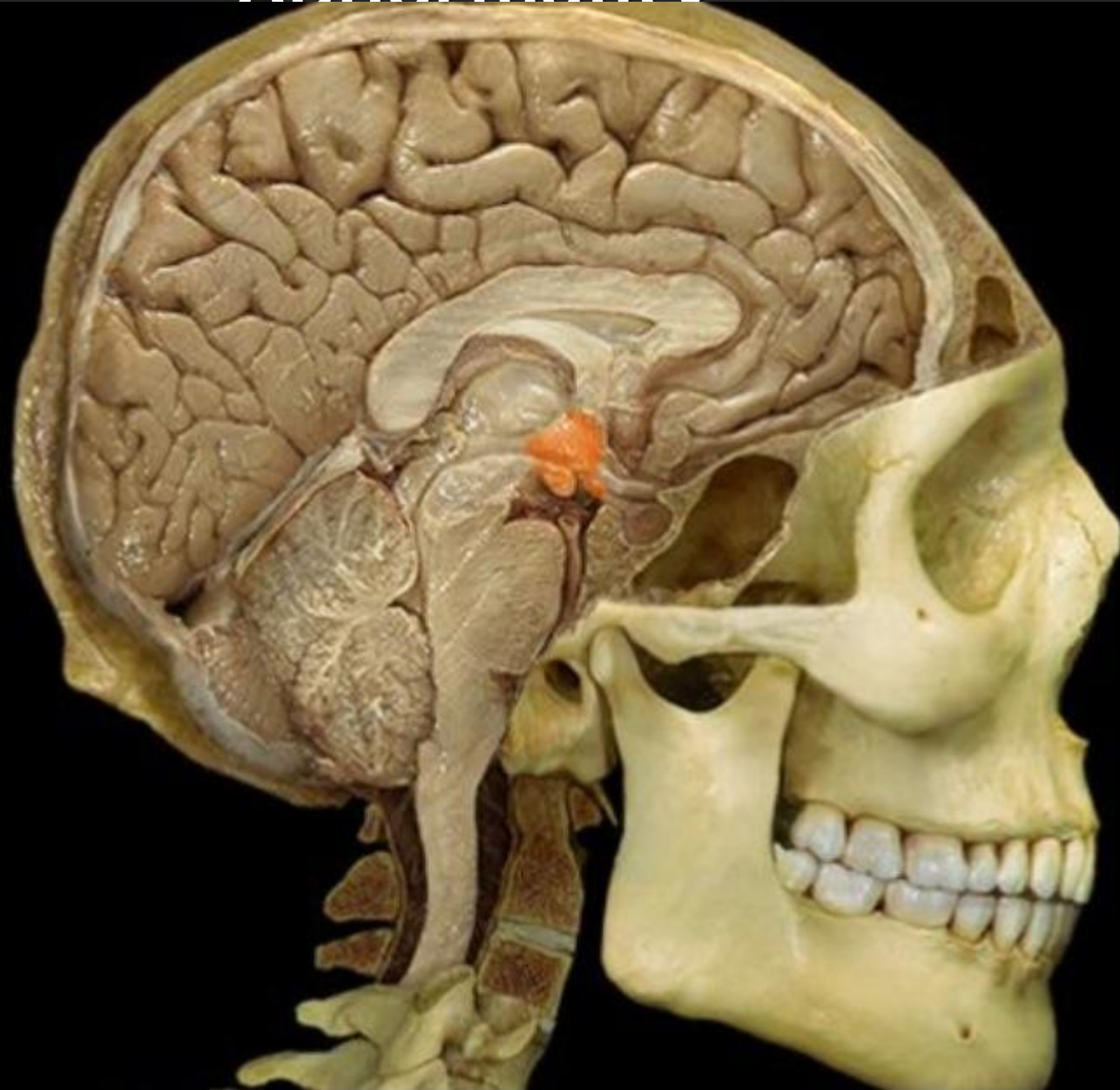
Hormonal Issues in patients with Substance Use Disorder

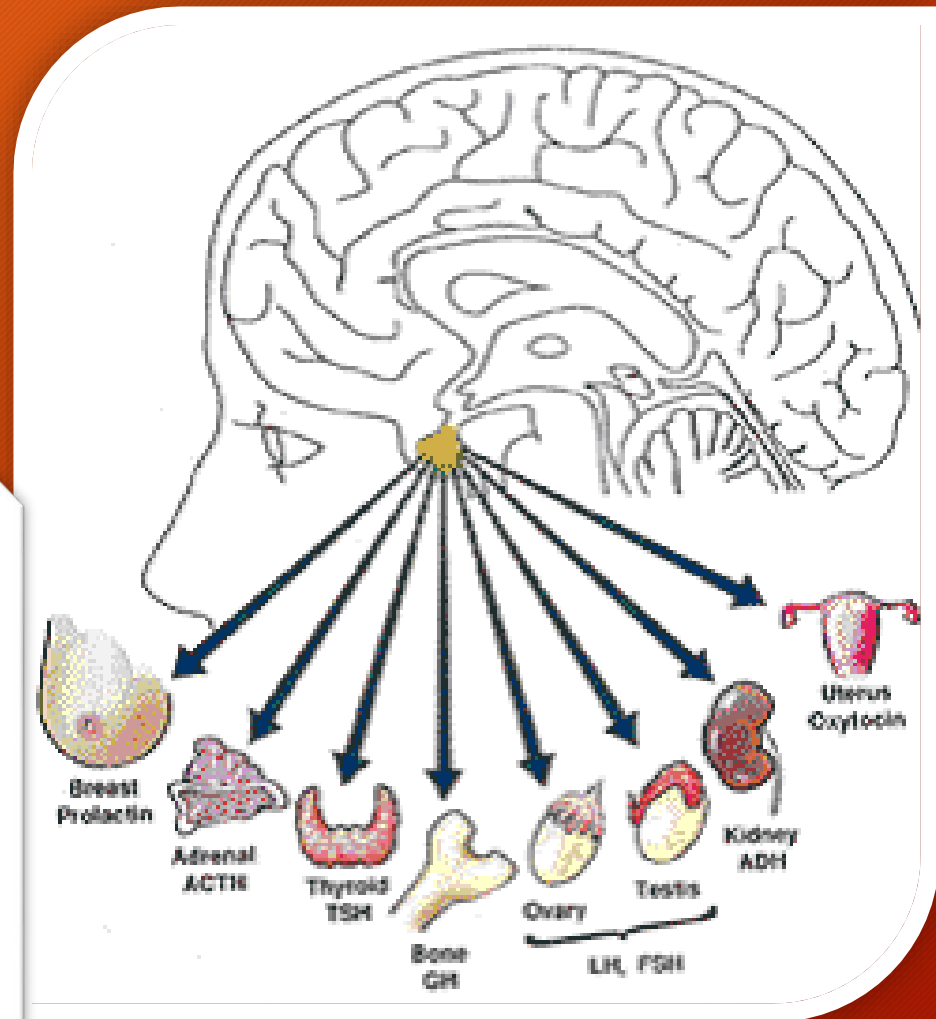
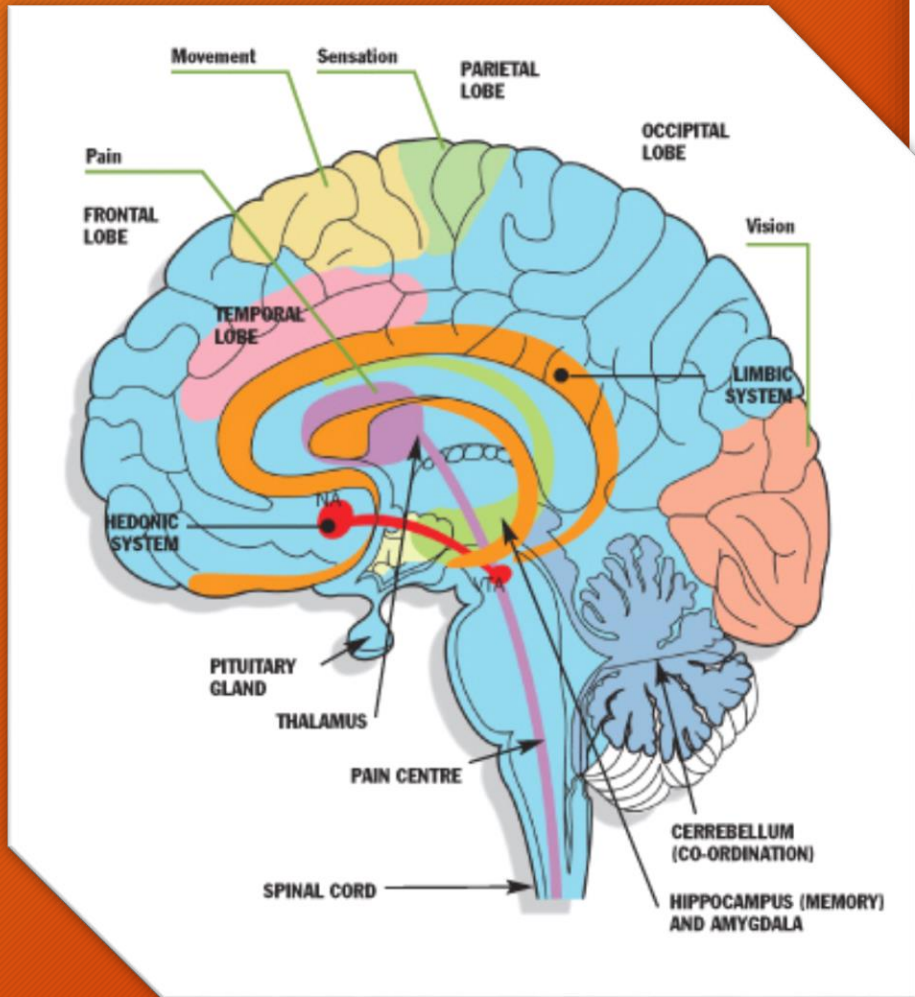
# The problem with Heroin



- Repeated heroin use changes the physical structure and physiology of the brain, creating long-term imbalances in neuronal and hormonal systems that are not easily reversed.
- Ignar, D.M.; and Kuhn, C.M. Effects of specific mu and kappa opiate tolerance and abstinence on hypothalamo-pituitary-adrenal axis secretion in the rat. *J Pharmacol Exp Ther* 255(3):1287-1295, 1990.
- 14. Kreek, M.J.; Raganath, J.; Plevy, S.; Hamer, D.; Schneider, B.; and Hartman, N. ACTH, cortisol and beta-endorphin response to metyrapone testing during chronic methadone maintenance treatment in humans. *Neuropeptides* 5(1-3):277-278, 1984.

# Head Trauma risk of pituitary Abnormality



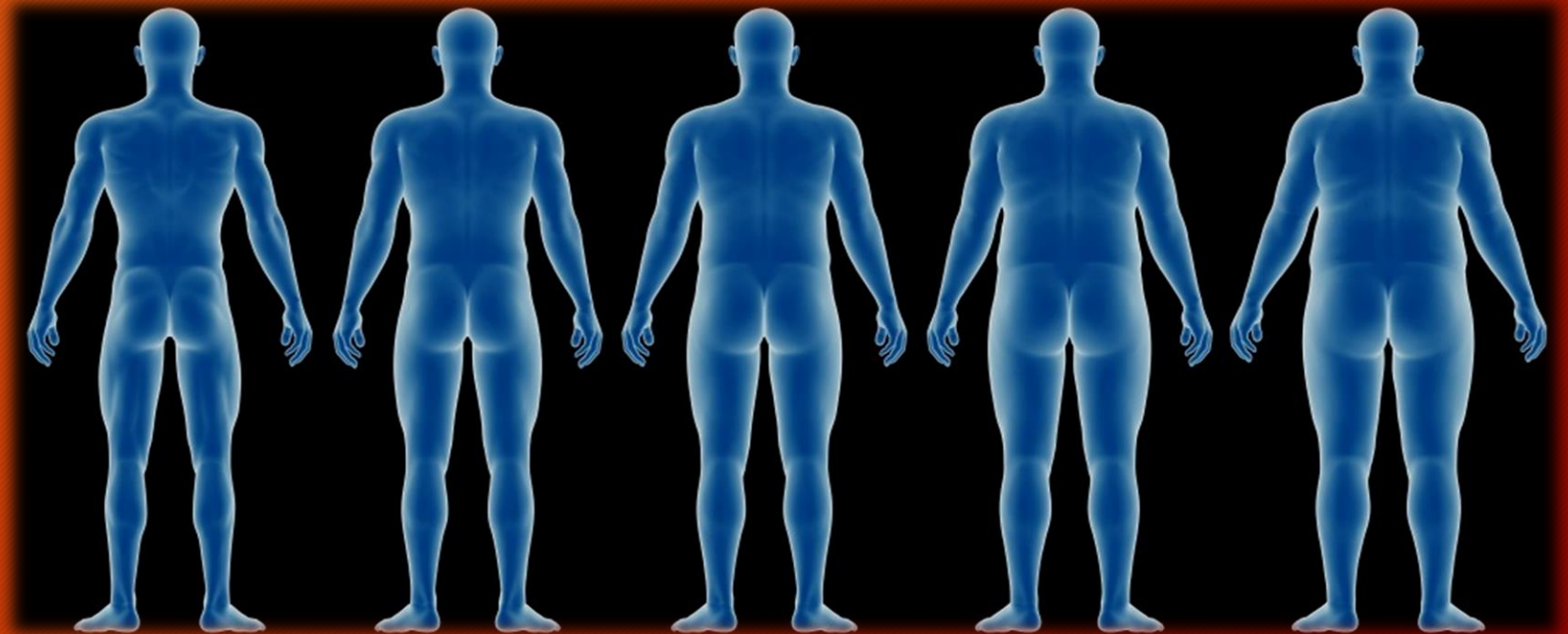






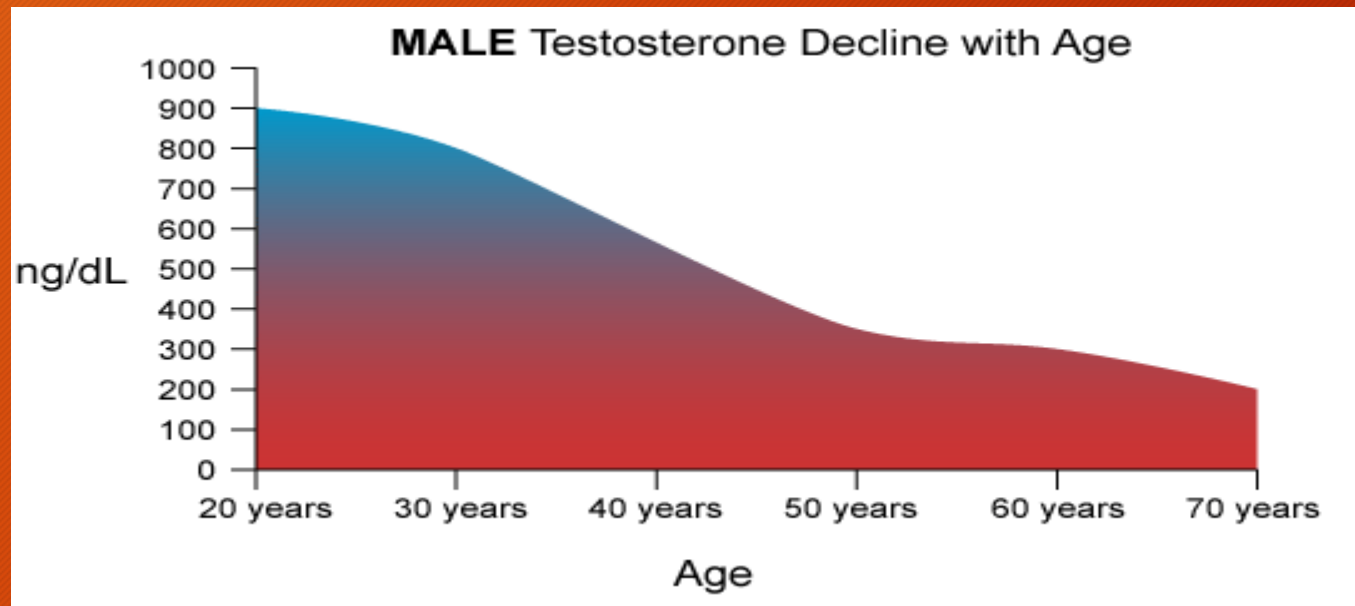
Hypogonadism is a relatively common endocrine disorder, in both men and women

- Increased body fat
- Decreased lean muscle mass
- Decreased bone density
- Increased Cholesterol levels
- Decreased insulin sensitivity
- Sexual dysfunction
- Depression
- Hair loss
- Anemia
- Fatigue
- Menstrual irregularities
- Vasomotor Instability



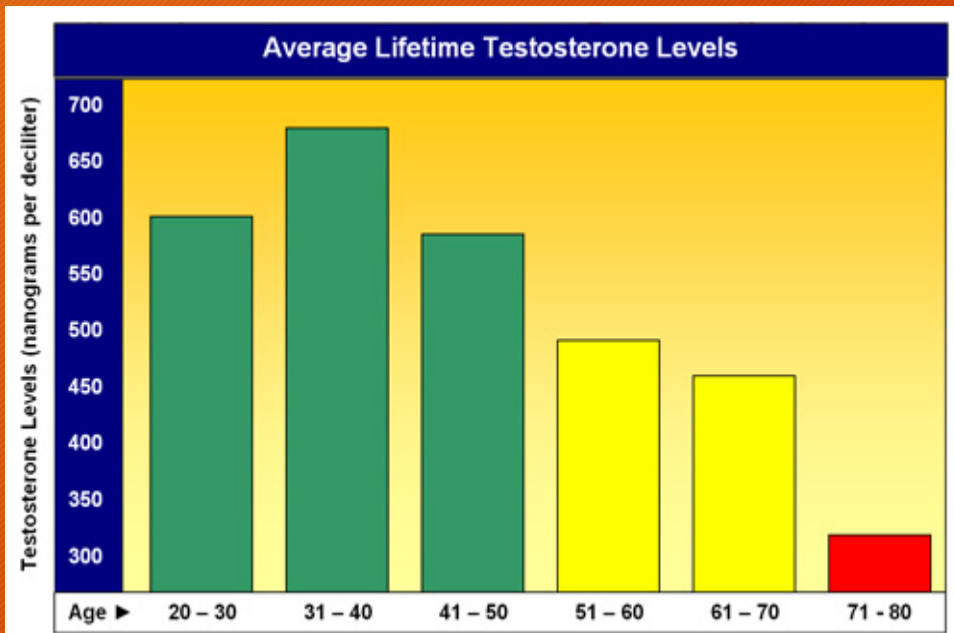
# 2013 Kaiser Permanente Study

- Men taking long-acting chronic pain medications are **5 times** more likely to have low testosterone levels
- **74% of men 26-79** years of age had levels of **250 or less**. (300-1100 ng/dl)

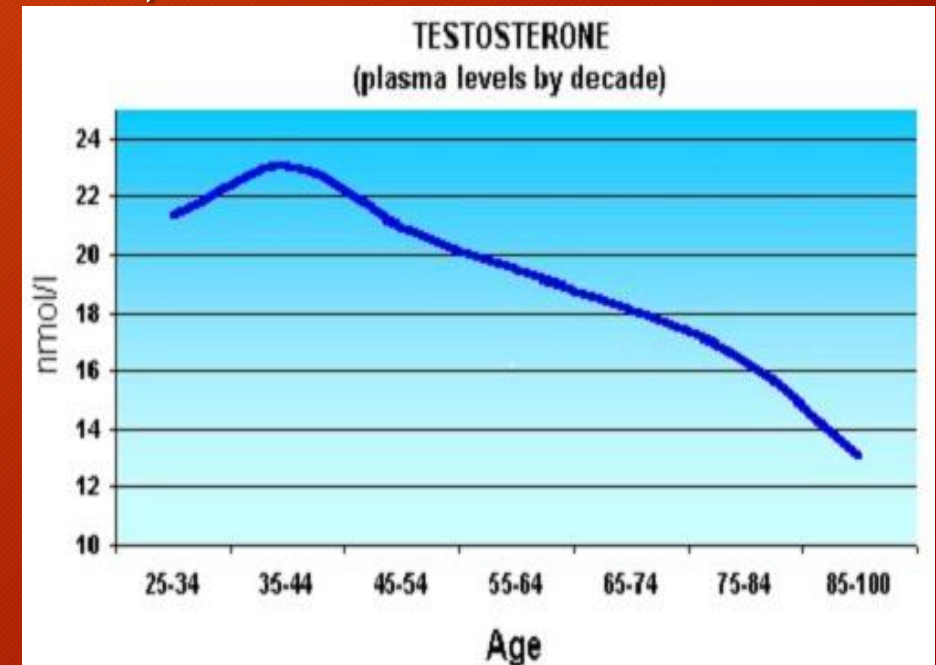


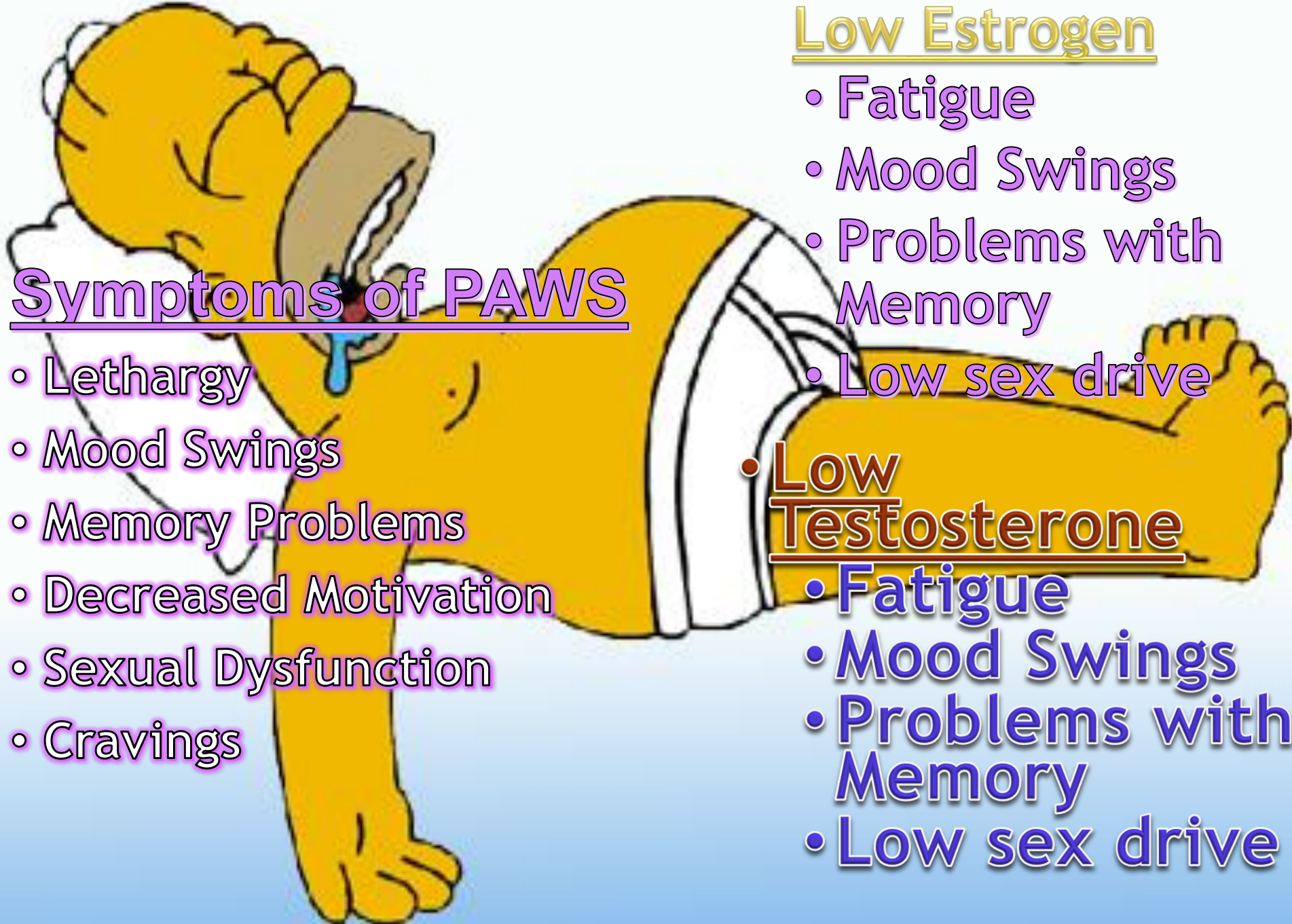
# Testosterone and Opiate Use

- Patient is 23 yrs old, 6' 3", 186 lbs
- College Student, long distance cyclist
- Testosterone Total **122** ng/dl (348-1197)
- Free Testosterone **4.2** ng/dl (9.3-26.5)



Source: Stephen J. Winters, M.D., University of Louisville





## Symptoms of PAWS

- Lethargy
- Mood Swings
- Memory Problems
- Decreased Motivation
- Sexual Dysfunction
- Cravings

## Low Estrogen

- Fatigue
- Mood Swings
- Problems with Memory
- Low sex drive

## • Low Testosterone

- Fatigue
- Mood Swings
- Problems with Memory
- Low sex drive

# Heroin and Hypogonadism

- The association of intravenous heroin use with decreased libido, erectile dysfunction and menstrual cycle abnormalities in women has been recognized for **DECADES**
- Heroin and methadone are also associated with depression, fatigue, hot flashes, sweating weight gain.
- 5 million men treated with sustained action opiates are **TESTOSTERONE Deficient**.

Azizi, F, et al Decreased serum testosterone concentrations in male heroin and methadone addicts. *STERIODS*, 1973, 195:296-302

# Methadone and Hypogonadism

- Despite the fact that this condition was well established as an adverse effect of methadone therapy in the **1970 and 1980**, screening for hypogonadism was not common!
- Reason: Clinics do not diagnose or treat conditions other than opiate dependence!!!!
- Treatment providers are unaware of the adverse endocrine effects!!!
- **FOR WHATEVER REASON:** countless individuals receiving methadone for addiction have not been diagnosed or treated for symptomatic endocrine deficiencies.

# Treatment for Hypogonadism

- Opiates decrease LH and FSH
- **Naloxone** increases these hormones \*
- Opiates decrease LH and FSH
- *B HCG will increased production\*\**



- \*Woodall, W.S “Opioids and the Endocrine System”, Advance Healthcare Network, 2013
- \*\*Mendelson, JH et al, Heroin and naltrexone effects on pituitary-gonadal hormones in man: interaction of steroid feedback effects, tolerance and supersensitivy. J Pharmacol Exp Ther.1980:214-503-506



# Hormones

## glucocorticoids

Cortisol

## mineralocorticoids

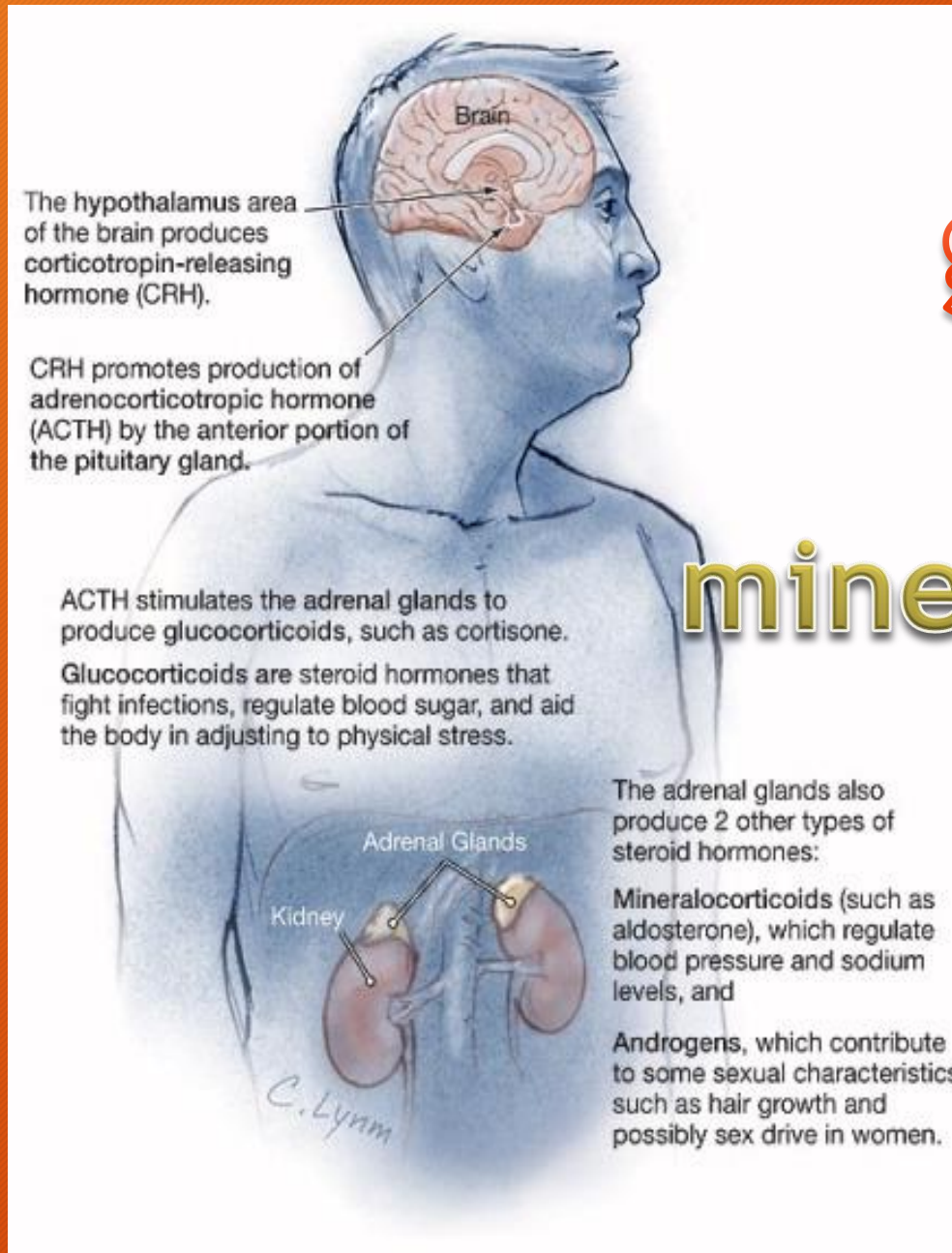
Aldosterone

## androgens

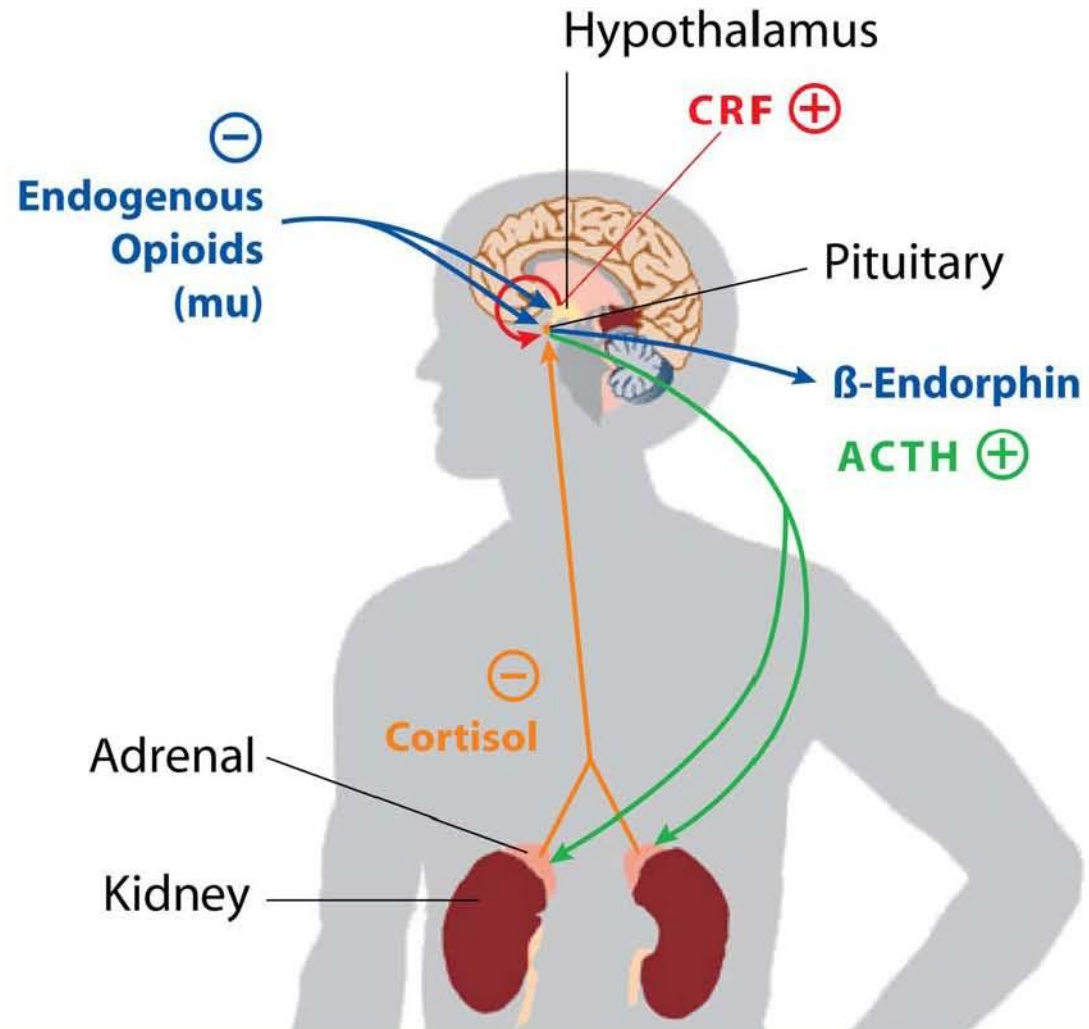
DHEA

Estrogens

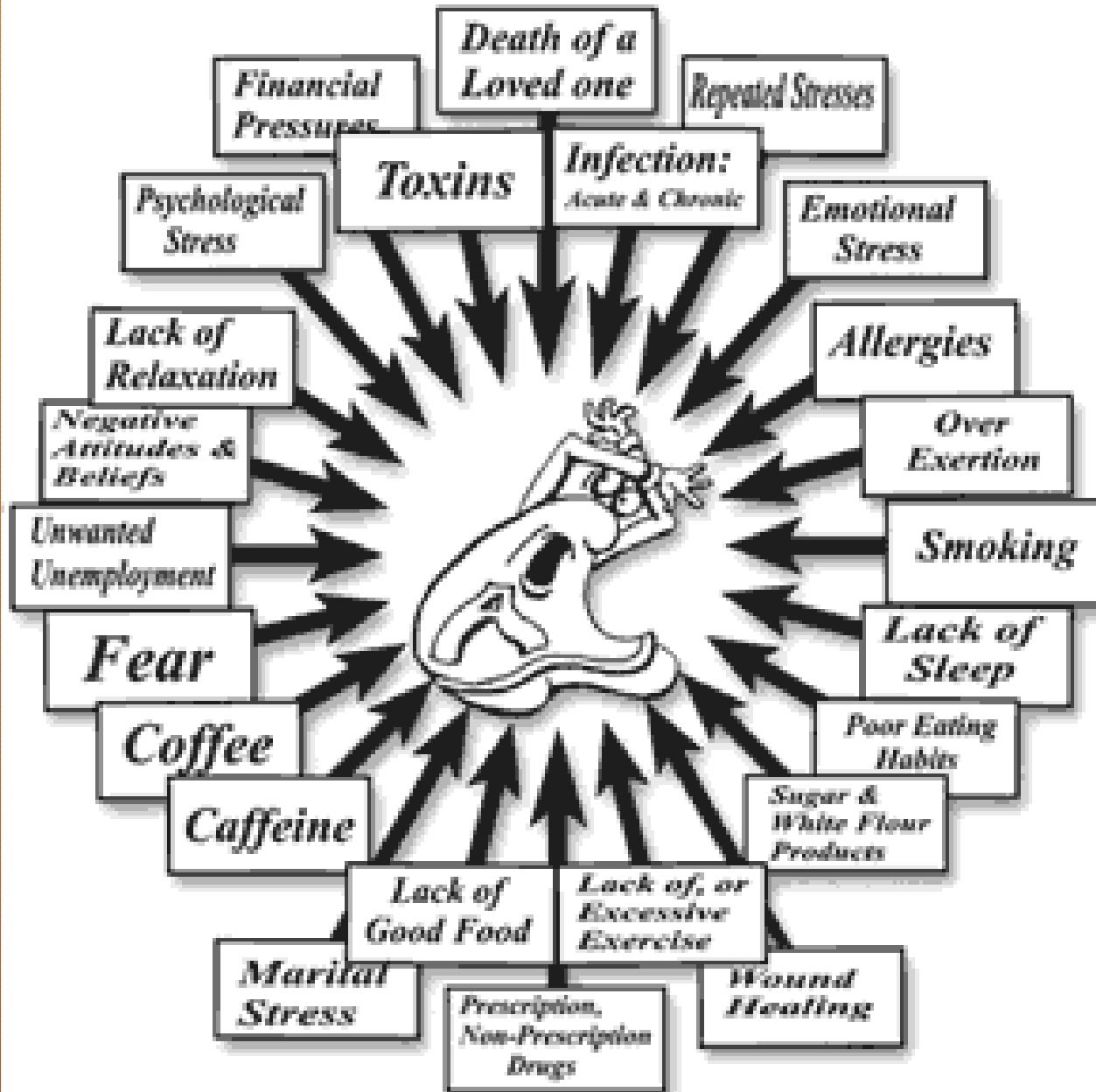
Testosterone



# Hypothalamic Pituitary Adrenal (HPA) Axis



# FACTORS AFFECTING THE ADRENALS



Cortisol is the only hormone that **Increases** with age!

# **Hypothesis — Atypical Responsivity to Stressors: A Possible Etiology of Addictions**

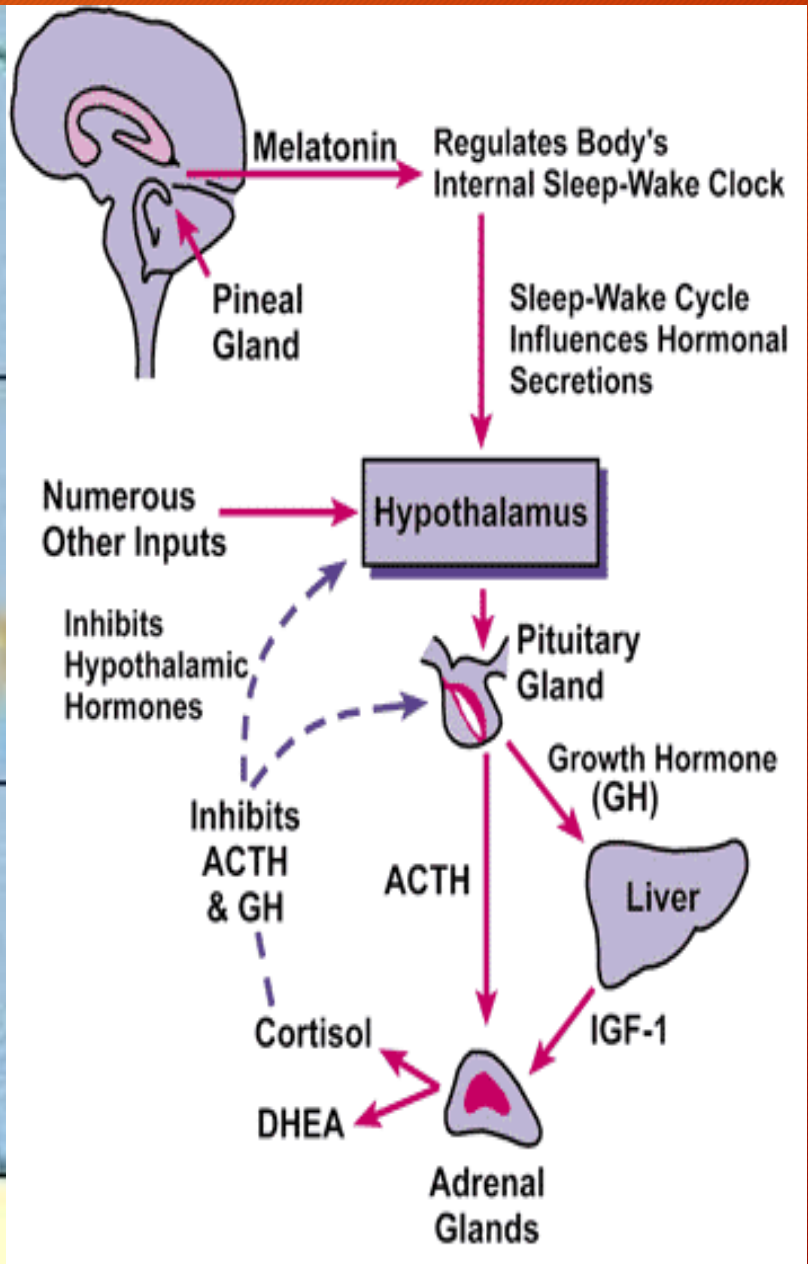
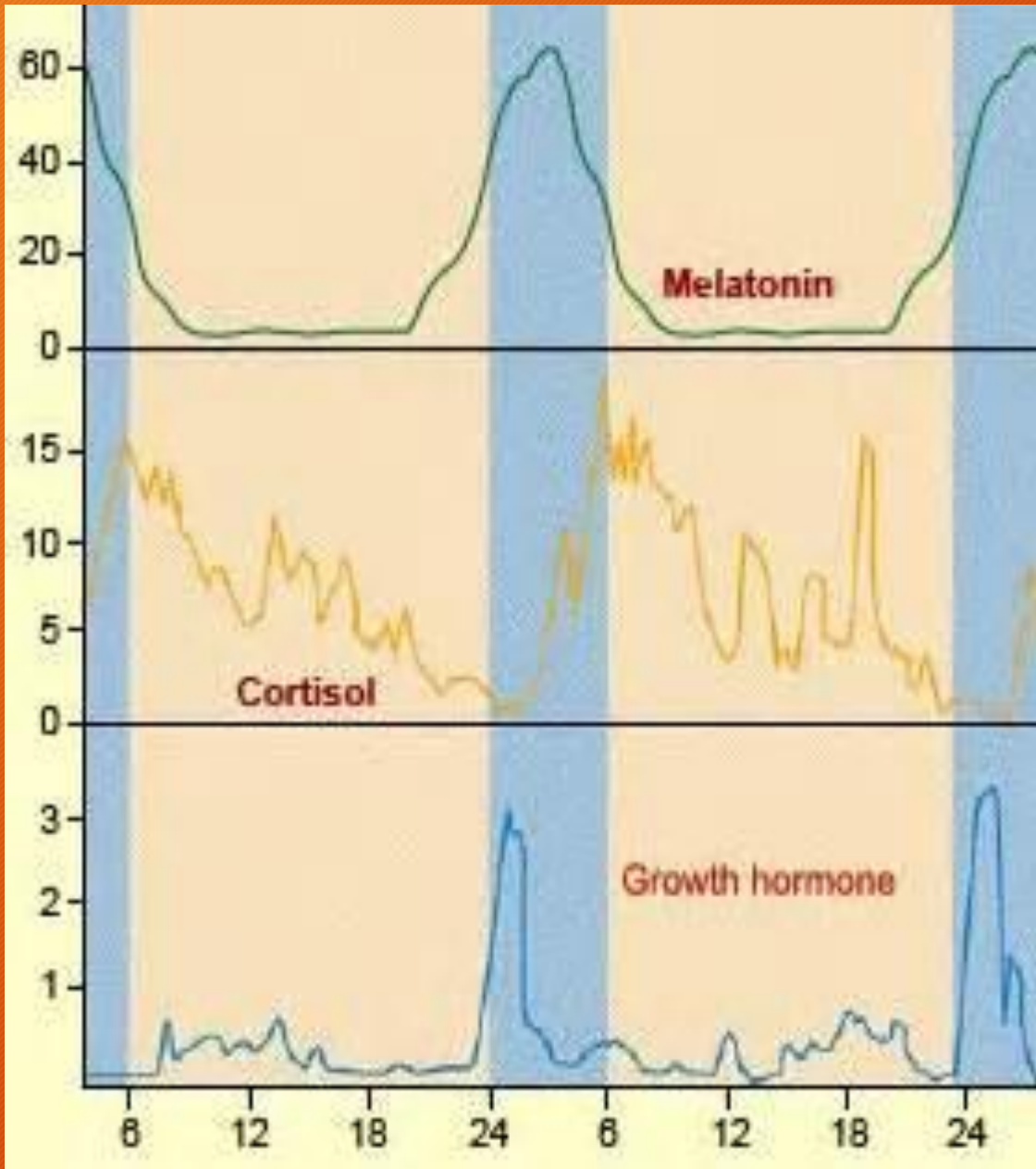
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**Atypical responsivity to stress and stressors may, in part, contribute to the persistence of, and relapse to, self-administration of drugs of abuse and addictions.**

**Such atypical stress responsivity in some individuals may exist prior to use of addictive drugs on a genetic or acquired basis, and lead to the acquisition of drug addiction.**

# Functions of Cortisol

- Balances Blood Sugar
- Weight Control
- Immune system response
- Bone turnover rate
- Stress reaction
- Sleep/wake cycle
- Protein Synthesis
- Mood and thoughts
- Testosterone & estrogen ratio
- DHEA/insulin ration
- Effects pituitary/thyroid/adrenal system
- Is anti-inflammatory



# Cortisol and An Emergency:

- Cortisol is released in response to **stress**
- Sparing available **glucose for the brain**
- Generating **new energy** from stored reserves
- **Diverting energy from low-priority activities** (such as the immune system) in order to survive immediate threats or prepare for the exertion of rising to a new day.







# Cortisol effects Memory

- Cortisol works with epinephrine (adrenaline) to create memories of short-term emotional events; this is the proposed mechanism for storage of flash bulb memories, and may originate as a means to remember what to avoid in the future.
- However, long-term exposure to cortisol damages cells in the hippocampus;
- This damage results in impaired learning.
- Furthermore, it has been shown that cortisol inhibits memory retrieval of already stored information

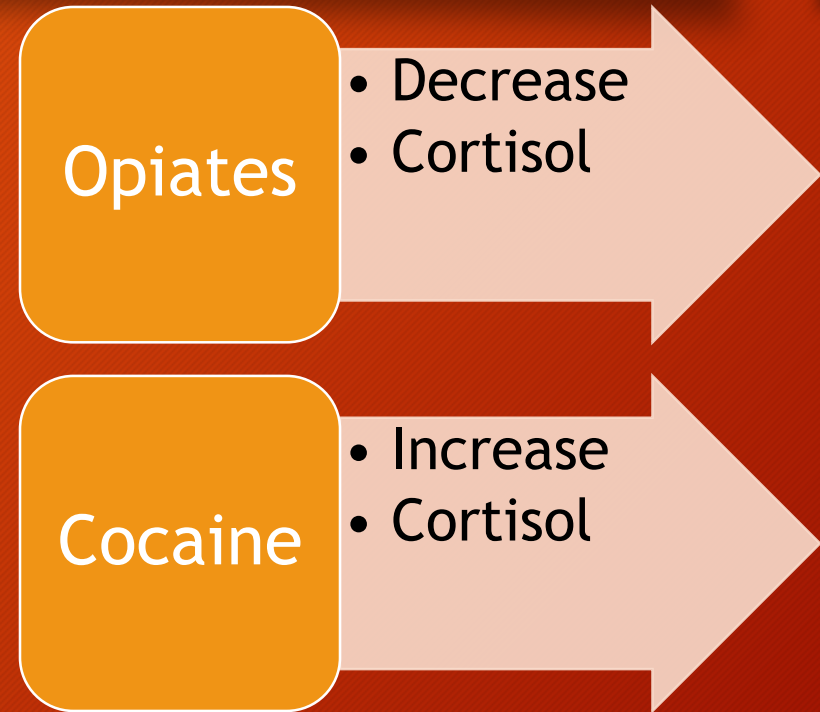


# Elevated Cortisol Effects IQ

- **Objective:** The objective of this study was to use Cushing's disease as a unique human model to elucidate the cognitive deficits resulting from exposure to chronic stress-level elevations of endogenous cortisol.
- **Methods:** Forty-eight patients with a first episode of acute, untreated Cushing's disease and 38 healthy control subjects were studied.
- **Results:** Scores for four of five verbal IQ subtests were significantly lower in patients with Cushing's disease; their scores were significantly lower for only one nonverbal performance IQ subtest (block design). Verbal, but not visual, learning and delayed recall at 30 minutes were significantly decreased among patients with Cushing's disease. Although verbal delayed recall was significantly lower in these patients, the retention index (percentage), which compares the amount of initially learned material to that recalled after the delay, was not significantly decreased. There was no significant association between depression scores and cognitive performance. A higher degree of cortisol elevation was associated with poorer performance on several subtests of learning, delayed recall, and visual-spatial ability.
- **Conclusions:** Chronically elevated levels of glucocorticoids have deleterious effects on particular domains of cognition. Verbal learning and other verbal functions seem more vulnerable than nonverbal functions. The results suggest that both the neocortex and hippocampus are affected.

# Adrenal Dysfunction in Drug Use

- **Opiates** inhibit CRH release leading to **decreased Cortisol** production resulting in adrenal insufficiency.
- Conversely, **Cocaine** administration results in enhanced HPA activity with **elevated levels of Cortisol**
- Both result in atypical circadian rhythm.

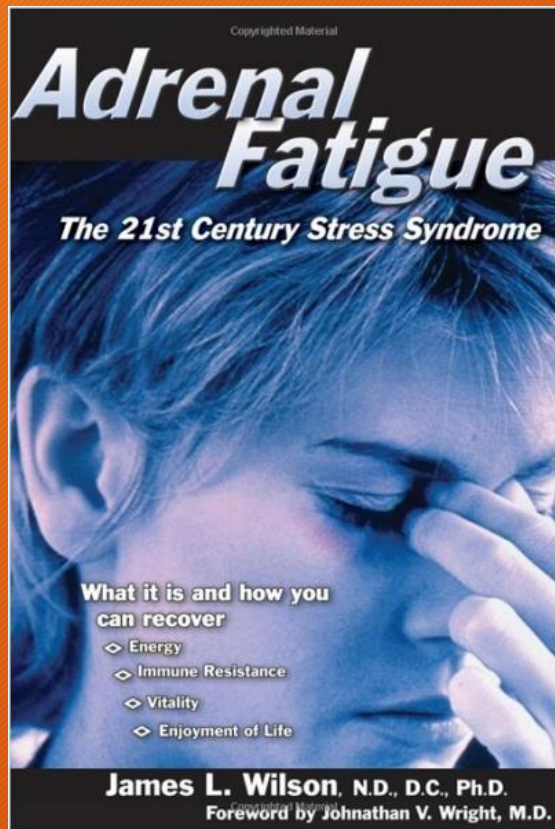


# Consequences of Elevated Cortisol

- Decreased immune system
- Increased osteoporosis risk
- Fatigue
- Irritability
- Sugar cravings
- Shakiness between meals
- Confusion
- Low Energy
- Night Sweats
- Binge eating
- Increased Blood Pressure, cholesterol, triglycerides, blood sugar
- Weight gain around the middle
- Impaired conversion of T4 to T3

# Symptoms of Adrenal Fatigue

- Difficulty getting up in the morning
  - Continuing Fatigue not relieved by sleep
  - Craving for salt or salty food
  - Lethargy
  - Increased effort to do every day tasks
  - Thoughts less focused/fuzzy
  - Memory less accurate
  - Decreased sex drive
  - Decreased ability to handle stress
  - Increased time to recover from illness, injury or trauma
  - Light-headed when standing up quickly
  - Increased PMS
  - Sx increase if meals are skipped or inadequate
- \*3 or more symptoms suggest adrenal problems



**Chocolate cravings:**  
may be caused in part by low levels of **Magnesium**  
So consider adding magnesium to  
Tame cravings and to help calm  
Frayed nerves and assist in restful sleep.

# Consequences of adrenal and gonadal abnormalities

## Cravings

- When drugs are withdrawn, the brain releases CRH with stress which causes cravings and the desire to use.
- HPA de-activation during drug use reinforces cravings and drug seeking behavior

## Relapse

- Increased CRH creates anxiety and increased the adverse effects of drug withdrawal.
- Low Estrogen and Testosterone levels decrease endogenous opiate levels and contribute to cravings and relapse

# Consequences of adrenal and gonadal abnormalities

## Depression and Gonads

- Estrogen and Testosterone have a direct effect on Serotonin synthesis.
- If there are low levels due to gonadal dysfunction with addiction, the patients can suffer from depression, sadness and anger that **does NOT respond to antidepressants**

## Depression and Adrenals

- Reduced Cortisol has been linked to depressive symptoms, apathy, profound fatigues and even delusional behavior
- Moderate to severe depression has been identified in more than 50% of people with addiction



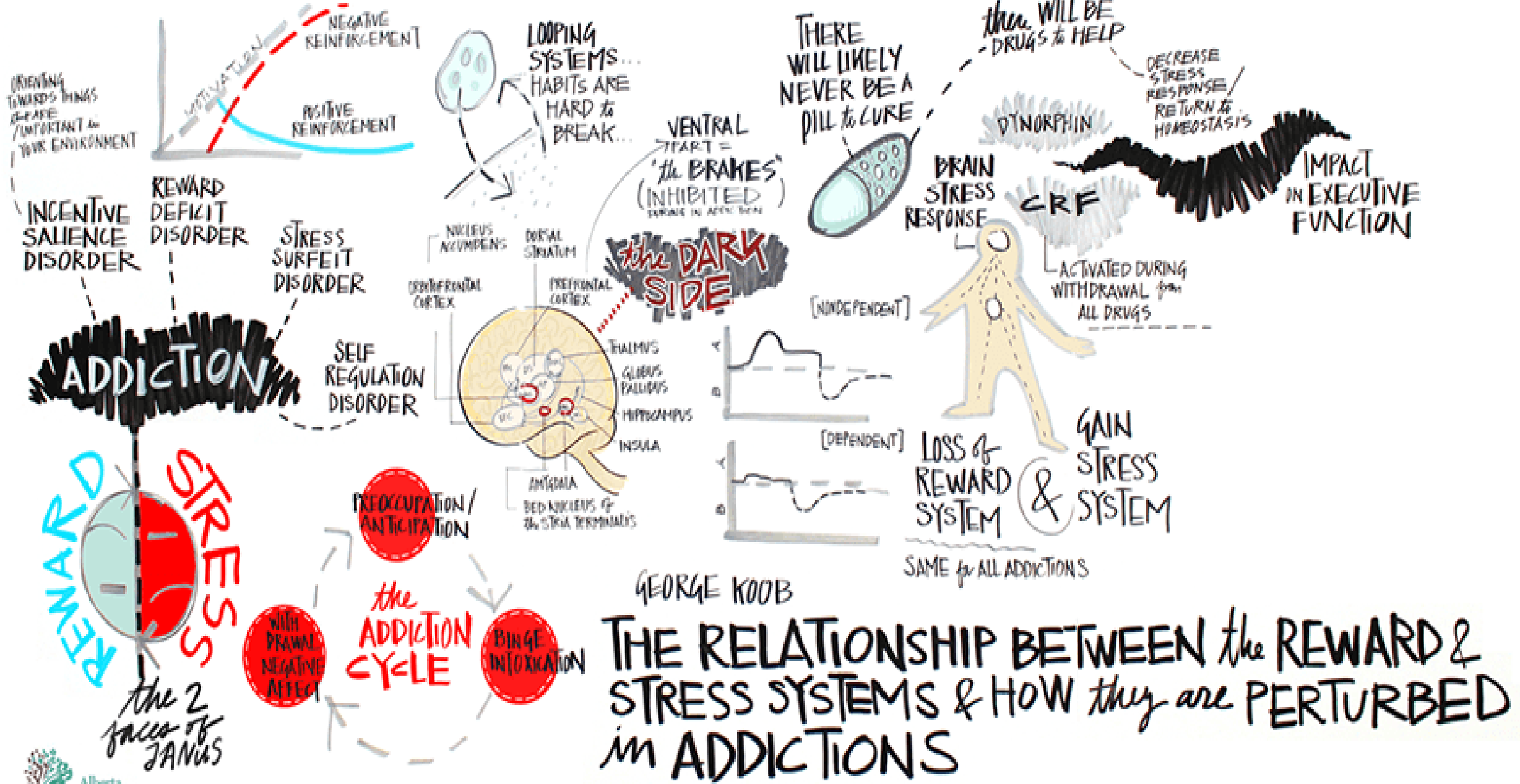
# Our Autonomic Nervous system

## Sympathetic: Flight or Flight

- Increased cortisol and adrenaline cause a number of physical and hormonal changes
- Increase a person's risk of relapse by creating an emotional and physiological state of over- stimulation
- Impair healing, interfere with memory production, increase risk of disease, including cancer
- Negatively impacts sleep cycle.

## Parasympathetic: Rest and Digest

- Yoga: Breathing and poses help to engage the parasympathetic nervous system, allowing our bodies to counter balance the stress response
- Meditation: Breathing and mindfulness allow us to remain in the present, not in the past (depression) or in the future (anxiety)
- Exercise (moderate) especially upper body work to release energy created by anger
- Adaptogens
- Tapping



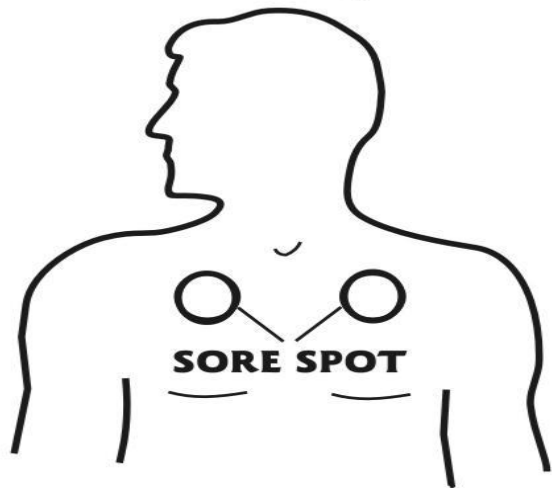
# #1...The Setup

1) Repeat 3X

*Even though I have this \_\_\_\_\_ (problem) \_  
I deeply & completely accept myself.*

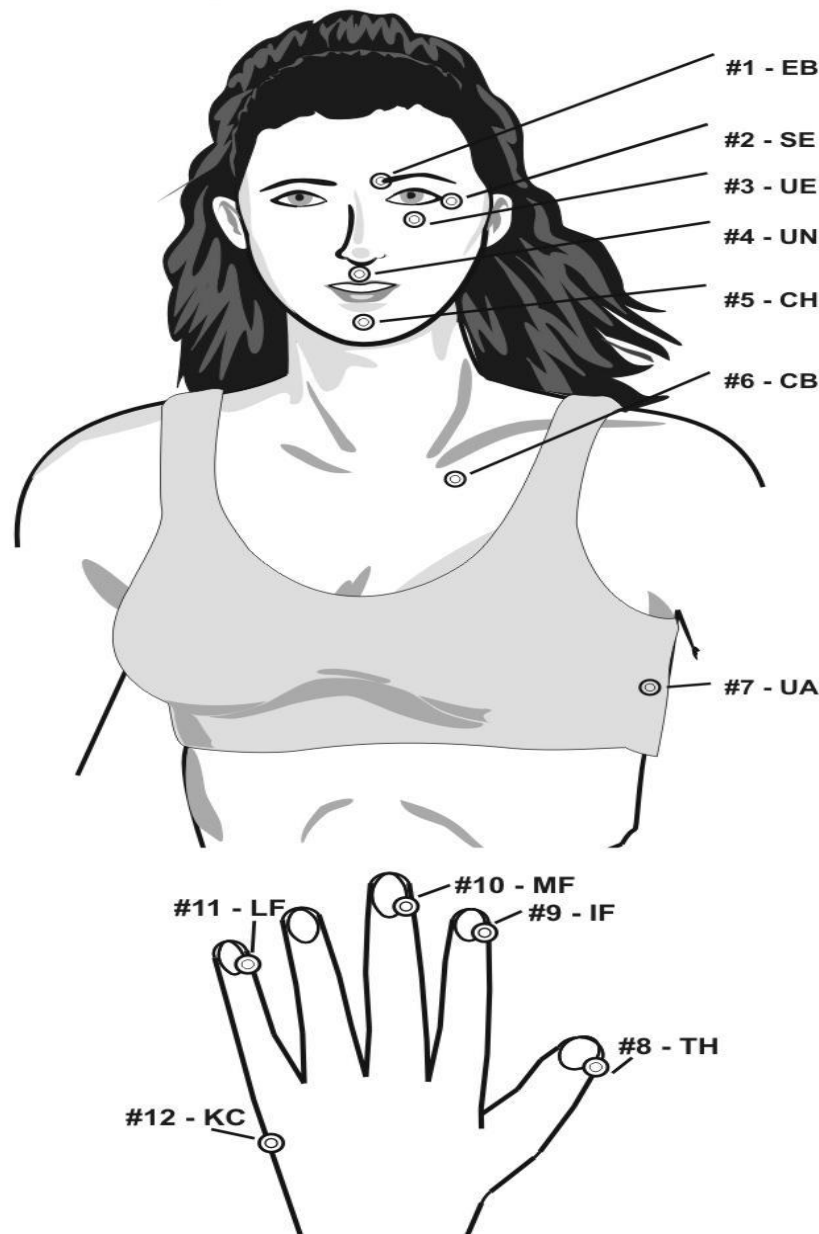
2) While continuously rubbing the “Sore Spot” or tapping the “Karate Chop” point.

## The Sore Spot/ Karate Chop Point

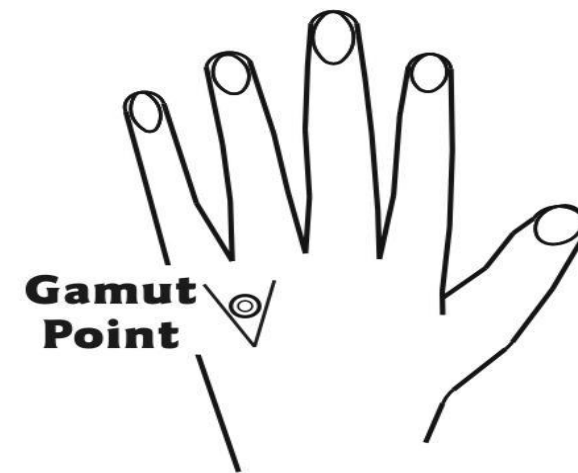


# #2...The Sequence

Tap about 5X on each point



# #3...The 9 Gamut



Perform 9 actions while tapping the GAMUT POINT continuously:

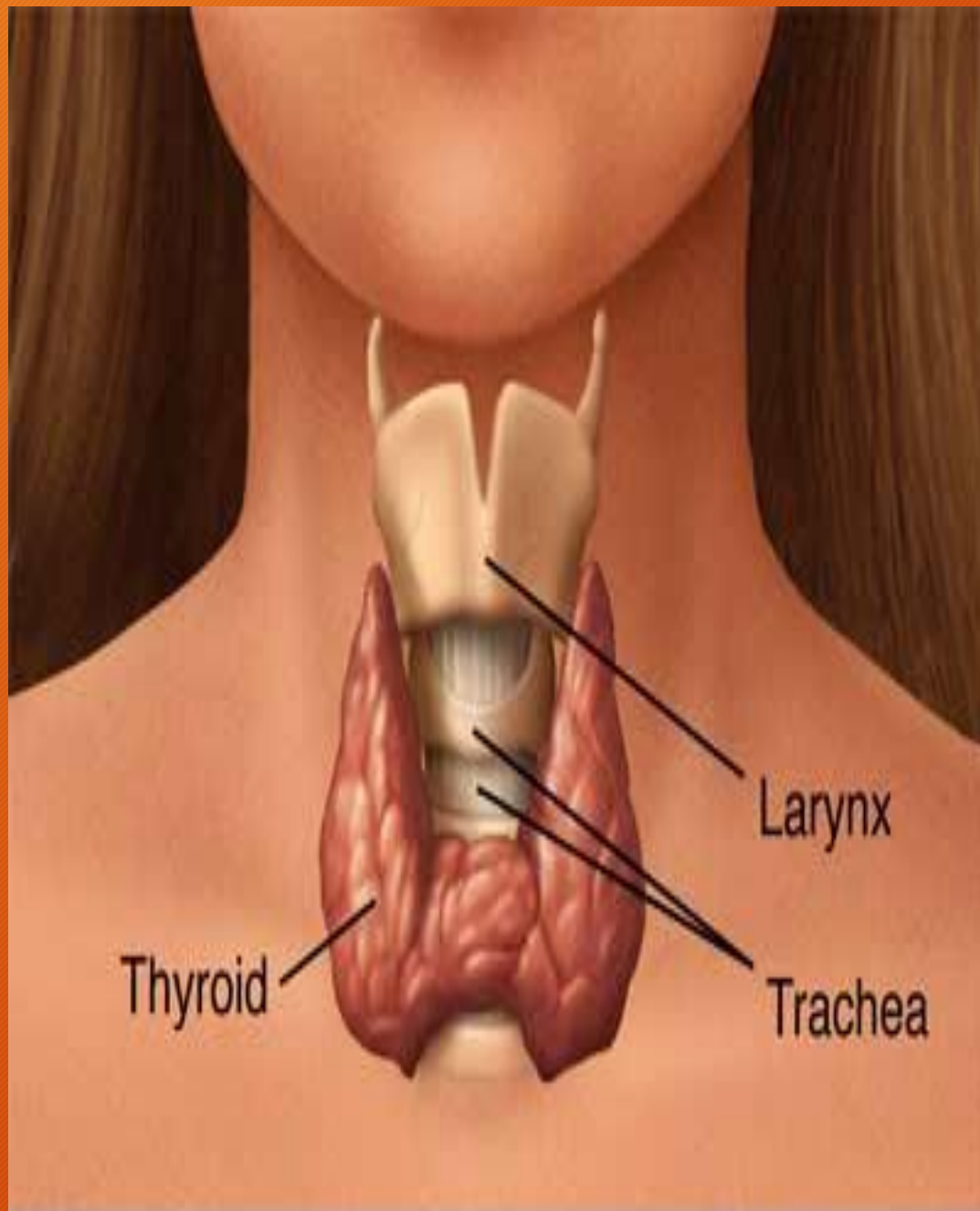
- 1) Eyes closed
- 2) Eyes open
- 3) Eyes hard down right (head steady)
- 4) Eyes hard down left (head steady)
- 5) Roll eyes in a circle
- 6) Roll eyes in opposite direction
- 7) Hum 5 seconds of song (Happy Birthday)
- 8) Count from 1 to 5
- 9) Hum 5 seconds of a song again.

## #4...Repeat (#2) The Sequence

NOTE: In subsequent rounds of tapping, change the setup language to “*Even though I STILL have SOME OF this problem...*” and use “*REMAINING problem*” as a reminder phrase.

Stressed spelled backwards  
DESSERTS





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## Some Common Thyroid Symptoms\*

\*That Your Doctor Probably Ignores or Explains Away

- Fatigue
- Weight gain
- Inability to lose weight
- Hair loss/thinning
- Eyebrow loss/thinning
- Fertility problems
- Low sex drive
- Muscle aches/pains
- Depression
- Brain fog

**GET TESTED! TSH, FT4, FT3, TPO!**

[www.facebook.com/ThyroidSupport](http://www.facebook.com/ThyroidSupport)

# Thyroid Gland



Pituitary

**TSH**  
Thyroid Stimulating  
Hormone

Zinc, B1, B6  
Tyrosine  
Iodine  
Vanadium  
B2  
Vit C



**T4** Is Inactive Hormone  
Thyroxine

Progesterone  
Selenium

Reverse T3

**T3** Is Active Hormone  
Tri-iodothyronine



T3 activates and energises all cells  
of the body

Tests to Run  
TSH  
Free T3  
Free T4  
Reverse T3  
TPO

# Thyroid Pathology

Physiologic state	Serum TSH	Serum Free T4	Serum T3	24-h radioiodine uptake
Hyperthyroidism, untreated	Low	High	High	High
Hyperthyroidism, T3 toxicosis	Low	Normal	High	Normal or High
Primary Hypothyroidism, untreated	High	Low	Low or Normal	Low or Normal
Hypothyroidism secondary to pituitary disease	Low or Normal	Low	Low or Normal	Low or Normal
Euthyroid, on exogenous thyroid hormone	Normal	Normal on T4, Low on T3	High on T3, Normal on T4	Low

# Neurocognitive Impairments with Hypothyroidism

- Purpose: (1) to evaluate objectively changes in cognitive function and electrophysiologic characteristics associated with hypothyroidism of varying severity and duration in primarily older persons; (2) to determine whether these changes are reversible when a euthyroid state has been attained after treatment with thyroid hormone.
- Subjects and Methods: 54 non-demented hypothyroid patients with biochemical evidence of hypothyroidism and 30 euthyroid controls. Evaluated attention, orientation, memory, learning, visual-spatial abilities, calculation, language, visual scanning, and motor speed using standardized neuropsychological tests
- Results: Hypothyroid patients showed significantly lower scores on the Mini-Mental Status Test (MMS) and on five of 14 neuropsychological tests as compared to controls.
- Conclusion: Hypothyroidism in non-demented older adults is associated with impairments in learning, word fluency, visual-spatial abilities, and some aspect of attention, visual scanning, and motor speed. The MMS by itself was sensitive in differentiating hypothyroid patients with cognitive deficits from controls, while electrophysiological measures did not generally differentiate the hypothyroid patients from normal controls. The MMS was not sensitive to treatment effects, but **treatment was associated with significant improvements in three of the most sensitive measures of cognitive dysfunction.**



# Nutrients and Cognitive Impairment

And now for some practical  
things we can do.....

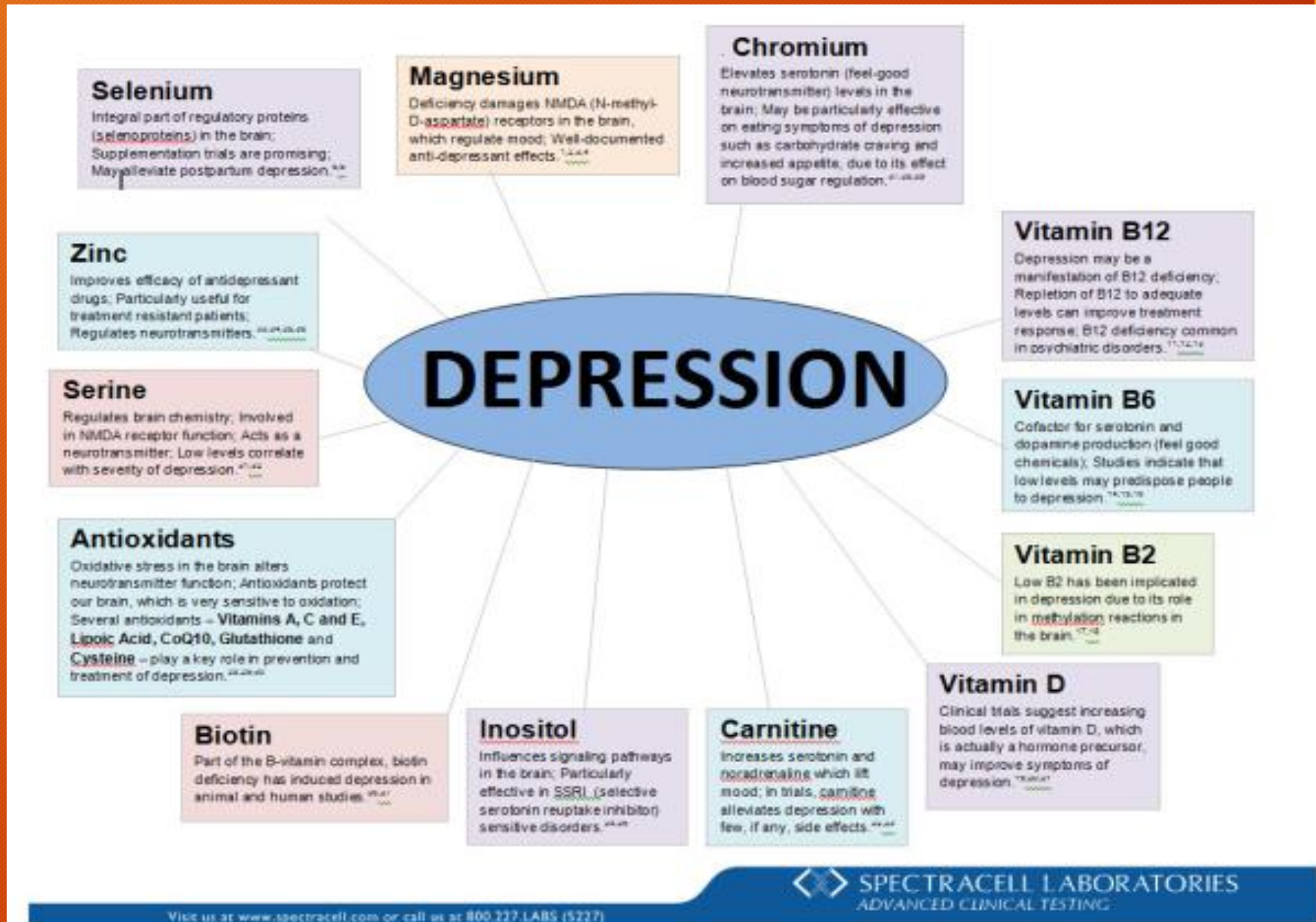


# Ageing, hippocampal synaptic activity and magnesium

(Billard, 2006)

- Calcium dysregulation has been extensively investigated in brain ageing but the role of magnesium has received less attention though ageing constitutes a risk factor for magnesium deficit.
- One of general properties of magnesium at presynaptic fiber terminals is to reduce transmitter release.
- At the postsynaptic level, it closely controls the activation of the N-methyl-D-aspartate receptor, a subtype of glutamate receptor, which is critical for the expression of long-term changes in synaptic transmission.
- In addition, magnesium is a cofactor of many enzymes localized either in neurons or in glial cells that control neuronal properties and synaptic plasticity such as protein-kinase C, calcium/calmodulin-dependent protein kinase II and serine racemase.
- It is therefore likely that a change in magnesium concentration would significantly impair synaptic functions in the aged hippocampus.
- Recent data indicate that magnesium is involved in age-related deficits in transmitter release, neuronal excitability and in some forms of synaptic plasticity such as long-term depression of synaptic transmission.

# Potential Nutritional Causes of Depression



# MAGNESIUM RICH FOODS

SESAME SEEDS			SUNFLOWER SEEDS
SPEARMINT			DILL
WATERMELON SEEDS			BASIL
PINE NUTS			BROCCOLI
ALMONDS			OKRA
PUMPKIN SEEDS			FLAX SEEDS
BRAZIL NUTS			SPINACH
CACAO			CHIVES

Rawforbeauty

## Serum Levels of Magnesium

After a 150 mg elemental dose from four different magnesium sources

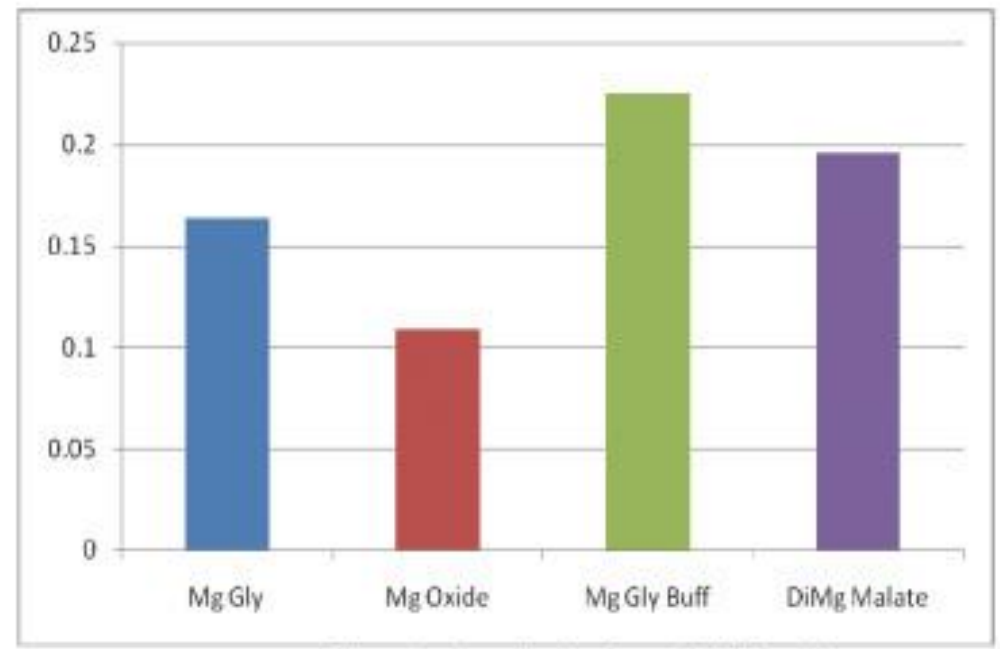


Figure 2. Area Under Curve (AUC) for 8 hours.

Magnesium Glycinate Chelate Buffered (Mg Gly Buff)	0.225
DiMagnesium Malate (DiMag Malate)	0.196
Magnesium Glycinate Chelate (MgGly)	0.164
Magnesium Oxide (Mg Oxide)	0.109

Source: Bioavailability and tolerability of various Albion manufactured organic magnesium sources compared to magnesium oxide.

# b vitamins



Sunflower Seeds



Nutritional Yeast



Avocado



Kombucha



Spinach

THIAMINE (B1), RIBOFLAVIN (B2), NIACIN (B3),  
PYRIDOXINE (B6), PANTOTHENIC ACID (B5),

## B Vitamins

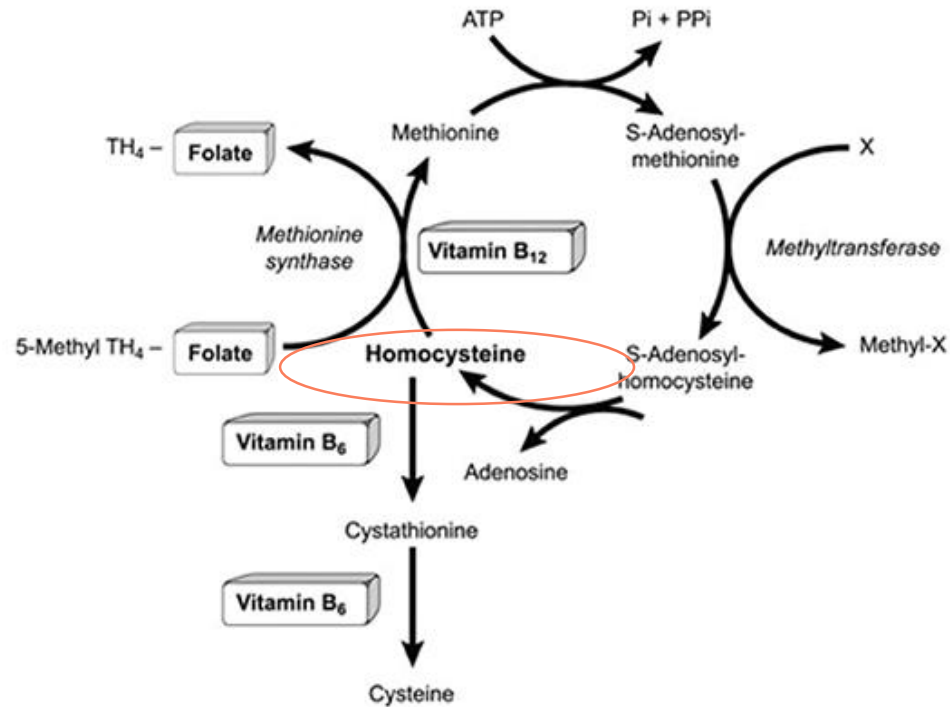
# Vit B1: Thiamine Deficiency and Cognitive Dysfunction

- *a reduction in thiamine can interfere with numerous cellular functions, leading to serious brain disorders, including Wernicke-Korsakoff syndrome, which is found predominantly in alcoholics.*
- *Chronic alcohol consumption can result in thiamine deficiency by causing inadequate nutritional thiamine intake, decreased absorption of thiamine from the gastrointestinal tract, and impaired thiamine utilization in the cells.*
- *People differ in their susceptibility to thiamine deficiency, however, and different brain regions also may be more or less sensitive to this condition.*

# Low B12, Folate and B6 High Homocysteine

- Low B vitamin and high homocysteine concentrations predict cognitive decline. Spatial copying measures appear to be most sensitive to these effects in a general population of aging men. (Tucker, et al 2005)
- Low B12 and Folate associated with poor performance on digit span. (Morris et al 2007)
- In high-functioning older adults, low folate levels appear to be a risk factor for cognitive decline. The risk of developing cognitive decline might be reduced through dietary folate intake. (Kado, et al, 2004)

Figure 1. Involvement of B Vitamins in Homocysteine Metabolism



S-adenosyl homocysteine is formed during S-adenosyl methionine-dependent methylation reactions, and the hydrolysis of S-adenosyl homocysteine results in homocysteine. Homocysteine may be remethylated to form methionine in a reaction that requires both folate and vitamin B<sub>12</sub>. Alternately, homocysteine may be metabolized to the amino acid, cysteine, in reactions catalyzed by two vitamin B<sub>6</sub>-dependent enzymes.

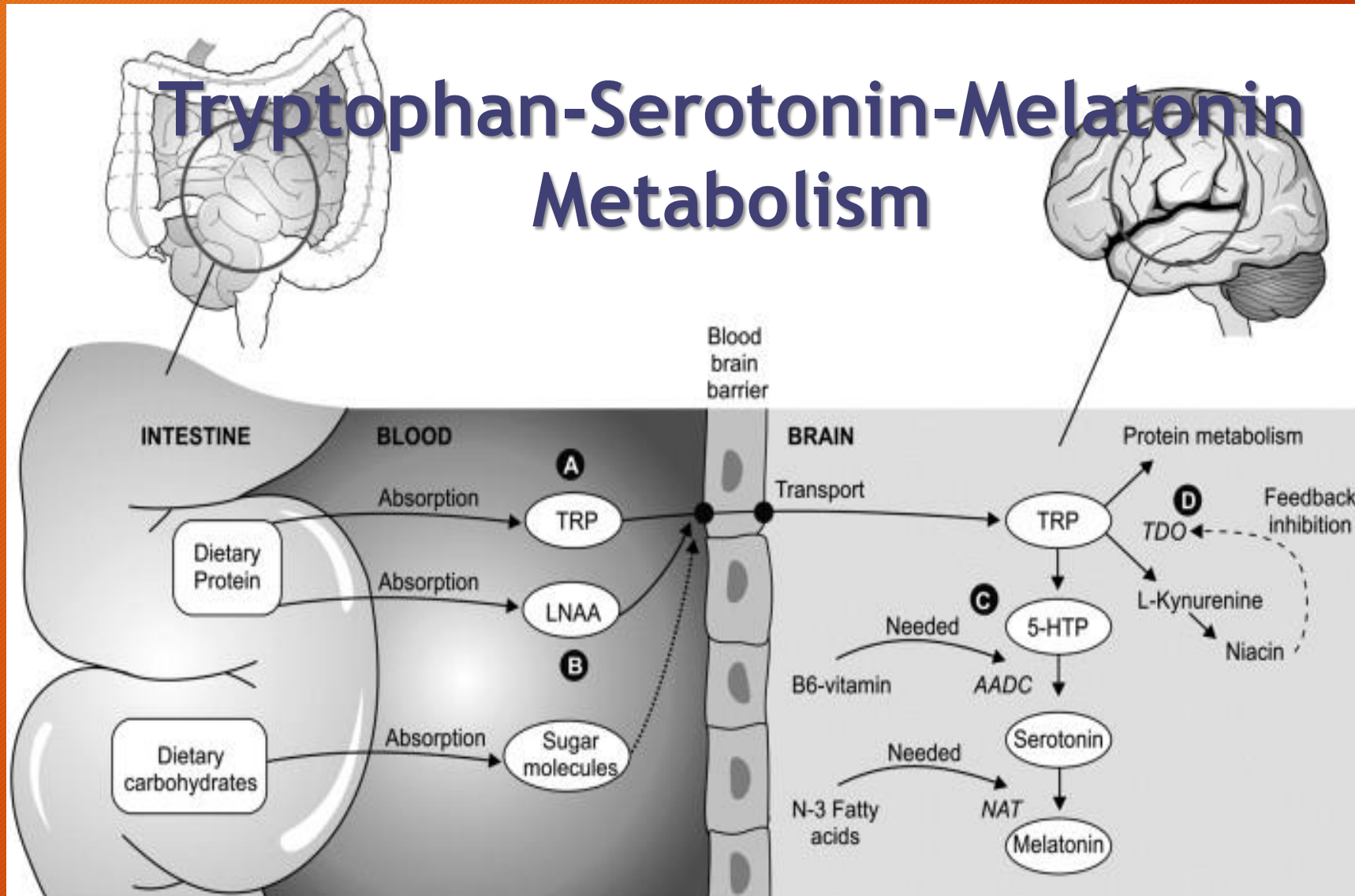


# Methylfolate and Methylcobalamine

According to Dr. Lawrence Ginsberg, past studies show nearly 70% of depressed individuals will not reach remission by taking 1 antidepressant alone, "so clearly a new approach is needed."

70% of people who have depression may have a specific genetic factor that compromises their ability to convert folic acid into L-methylfolate, "the only form of folate that can cross the blood-brain barrier and regulate serotonin, norepinephrine, and dopamine."

# Tryptophan-Serotonin-Melatonin Metabolism



5-HTP, 5-hydroxytryptophan, AADC, aromatic l-amino acid decarboxylase, LNAAs, large neutral amino acid, TDO, tryptophan 2,3-dioxygenase, TRP, tryptophan

# Tryptophan

- You need 1 gm of tryptophan for low mood
- You need 3 gm of tryptophan for treatment of depression
- You must eat tryptophan with carbohydrate for absorption across the blood brain barrier
- Promotes sleep, so best taken at night
- (If sugar gives you a lift, or if high protein diets make you depressed, you may be low in serotonin)

# Tryptophan: 5 ways to eat 500 mg

- Oatmeal, with soy milk and 2 scrambled eggs
- Baked potato with cottage cheese and tuna salad
- Chicken breast potatoes au gratin and green beans
- Whole-wheat spaghetti with bean, tofu or meat sauce
- Salmon filet, quinoa and lentil pilaf and green salad with yogurt dressing

# Is Apathy a Tyrosine Deficiency?

- **Phenylalanine and tyrosine are needed to make dopamine and norepinephrine**
- **150-200 mg of phenylalanine improved 31/40 depressed patients at Rush Medical Center**
- **Military has long known that tyrosine improves mental and physical performance under stress.**

- L-Phenylalanine
  - Needs B6 (pyridoxine), Mg, Mn, Fe, Cu, Zn, Vit C
- L-Tyrosine (apathy)
  - Needs B9(folate) Mg. Mn, Fe, Cu, Zn, Vit C
- L-Dopa
  - Needs B6 and Zn

**Blood**

- Dopamine

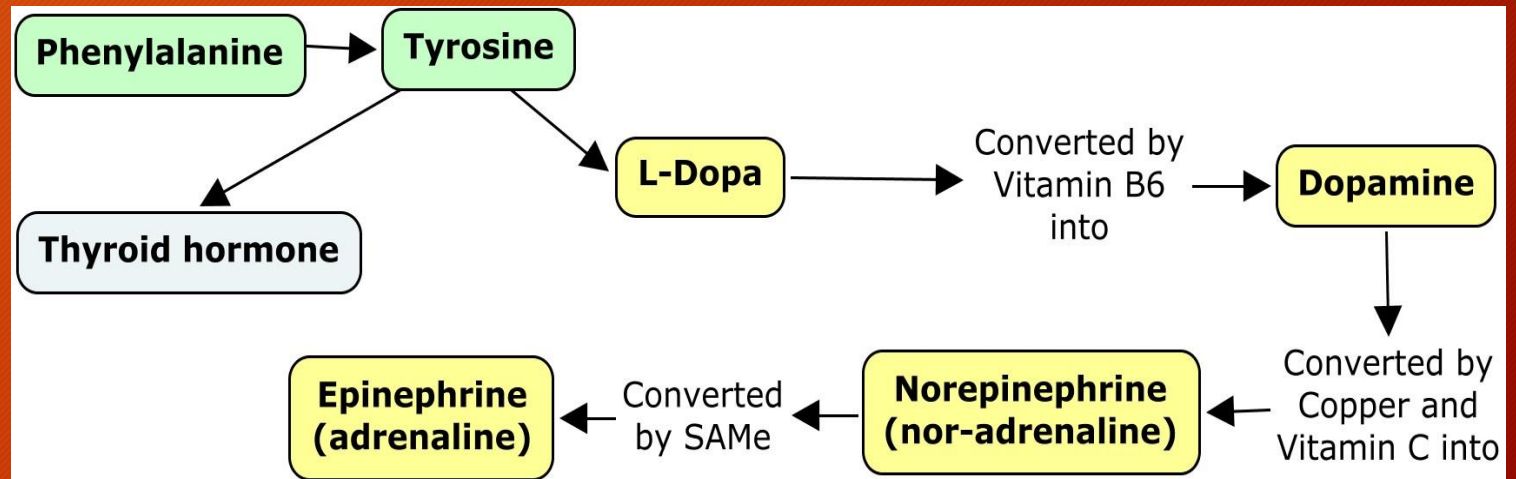
- Needs Vit C

Norepinephrine

**Needs SAME**

- Epinephrine

**Brain Barrier**



# Sources For Vitamin D3

## Vitamin D Deficiency

Lack of Sunlight



# Important protective role of Vitamin D3

- In a recent review, Buell and Dawson-Hughes (2008) emphasize that vitamin D may be neuroprotective through antioxidative mechanisms, immunomodulation, neuronal calcium regulation, detoxification mechanisms, and enhanced nerve conduction
- Vitamin D may play a role in brain detoxification pathways by reducing cellular calcium, inhibiting the synthesis of inducible nitric oxide synthase, and increasing levels of the antioxidant glutathione.
- Vitamin D is also an immunosuppressor and may inhibit autoimmune damage to the nervous system. (Garcion, 2002)



# Effects of Low Vit D3 on Cognitive Functioning

- Elderly subjects with low levels of 25(OH)D had a higher relative risk of substantial cognitive decline over a 6-year period and that this association remained after adjusting for potential confounders
- Assessment of cognitive performance included the MMSE, the most widely used measure of cognitive function, and Trails A and B, which are also commonly used. (Llewellyn, et al, 2010)
- 25-Hydroxyvitamin D deficiency was associated with cognitive impairment in this cohort of community-dwelling older women.
- Cognitive impairment was defined as a Pfeiffer Short Portable Mental State Questionnaire (SPMSQ) score <8. (Annweiler, 2008)

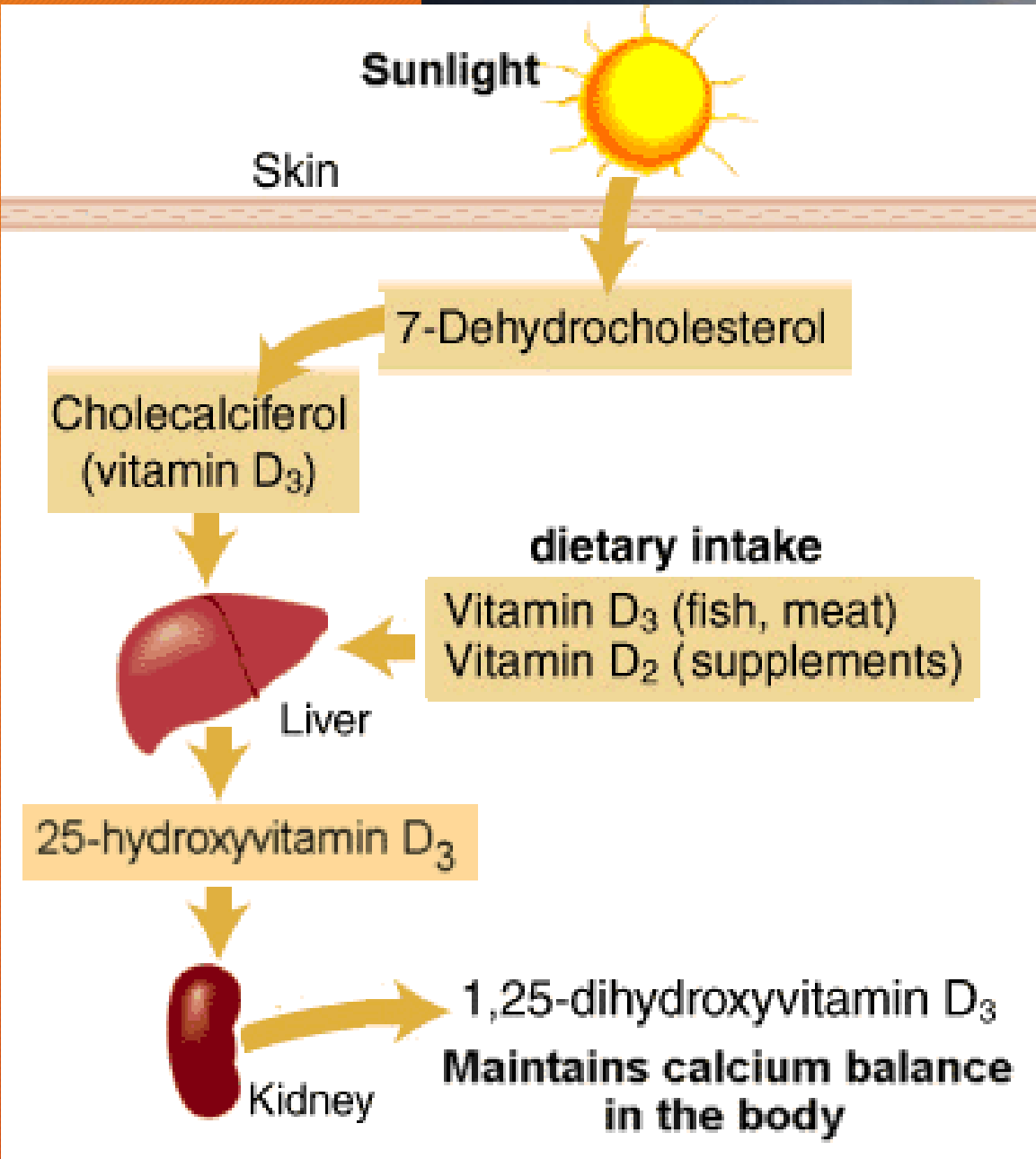
# VITAMIN D LEVELS

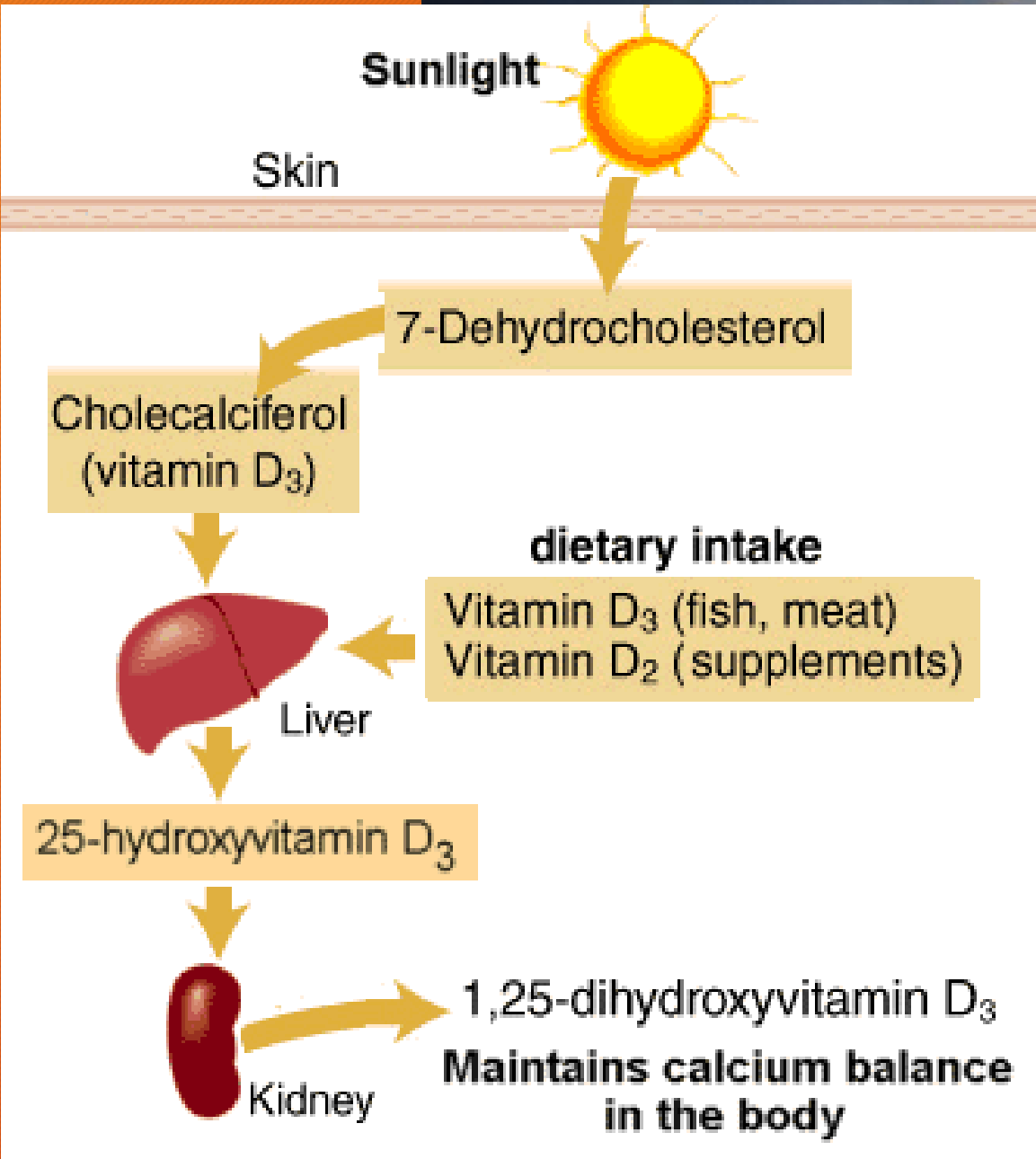
## 25 HYDROXY D

DEFICIENT	OPTIMAL	THERAPEUTIC LEVEL (DISEASE TREATMENT)	EXCESS
<50 ng/mL	50-70 ng/mL	70-100 ng/mL	>100 ng/mL

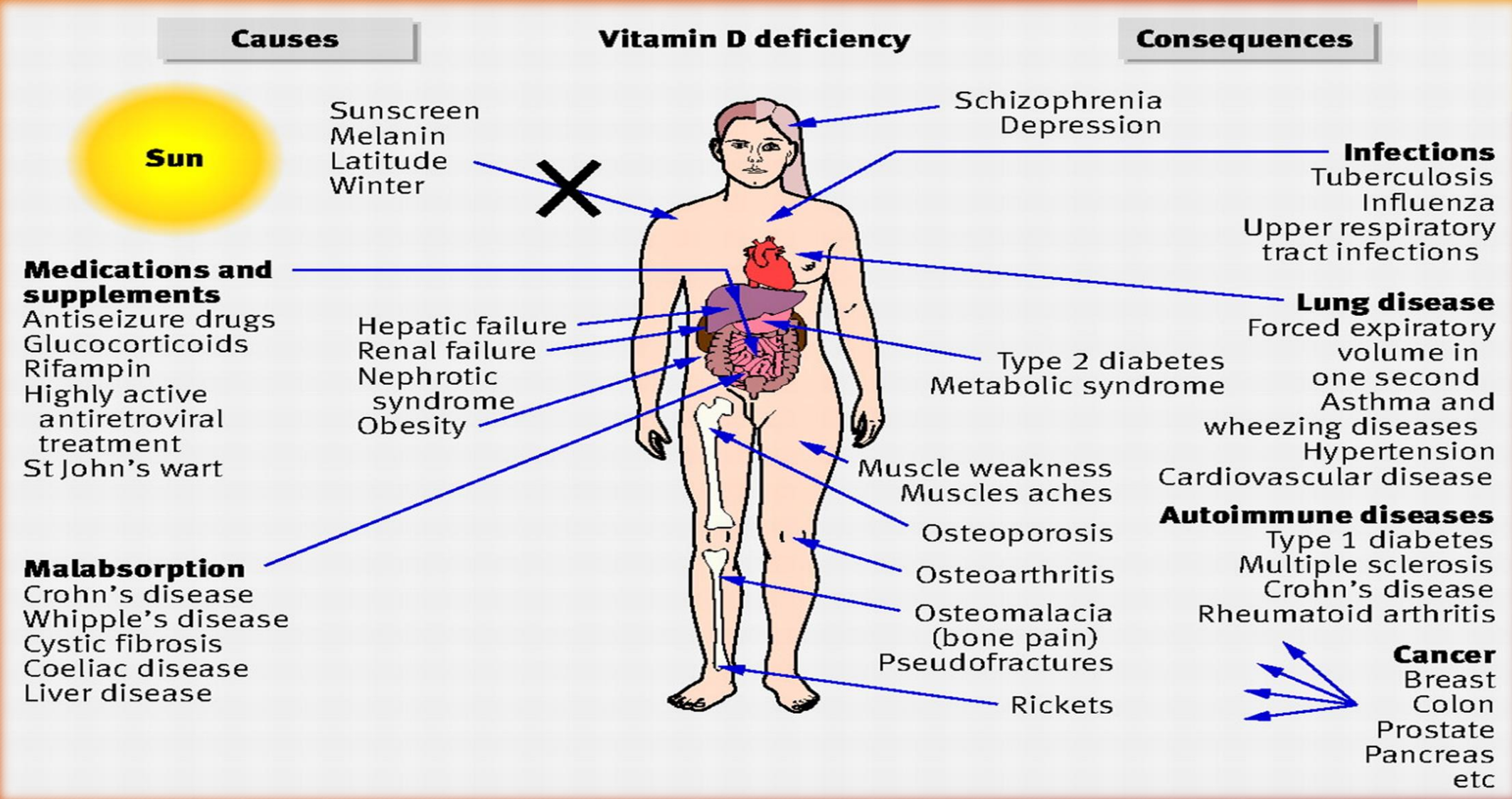
Multiply ng/mL by 2.5 to convert to nmol/litre







# Vitamin D: Depression (and about 300 other problems)





# Omega 3 Deficiency

Chicken of the Sea



# Omega III Fatty Acids and Cognitive Impairment

- Higher intake of omega-3 fatty acids (n-3 FAs) is associated with a reduced risk of Alzheimer's disease (AD) and milder forms of cognitive impairment
- Meta Analysis revealed: benefit for immediate recall was detected in Cognitive Impairment Not Dementia (CIND).
- A benefit for attention and processing speed was also detected in CIND, but not healthy subjects
- These results suggest an effect of n-3 FAs within specific cognitive domains in CIND, but not in healthy or AD subjects. (Mazereeuw, et al 2012)

# Omega 3 Fish Oil

EPA + DHA = 1-3000 mg

- Six of 10 patients receiving EPA had a 50% reduction in Hamilton depression score compared with 1 of 10 patients receiving placebo.
- Mean reduction in Hamilton score was 12.4 points in the E-EPA group and 1.6 points in the placebo group.
- There were no significant adverse effects and no reports of fishy taste or odors.

Amount Per Serving	% Daily Value	
Calories	10	*
Calories from Fat	10	*
Total Fat	1	2%
Saturated Fat	0.5g	3%
Polyunsaturated Fat	Less than 0.5	*
Monounsaturated Fat	0g	*
Cholesterol	5mg	2%
Fish Oil Concentrate	1,000mg	*
EPA (Eicosapentaenoic Acid)	180mg	*
DHA (Docosahexaenoic Acid)	120mg	*



## Journal of American College of Nutrition

**EPA but Not DHA Appears To Be Responsible for the Efficacy of Omega-3 Long Chain Polyunsaturated Fatty Acid Supplementation in Depression: Evidence from a Meta-Analysis of Randomized Controlled Trials**

---

Julian G. Martins, MA, MBBS

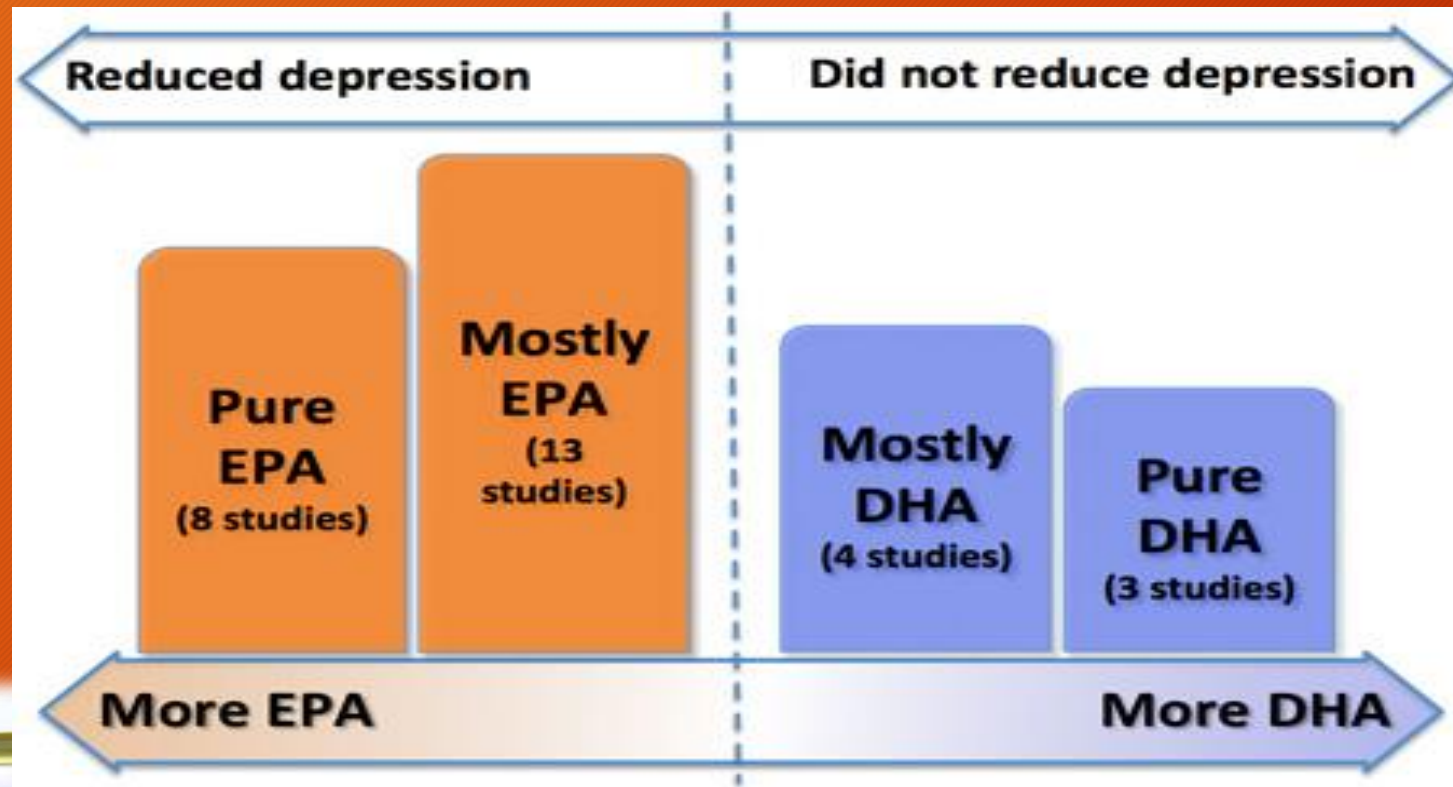
## Molecular Psychiatry

**EPA in major depressive disorder**

Eicosapentaenoic acid appears to be the key omega-3 fatty acid component associated with efficacy in major depressive disorder: a critique of Bloch and Hannestad and updated meta-analysis

JG Martins, H Bentsen and BK Puri

**1000 to 2000 mg of EPA is an effective dose to help with depression.**



## Take home message:

- 1. Good (chewable) multivitamin with minerals
- 2. B Vitamins:
  - B1-100 mg (Thiamine)
  - B6 20 mg
  - B12 10 mcg (Methylcobalamine)
  - B9 folate 200 mcg (Methylfolate)

## Take home message:

- 3. *Magnesium, preferably NOT oxide (500-1500 mg per day)*
- 4. *Vit D3 with Vit K2 (4000 units per day)*
- 5. *Omega 3 Fish Oil 1000-4000 units per day of DHA + EPA=1000-4000.*

Questions?



What can we do when anti-depressants  
don't work?

# Sex and Serotonin

- A man's average production of Serotonin is about 52% greater than a woman's
- In women, low serotonin is associated with depression and anxiety
- In men, low serotonin is related to aggression and alcoholism
- Men *act out* their mood
- Women *act in* their moods

# Depression in Addiction

- Male addicts have a rate of depression three times higher than the general public
- Female addicts have a rate that's four times higher [source: [Albrecht, Herrick](#)].





**“Depression is often anger,  
without enthusiasm”**

**Patrick Holford,**  
*New Optimum Nutrition for the Mind*

# Depression in Addiction

The link between depression and addiction holds true for more traditional substance addictions like nicotine and alcohol as well as more recently recognized impulse-control addictions, such as compulsive gambling.

Is it any wonder then that Nevada, with the smoky, cocktail-fueled casinos of Las Vegas, ranked as **one of the 10 most depressed states in 2007**



# Truth about Antidepressants

*The Truth.....*



# A word about Mania and Antidepressants

- Review of 173 studies to assess the quality of the evidence for antidepressant use in bipolar patients
- "The take-home message is that antidepressants have a questionable benefit-risk and should only be used in certain cases in bipolar disorder,"

*Vieta, Nolen* 10th International Conference on Bipolar Disorders (ICBD).  
Abstract 13. Presented June 14, 2013.

# A word about Mania and Antidepressants

- "First, they shouldn't be used in mania or in mixed episodes
- They should only be used in bipolar depression in patients with a history of a good response in the past to antidepressants and no history of rapid cycling or switches into mania right away," he said

*Vieta, Nolen* 10th International Conference on Bipolar Disorders (ICBD).  
Abstract 13. Presented June 14, 2013.

# CDC Report on Antidepressants

- **1 in 9** Americans over age 12 takes antidepressants
- **1 in 4** women between 40 and 59
- Since the early 1990s antidepressant use has increased **400%** across all age groups
- **1 in 12** takes antidepressants despite having no depressive symptoms whatsoever.
- Less than **1/3** of those taking antidepressants have had a checkup with a mental health professional in the last year
- **1 in 7** has been on antidepressants for more than a decade.

# Antidepressants without a DX

- Nearly 3/4 of all antidepressant prescriptions are written without any diagnosis of a psychiatric problem.
- **Primary-care** physicians are much more likely to prescribe these drugs than specialists
- 1 in 11 visits to a primary-care physician results in a new antidepressant prescription or refill.
- In nearly 80% of these office visits where there's no psychiatric diagnosis, there's also no specific psychiatric complaint from the patient.



# Antidepressants and Placebo Response

- A review of 96 studies published from 1980 to 2005 concluded the placebo effect was likely responsible for **68%** of the improvement seen in patients taking antidepressants.
- Another review pegged it at **84%**.
- What's more, the placebo effect appears to be growing over time.

Khan, Arif et al. "Why Has the Antidepressant-Placebo Difference in Antidepressant Clinical Trials Diminished over the Past Three Decades?" *CNS Neuroscience & Therapeutics* 16 (2010): 217-226.

Kirsch, Irving "Antidepressants and the placebo response" *Epidemiologia e Psichiatria Sociale* 18.4 (2009): 318-322.

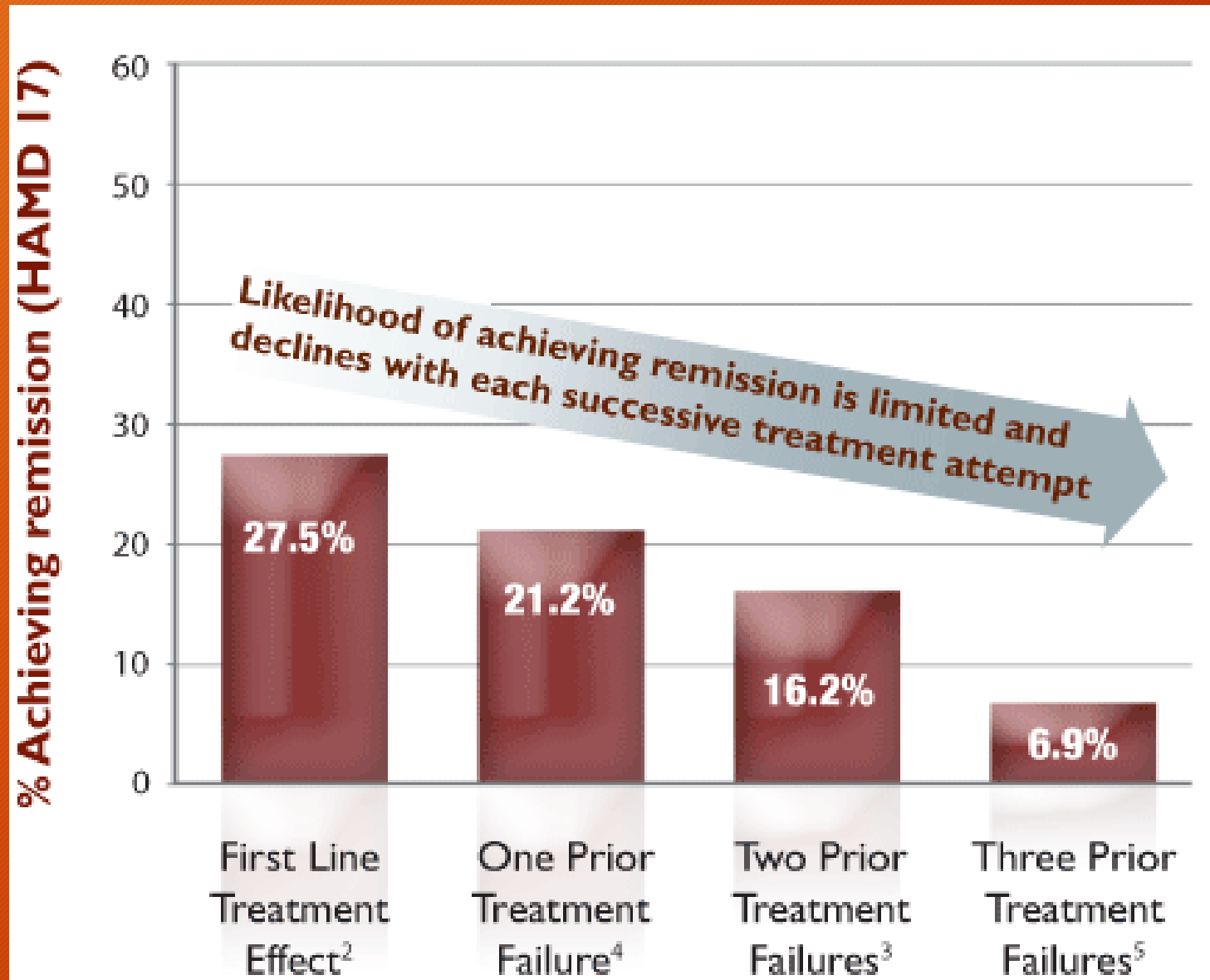
# Placebo v. Antidepressants v. Therapy

- A review of 177 studies involving more than 24,000 depressed patients found **placebos alleviated symptoms in 38%**, while **antidepressants reduced them in 46%**.
- **Psychotherapy alone reduced symptoms in 47 percent**, about the same as antidepressants but usually at higher cost.
- Best of all was combining antidepressants and psychotherapy, with a **52% success rate**.

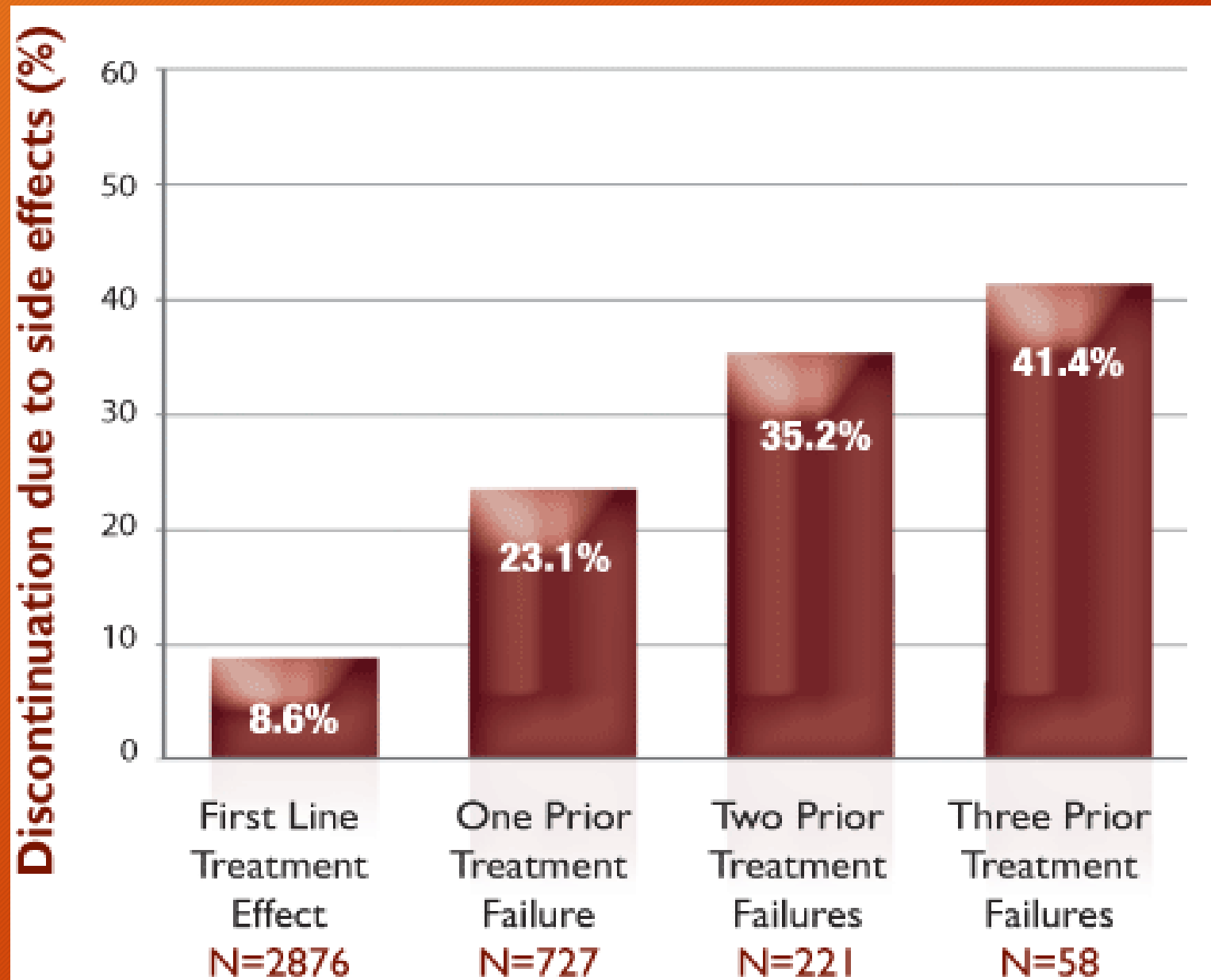
# Antidepressants and the placebo response

- Some research says there's *no* medicinal benefit.
- A European study of “active placebos” (where the placebo mimicked the drug's side effects) found **no significant difference between placebos and antidepressants.**

The STAR\*D study is the largest and longest study ever conducted to evaluate depression medication<sup>2,3</sup>



# Likelihood of discontinuing treatment increases with each new medication attempt<sup>2</sup>,



# Antidepressants and Nutrients

- Antidepressants DEplete **melatonin** which is important for sleep as well as one of the most powerful antioxidants in the body
- **Deficiency of B Vitamins**

# What else looks like depression?

Another question to ask.....

# Alternative Causes of Depression

- Low estrogen in women, low testosterone in men
- Not enough full spectrum light
- Not enough exercise
- Too much stress, especially for women
- Not enough co-factor vitamins and minerals
- Blood Sugar Imbalances

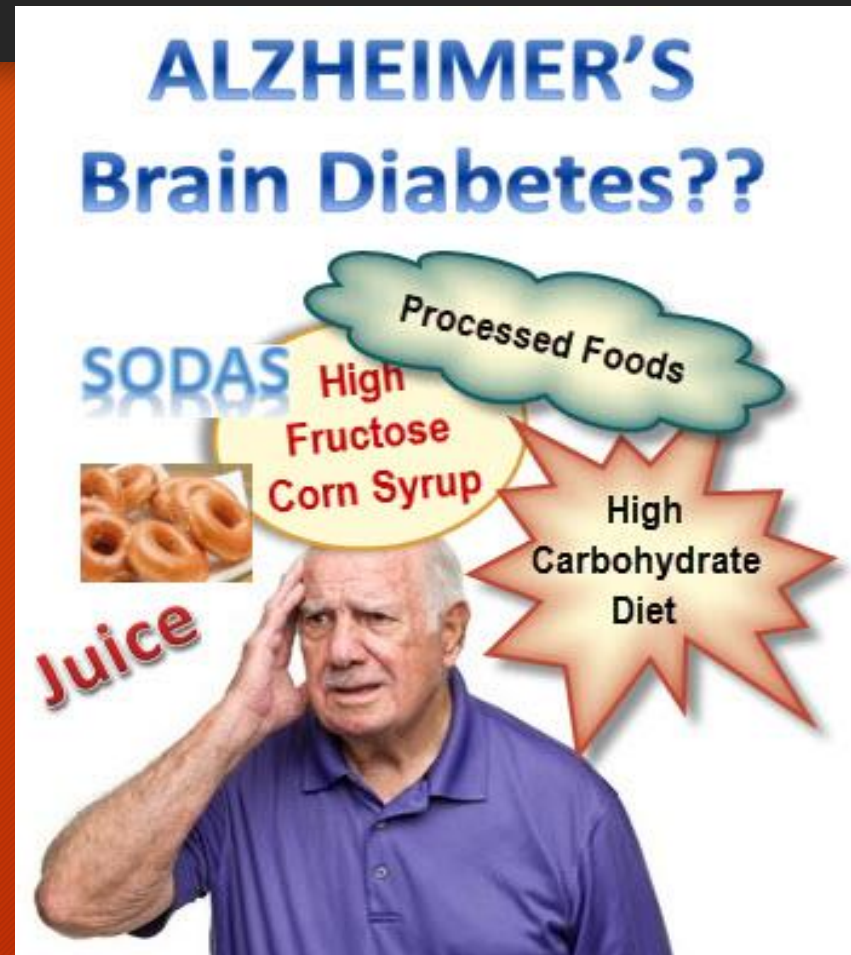


# Diabetes Connection

Blood Sugar and Depression

# Let's look at Diabetes

- Type I- autoimmune insulin dependent
- Type II- insulin resistance
- Gestational Diabetes
- Surgical/injury related
- Type 1.5-delayed autoimmune insulin dependent
- Type 3- Alzheimers



# Depression and Diabetes

- Studies have shown that **people with diabetes are more likely to have depression** than individuals who do not have diabetes. However the mechanisms linking these conditions are not entirely clear.
- A review of studies found that depression was associated with a **60% increase of type 2 diabetes** while type 2 diabetes was only associated with a moderate (15%) increase in risk of depression

# Depression, Diabetes and VAT

- The women who showed signs of depression (assessed using the CES-D scale) had 24.5% more visceral belly fat than the women with fewer depressive symptoms.
- No association was found between depression and subcutaneous belly fat (non-visceral)

Researchers from Rush University Medical Center looked at over 400 women “who were participating in the Women in the South Side Health Project (WISH) in Chicago, a longitudinal study of the menopausal transition”.

**They screened the women for depression and measured their visceral fat with a CT scan**

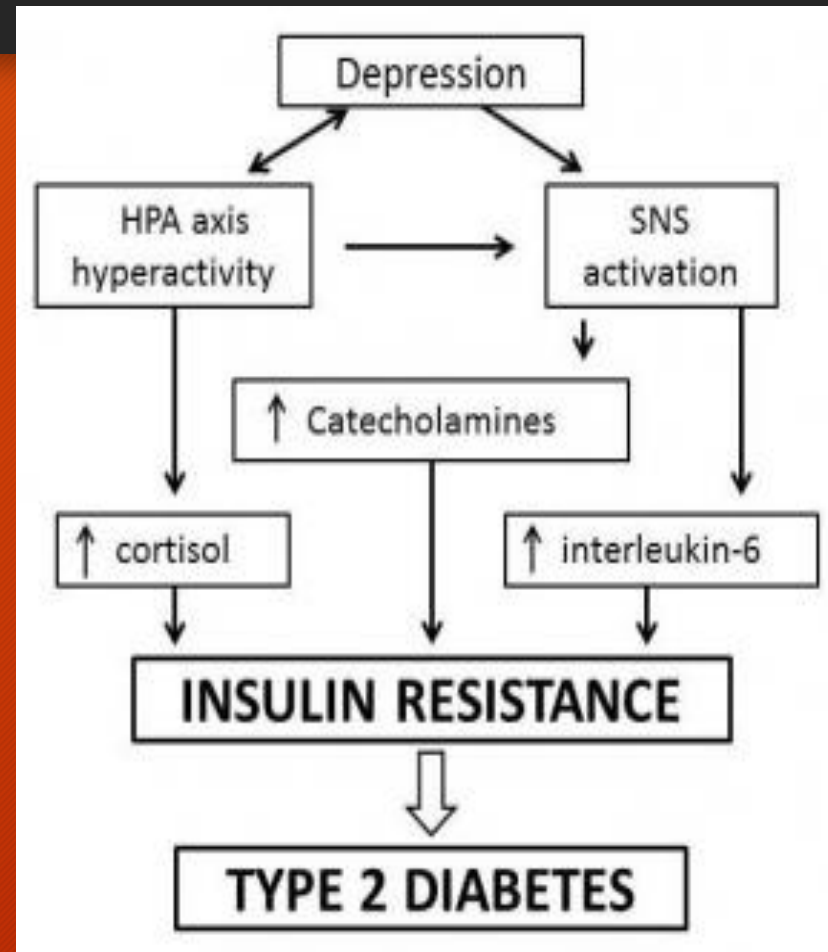


# why is depression linked to increased visceral fat, diabetes and cardiovascular disease?

- Alterations of the HPA axis : resulting in excess cortisol production
- The excess cortisol could lead to increased visceral fat because glucocorticoid receptor density is higher in VAT than in other types of adipose tissue
- Depression is also associated with increased inflammation. Various markers of inflammation (C-RP, fibrinogen, interleukin-6 and tumor necrosis factor. All of these markers have been noted to be elevated in individuals suffering from obesity, diabetes and atherosclerotic vascular disease.

# Why is depression linked to increased visceral fat, diabetes and cardiovascular disease?

- Adipose tissue, particularly VAT, secretes a host of inflammatory markers and is associated with increased systemic inflammation



By 2010, over one third of the kids and also adults were overweight.

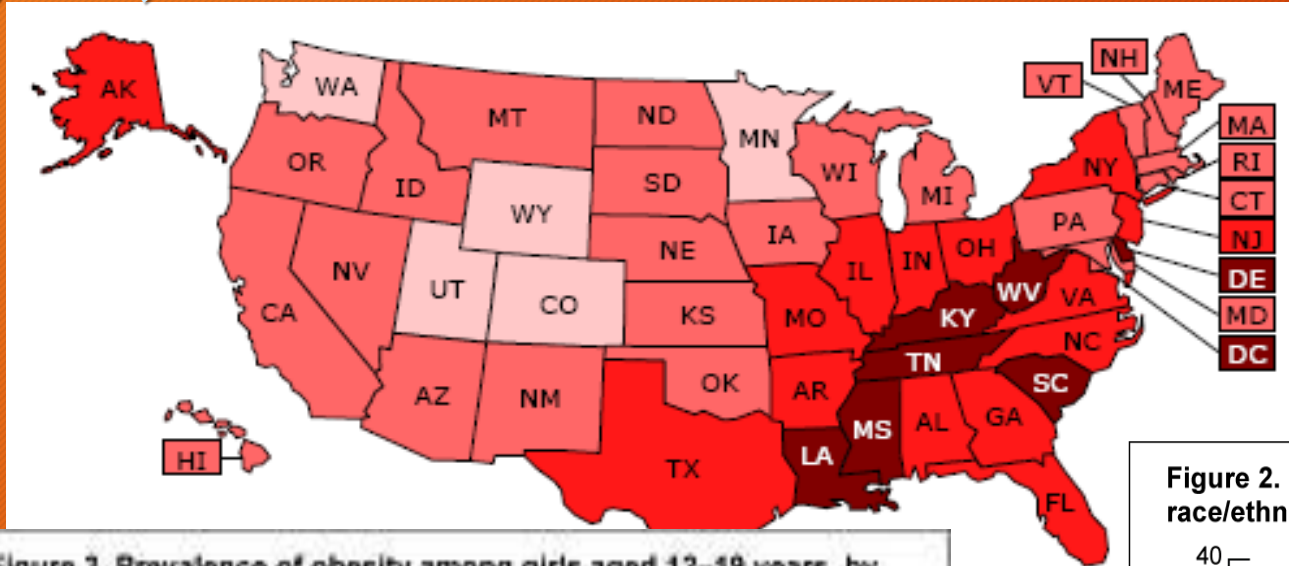
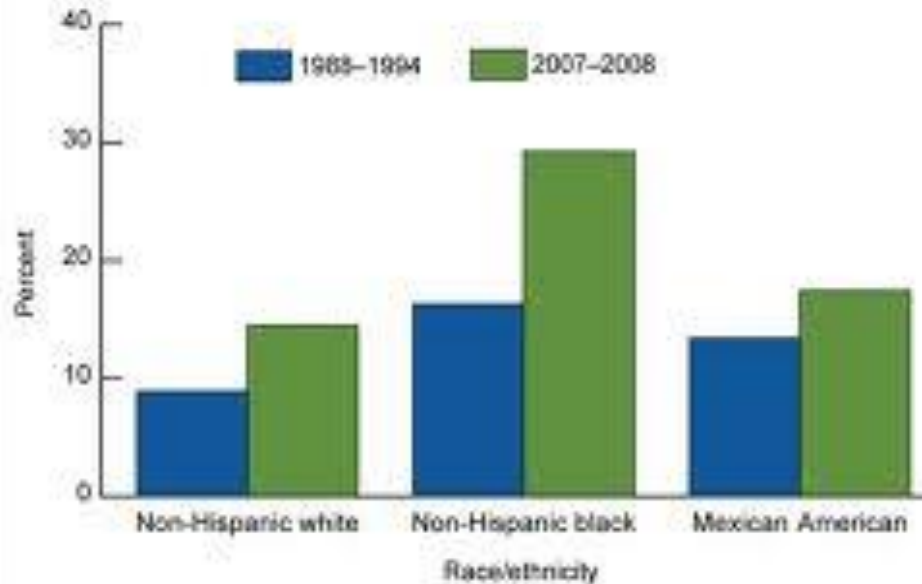
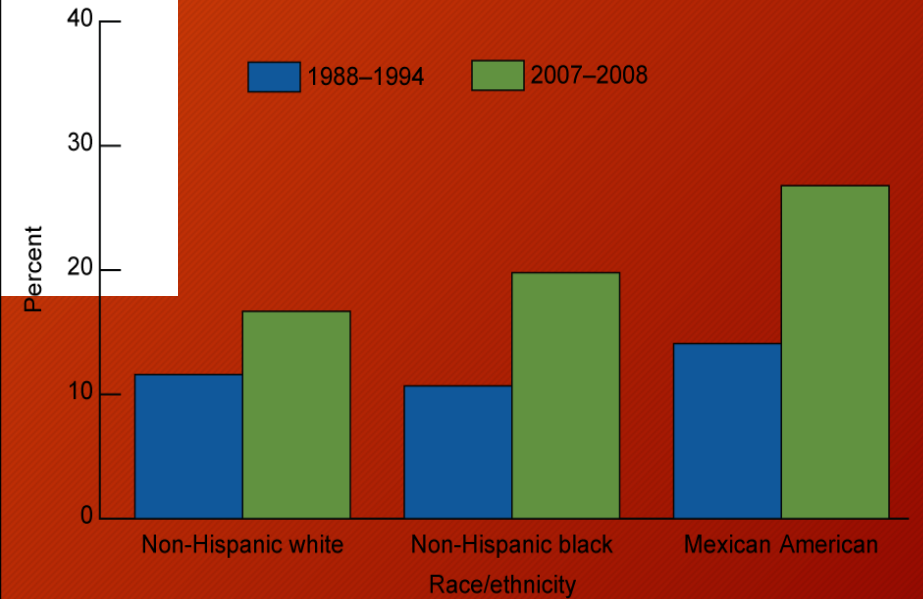


Figure 3. Prevalence of obesity among girls aged 12–19 years, by race/ethnicity: United States, 1988–1994 and 2007–2008



NOTE: Obesity is defined as body mass index (BMI) greater than or equal to sex- and age-specific 95th percentile from the 2000 CDC Growth Charts.  
 SOURCES: CDC/NCHS, National Health and Nutrition Examination Survey (NHANES) III 1988–1994 and NHANES 2007–2008.

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 SOURCES: CDC/NCHS, National Health and Nutrition Examination Survey (NHANES) III 1988–1994 and NHANES 2007–2008.



# ADRENAL GLANDS

Multiple responsibilities

# DHEA in Women and Men

- Important Adrenal Hormone
- Decreased postmenopausal bone loss
- Improves muscle strength
- Improves sexual performance
- Improves memory
- Improve weight loss efforts
- Can raise testosterone levels without some of the side effects of T replacement (acne, hirsutism, or deepening of voice)

## Some CAM Therapies May Reduce Major Depression Symptoms

Here's a brief look at the effectiveness, safety, and costs of some CAM treatments that have been evaluated in major depression.

Treatment	Effectiveness	Safety	Cost
Omega-3 fatty acids	Evidence of effectiveness when used as an antidepressant supplement	Low risk	Low cost
SAMe	Evidence of effectiveness when used as a monotherapy	Relatively low risk	Expensive
Exercise	Evidence of effectiveness both as monotherapy and as antidepressant adjunct	Few medical contraindications	Low cost
Light therapy	Evidence of effectiveness when used as an adjunct to antidepressants	Low risk	Cost of light box
Folate	Possibly effective	Can mask pernicious anemia	Low cost

Source: Marlene Freeman, M.D., et al., *Journal of Clinical Psychiatry*, June 2010

# DHEA and Opiates for Pain

- *Daniell*\* studied patients treated with sustained-action oxycodone, sustained released morphine, transdermal fentanyl or methadone for at least one month.
- DHEA Levels were **below normal in 67% of study participants.**
- Only **25% of men** and **32% of women** had DHEA-S levels within normal age related values

Daniell HW, DHEAS deficiency during consumption of sustained-action prescribed opioids: evidence for opioid-induced inhibition of adrenal androgen production. *J Pain* 2006;7:901-907

# Consequences of adrenal and gonadal abnormalities

- Depression and Gonads

- **Estrogen and Testosterone have a direct effect on Serotonin synthesis.**
- **If there are low levels due to gonadal dysfunction with addiction, the patients can suffer from depression, sadness and anger that **does NOT respond to antidepressants****

- Depression and Adrenals

- **Reduced Cortisol has been linked to depressive symptoms, apathy, profound fatigue and even delusional behavior**

# Light Therapy and SAD

- Serotonin levels are lowest in the winter
- The amount of Serotonin produced is directly related to how much daylight we are exposed to
- Light therapy can improve sleep problems, lethargy, overeating, anxiety loss of libido and depression

# Supplements that can Help

<b>Supplement Facts</b> <sup>v1</sup>		
Serving Size 4 Capsules Servings Per Container 15, 30		
4 capsules contain	Amount Per Serving	% Daily Value
Vitamin C (as Ascorbic Acid USP)	50 mg	83%
Niacin (as Niacinamide USP)	10 mg	50%
Vitamin B6 (as Pyridoxal 5'-Phosphate)	10 mg	500%
Folate (as Quatrefolic® (6S)-5-Methyltetrahydrofolic acid glucosamine salt)	400 mcg	100%
Vitamin B12 (as Methylcobalamin)	200 mcg	3,333%
Magnesium (as DiMagnesium Malate)	75 mg	19%
Zinc (as TRAACS® Zinc Bisglycinate Chelate)	5 mg	33%
Inositol NF	1,000 mg	*
L-Tyrosine USP	400 mg	*
Mucuna Pruriens Extract (Standardized to contain 10% L-Dopa)	400 mg	*
5-HTP	150 mg	*
L-Theanine	100 mg	*
PharmaGABA™	100 mg	*

\* Daily Value not established

<b>Supplement Facts</b> <sup>v1</sup>		
Serving Size 3 Capsules Servings Per Container 30		
3 capsules contain	Amount Per Serving	% Daily Value
Vitamin C (as Ascorbic Acid USP)	50 mg	83%
Niacin (as Niacinamide USP)	10 mg	50%
Vitamin B6 (as Pyridoxal 5'-Phosphate)	10 mg	500%
Folate (as Quatrefolic® (6S)-5-Methyltetrahydrofolic acid glucosamine salt)	400 mcg	100%
Vitamin B12 (as Methylcobalamin)	200 mcg	3,333%
Magnesium (as DiMagnesium Malate)	75 mg	19%
Zinc (as TRAACS® Bisglycinate Chelate)	5 mg	33%
Inositol NF	1,000 mg	*
Taurine	300 mg	*
L-Theanine	100 mg	*
PharmaGABA™	100 mg	*
5-HTP	75 mg	*

\* Daily Value not established