INTEGRATED TRAUMA INFORMED HEALING INTENSIVE IN CANMORE AB: NEUROSCIENCE, ATTACHMENT AND EVIDENCE-BASED PRACTICES

Presented by Jack Hirose & Associates. Sponsored by Sunshine Coast Health Centre and Georgia Strait Women's Clinic

If you have any questions, please contact your on-site coordinator.

PLEASE REMEMBER:

- Wear your name badge every day.
- Turn off your cell phone.

EVALUATION FORM:

- Complete your evaluation form each day using the QR code below.

SCHEDULE:

This schedule may vary depending on the flow of the presentation and participant questions

7:30am – 8:15am	Sign-In
8:15am – 10:00am	Morning Workshops Begin
10:00am – 10:15am	Mid-Morning Break (Refreshments Provided)
10:15am – 12:30pm	Workshop in Session
12:30pm	Complete Evaluation Forms (Use QR Code Above) & Sign-Out (CPA Members Only)

CERTIFICATES:

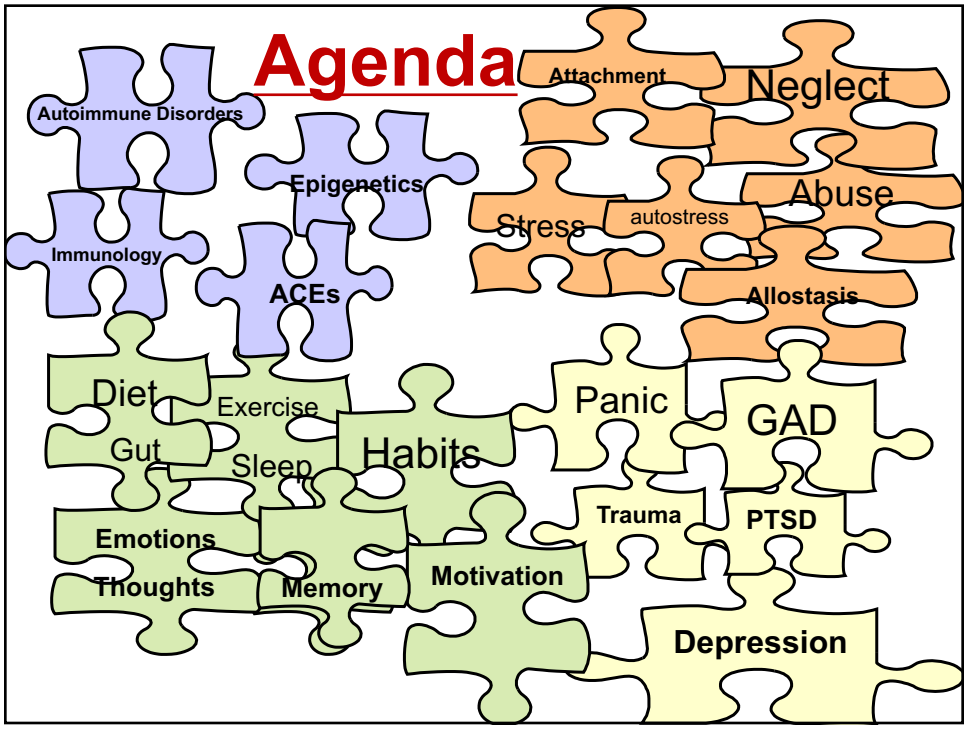
- Digital certificates are available for download on the final day for multi-day attendees at: http://registration.jackhirose.com/certificates

CPA MEMBERS

- A new policy requires you to request a form from your on-site coordinator, which must be submitted directly to the association.
- Please sign in after lunch and sign out at the end of the day. Early departures result in the loss of CPA credits.
- Certificates will be updated with CPA credits after form verification (allow 2-4 weeks).

Integrated Trauma Interventions

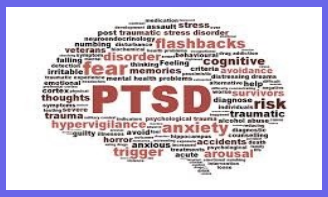
John B. Arden, PhD, ABPP



Refugee Crisis --100 Million

Re-traumatization caused by:

relentless war in throughout the world with a growing level of violence, traumatic experiences extreme deprivation in daily life



People Throughout the World

- Afghanistan—saying goodbye in the morning
- Syria—bomb and limbs
- Ukraine—soldier and partner
- Mexico—coyotes
- South Africa—necklaces
- USA—bullet
- Iraq—Shoot me
- Police—gun for 10 seconds

The Demise of the Medical Model

NIMH spent $20 billion of dollars, researchers have not found genetic risk for psychological disorders.

NIMH rejects DSM-5. The developers of DSM-IV also reject DSM-5 which was heavily funded by big Pharm.

"A system based on clusters of symptoms …not any objective, tested, reproducible, clinically actionable biomarkers for any psychiatric disorder."
(Insel, 2013)

Medications and the Medical Model

- Only 27% of the therapeutic response to drug effects.
- 50% of the responses to psychological factors surrounding the administration of the drug---10% to 70% placebo effect
- Down regulation of receptors

Therapy might have been different

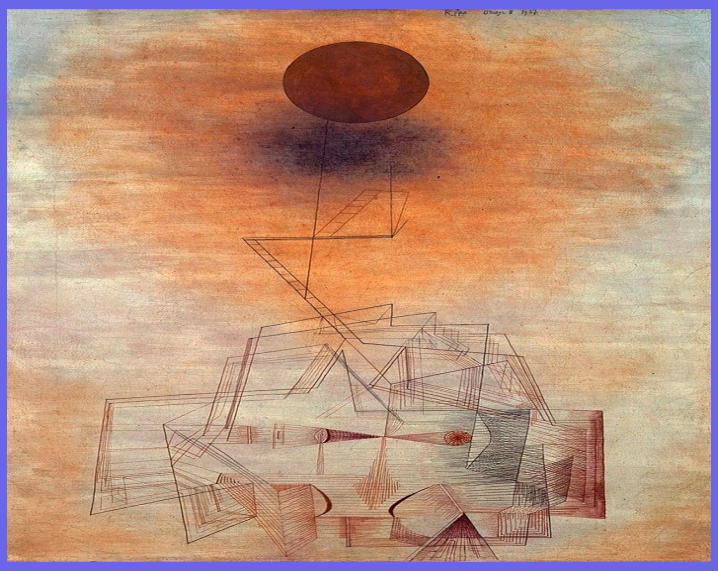
"We must recollect that all of our provisional ideas in psychology will presumably one day be based on an organic substructure."

--Sigmund Freud

"The act of will activates neural circuits" **But……**

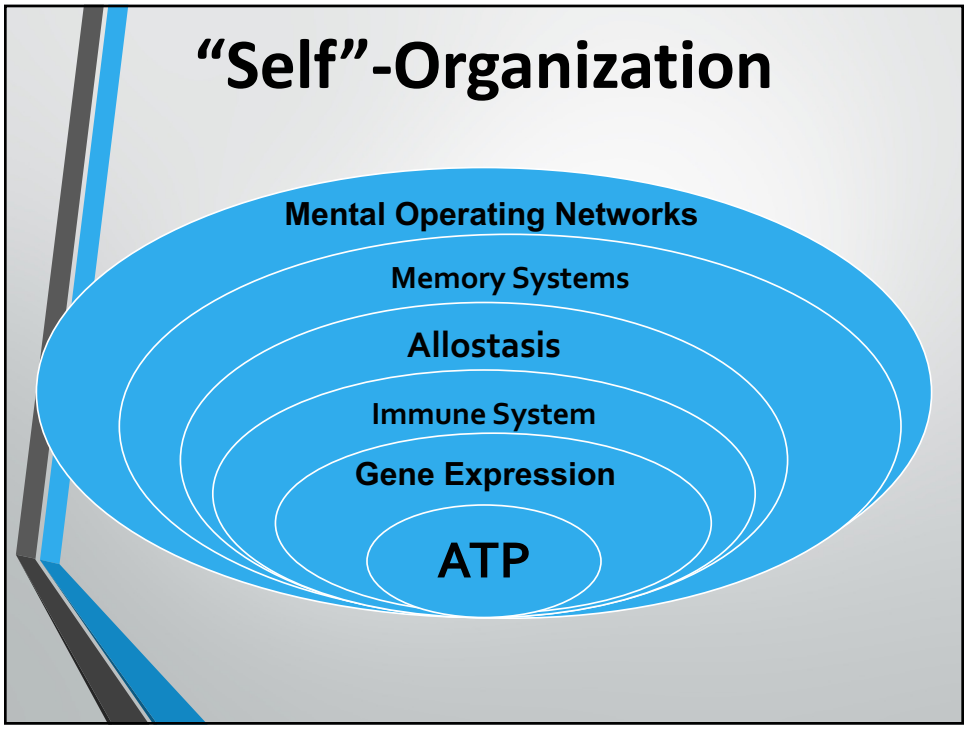
--William James

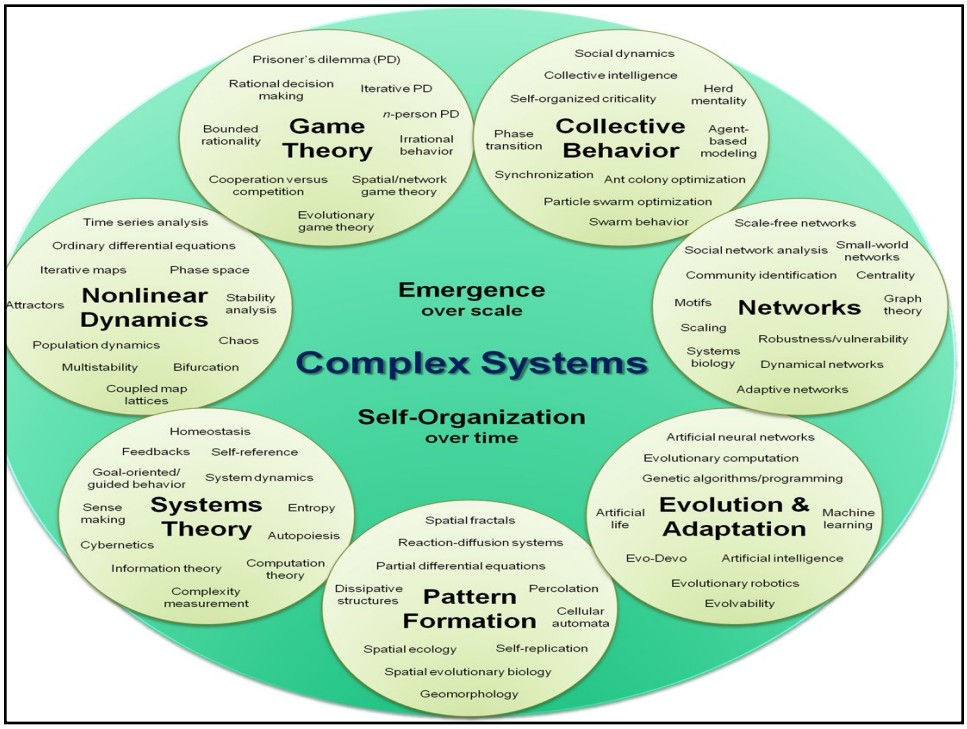
Limits of Understanding (Klee)



The **Cartesian** Blizzard

Abreaction therapy
ACT
Adlerian therapy
Adventure therapy
Analytical psychology
Art therapy
Attack therapy
Attachment-based psychotherapy
Attachment-based therapy (children)
Attachment therapy
Autogenic training
Behavior modification
Behavior therapy
Biodynamic psychotherapy
Bioenergetic analysis
Biofeedback
Body psychotherapy
Brief psychotherapy
Classical Adlerian psychotherapy
Chess therapy
Child psychotherapy
Client-centered psychotherapy
Co-counselling
Cognitive analytic therapy
CBT
Coherence therapy
Collaborative therapy
CFT
Concentrative movement therapy
Contemplative psychotherapy
Conversational model
Conversion therapy
Core process psychotherapy
Dance therapy
Depth psychology
Daseinsanalysis
DNMS
DBT
Drama therapy
Dreamwork
DDP
Ecological counseling
EFT
EFT
EMDR
Existential therapy
Exposure and response prevention
Expressive therapy
Family Constellations
Family therapy
Feminist therapy
Focusing
Freudian psychotherapy
FAP
Future-oriented therapy
Gestalt therapy
Gestalt theoretical psychotherapy
Group analysis
Group therapy
Guided affective imagery
Hakomi
Holotropic Breathwork
Holding therapy
Humanistic psychology
Human Givens
Hypnotherapy
Inner Relationship Focusing
Integrative body psychotherapy
Integral psychotherapy
Integrative psychotherapy
Intensive short-term dynamic psychotherapy
Internal Family Systems Model
Interpersonal psychoanalysis
Interpersonal psychotherapy
Jungian psychotherapy
Logotherapy
Marriage counseling
Milieu therapy
Mindfulness-based cognitive therapy
Mindfulness-based stress reduction
Mentalization-based treatment
MOL
MDT
Morita therapy
Motivational interviewing
Multimodal therapy
Multitheoretical psychotherapy
Music therapy
Narrative therapy
Nonviolent Communication
Nude psychotherapy
Object relations psychotherapy
Ontological hermeneutics
Orthodox psychotherapy
Parent–child interaction therapy
Parent management training
Pastoral counseling
Person-centered therapy
Play therapy
Positive psychology
Positive psychotherapy
Postural Integration
Primal therapy
Primal Integration
Process oriented psychology
Process psychology
Prolonged exposure therapy
Provocative therapy
Psychedelic therapy
Psychoanalysis
Psychodrama
Psychodynamic psychotherapy
Psychosynthesis
Pulsing
RET
RLT
Reality therapy
Rebirthing-breathwork
Recovered-memory psychotherapy
Re-evaluation Counseling
Reichian psychotherapy
Relationship counseling
Relational-cultural therapy
Remote therapy
Reprogramming
Rogerian psychotherapy
Sandplay Therapy
Schema Therapy
Self-relations
Psychotherapy
Sensorimotor psychotherapy
Sexual Identity Therapy
Sex therapy
Social Therapy
Solution focused brief therapy
Somatic Experiencing
Somatic psychology
Status dynamic psychotherapy
Supportive psychotherapy
Systematic desensitization
Systemic Constellations
Systemic therapy
T-groups
Therapeutic community
Thought Field Therapy
Transactional analysis
Transference focused psychotherapy


"Self"-Organization
Mental Operating Networks
Memory Systems
Allostasis
Immune System
Gene Expression
ATP


Complex Systems
Emergence over scale
Self-Organization over time
Game Theory
Prisoner's dilemma (PD)
Rational decision making
Iterative PD
n-person PD
Bounded rationality
Irrational behavior
Cooperation versus competition
Spatial/network game theory
Evolutionary game theory
Collective Behavior
Social dynamics
Collective intelligence
Self-organized criticality
Herd mentality
Phase transition
Agent-based modeling
Synchronization
Ant colony optimization
Particle swarm optimization
Swarm behavior
Nonlinear Dynamics
Time series analysis
Ordinary differential equations
Iterative maps
Phase space
Attractors
Stability analysis
Population dynamics
Chaos
Multistability
Bifurcation
Coupled map lattices
Networks
Scale-free networks
Social network analysis
Small-world networks
Community identification
Centrality
Motifs
Graph theory
Scaling
Robustness/vulnerability
Systems biology
Dynamical networks
Adaptive networks
Systems Theory
Homeostasis
Feedbacks
Self-reference
Goal-oriented/ guided behavior
System dynamics
Sense making
Entropy
Autopoiesis
Cybernetics
Information theory
Computation theory
Complexity measurement
Evolution & Adaptation
Artificial neural networks
Evolutionary computation
Genetic algorithms/programming
Artificial life
Machine learning
Evo-Devo
Artificial intelligence
Evolutionary robotics
Evolvability
Pattern Formation
Spatial fractals
Reaction-diffusion systems
Partial differential equations
Dissipative structures
Percolation
Cellular automata
Spatial ecology
Self-replication
Spatial evolutionary biology
Geomorphology

Characteristics of Complex Systems

- Open Systems
- Interdependence
- Feedback loops
- Non-linearity
- Emergence
- Self-organization

Free Energy Principle

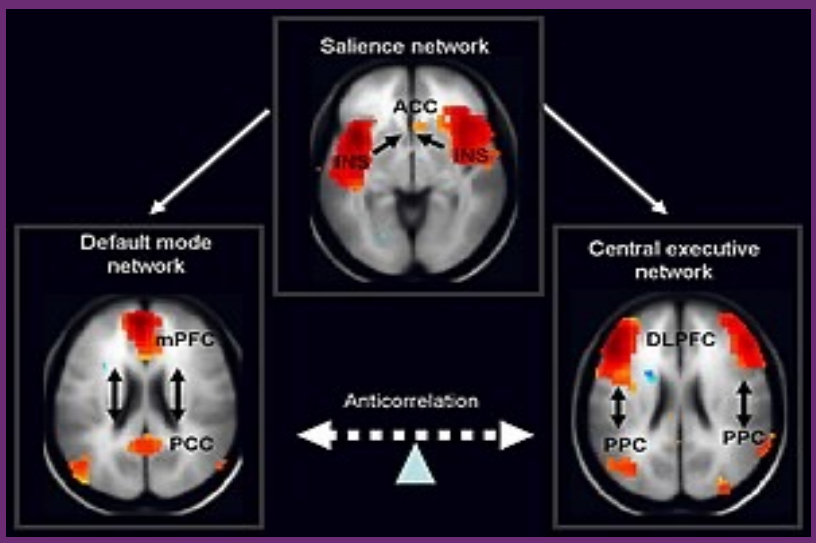
- **Minimize free energy**
- **Maximize energy efficiency**
- **Reduce uncertainty**
- **Prediction**

The Science has Changed

"Mental functions direct electrochemical traffic at the cellular level" Roger Sperry

"Psychotherapy works by producing changes in gene expression that alter the strength of synaptic connections…" Eric Kandel

The Mental Networks



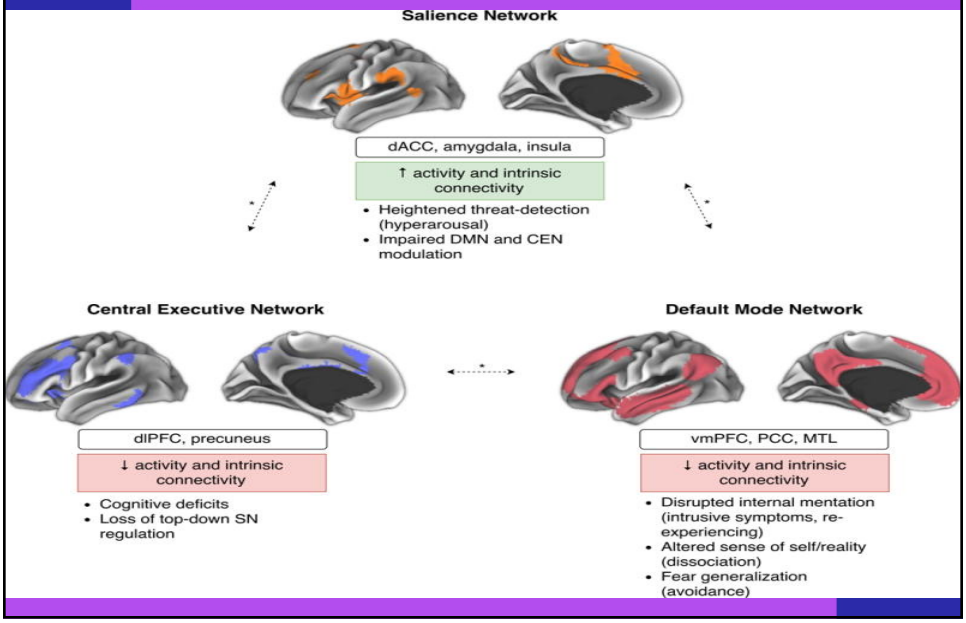
Life Satisfaction

- An indicator of brain flexibility and adaptability
- Self-construal (narrative) moderates the relationship
- Provides the infrastructure to minimize energy loss as we try to predict and adapt to new situations

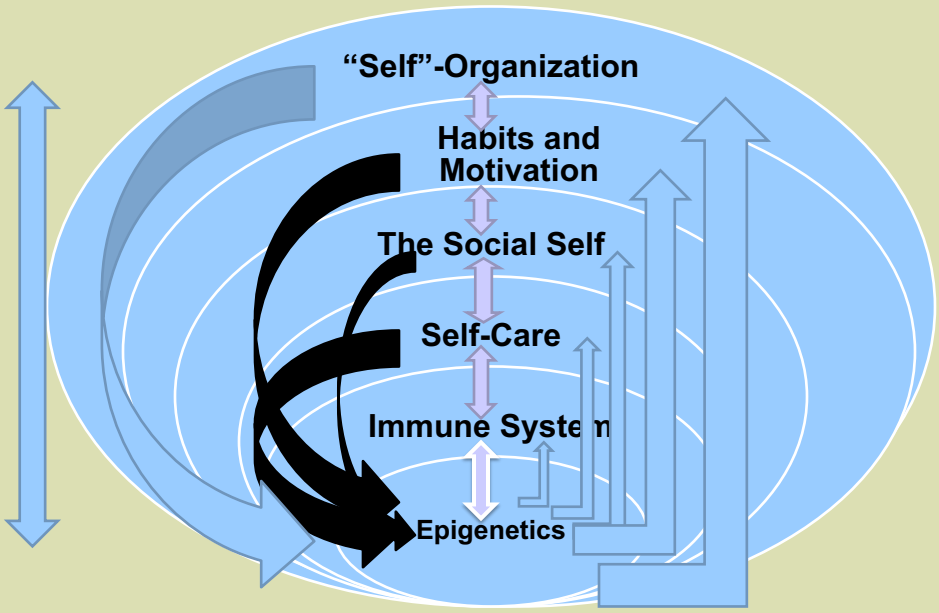
Life Satisfaction

- mPFC involved in the representation of self-referential information and affect regulation
- pCC is involved in the integration of self-referential info (narrative)
- Together they support mental health
- Greater life-satisfaction associated with neural variability between the DMN, EN, and SN

States of mind in conflict



Mind-Brain-Gene Feedback Loops



The ACE Study

- **Examined the health effects of ACE's throughout the lifespan among 17, 421 members of Kaiser Permanente in San Diego county**
- **What are Adverse Childhood Experience?**
  - **Childhood abuse and neglect**
  - **Growing up with domestic violence, substance abuse, parental discord, crime, or mental illness in the home**

Categories of Adverse Childhood Experiences

Abuse, by Category	**Category Prevalence (%)**
• Psychological (by parents)	11%
• Physical (by parents)	11%
• Sexual (anyone)	22%
Household Dysfunction, by Category	
• Substance Abuse in family	26%
• Mental Illness in family	19%
• Domestic Violence	13%
• Imprisoned Household Member	3%
• Loss of parent	23%

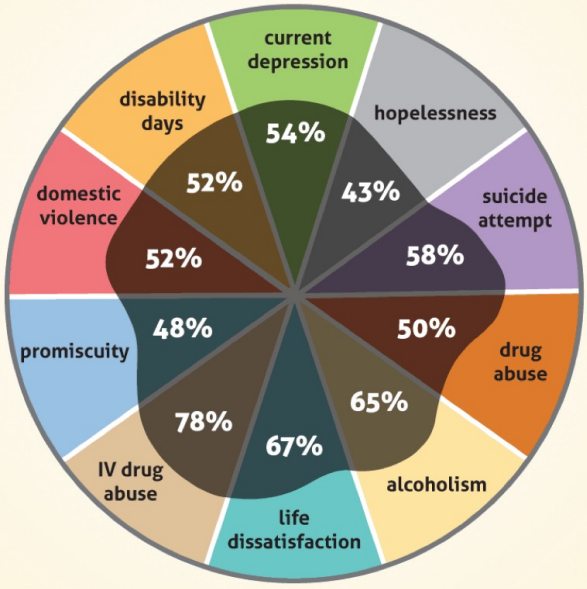
ACEs score percentages

Number of categories of childhood experiences are summed

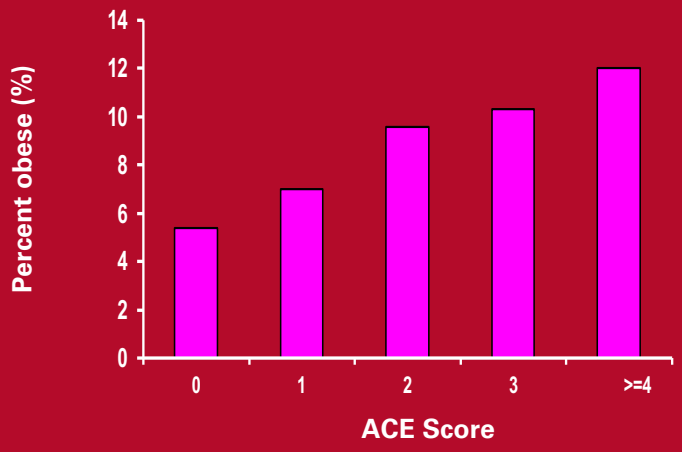
ACE Score	*Prevalence*
0	48%
1	25%
2	13%
3	7%
4	7%

- More than *half have at least one ACE*
- Slightly more than one quarter have experienced 2 – 4 ACE categories

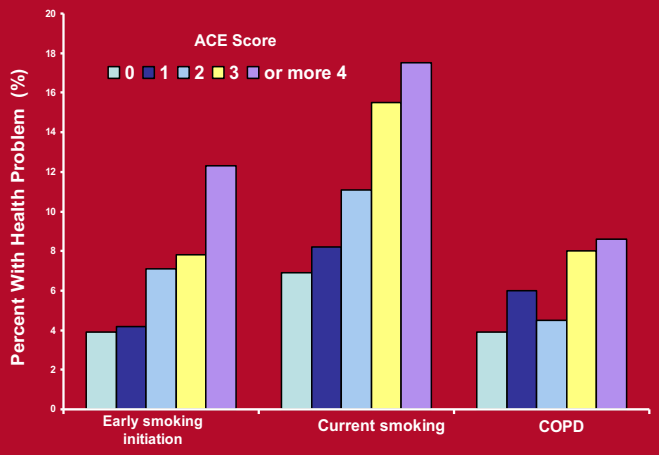
ACEs and Population Attributable Risks

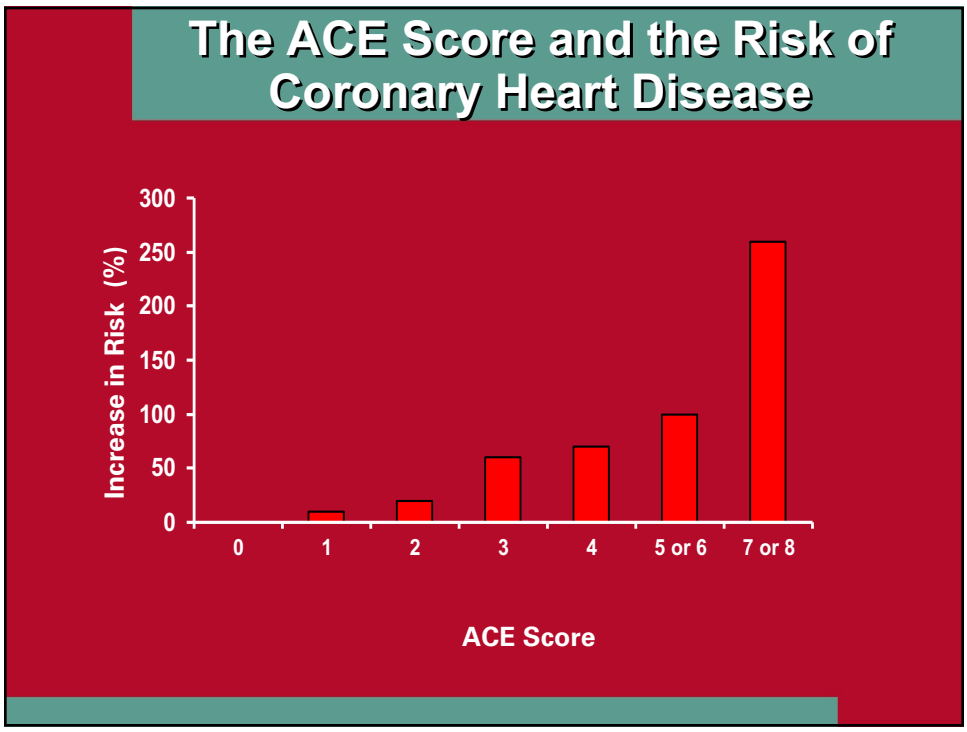


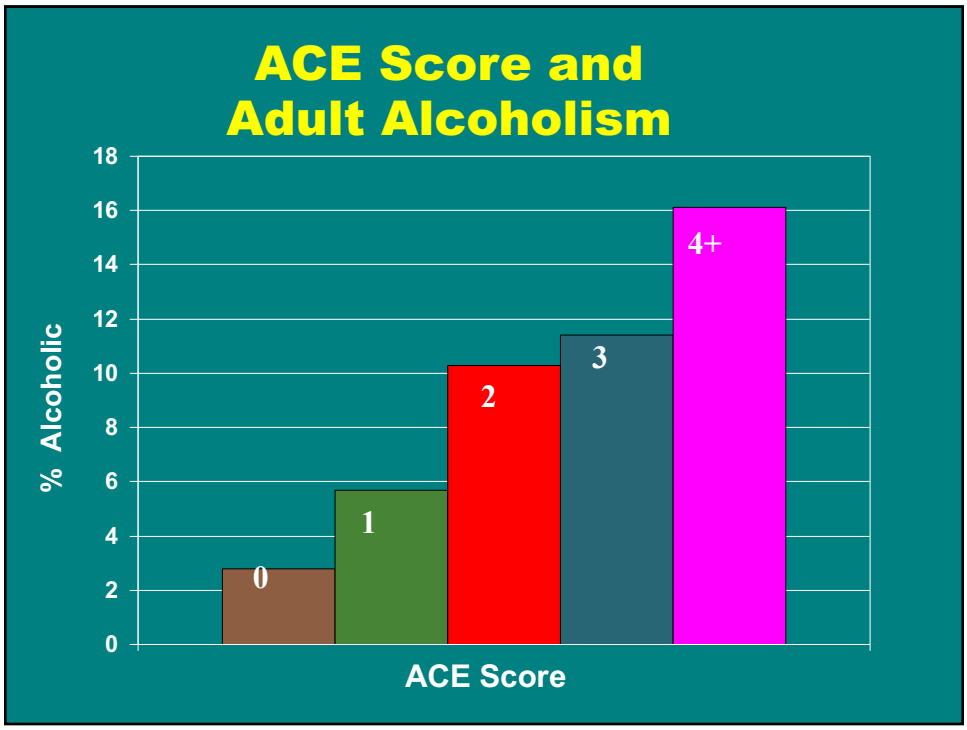
The ACE Score and the Prevalence of Severe Obesity (BMI>35)



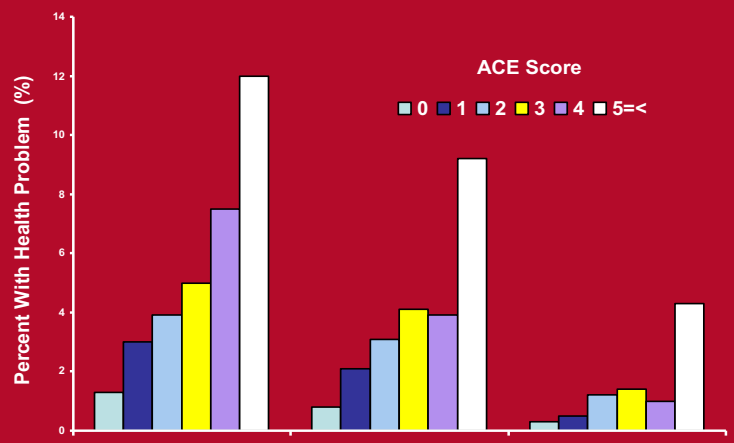
ACE's Smoking and Lung Disease



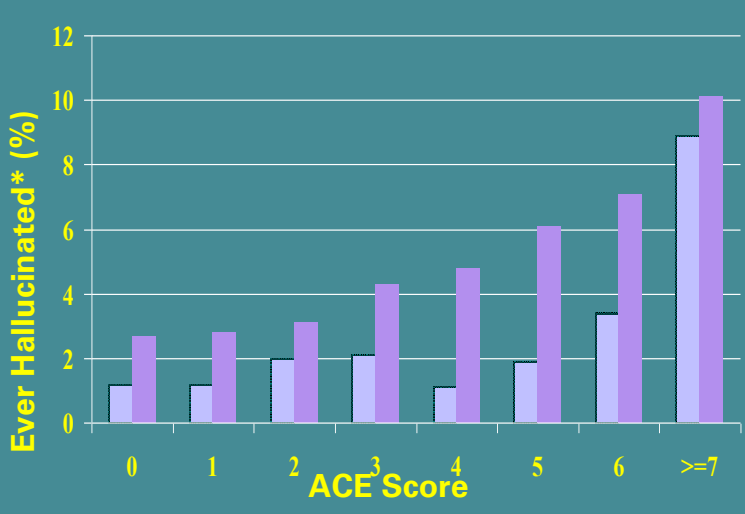

The ACE Score and the Risk of Coronary Heart Disease
Increase in Risk (%)
300
250
200
150
100
50
0
0
1
2
3
4
5 or 6
7 or 8
ACE Score


ACE Score and Adult Alcoholism
% Alcoholic
18
16
14
12
10
8
6
4
2
0
0
1
2
3
4+
ACE Score

The ACE Score and Drug Addiction

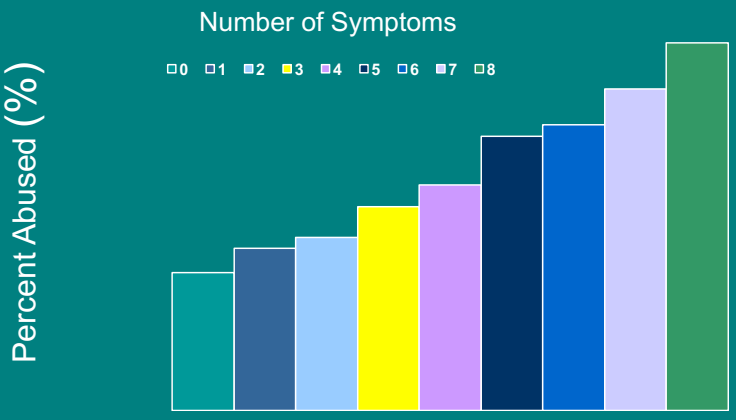


ACE Score and Hallucinations



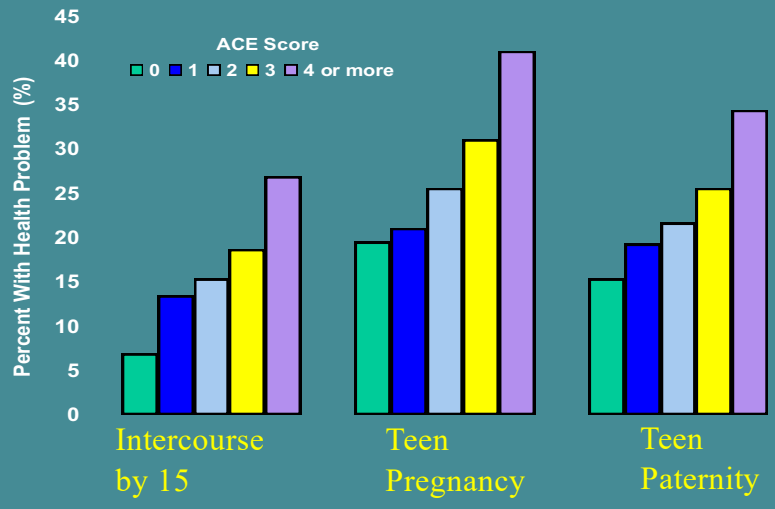
*Adjusted for age, sex, race, and education.

Childhood Sexual Abuse and the Number of Unexplained Symptoms

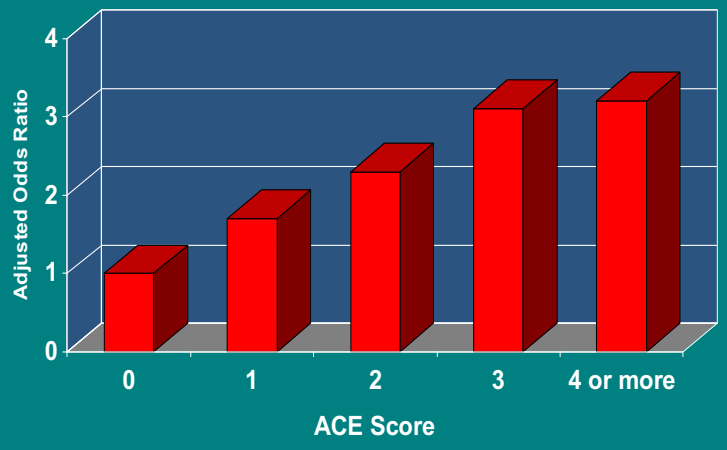


History of Childhood Sexual Abuse

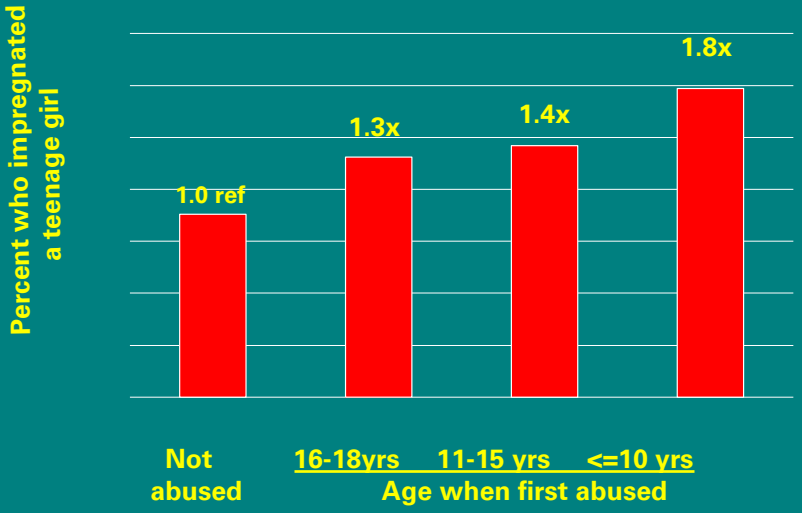
ACE Score and Teen Sexual Behaviors



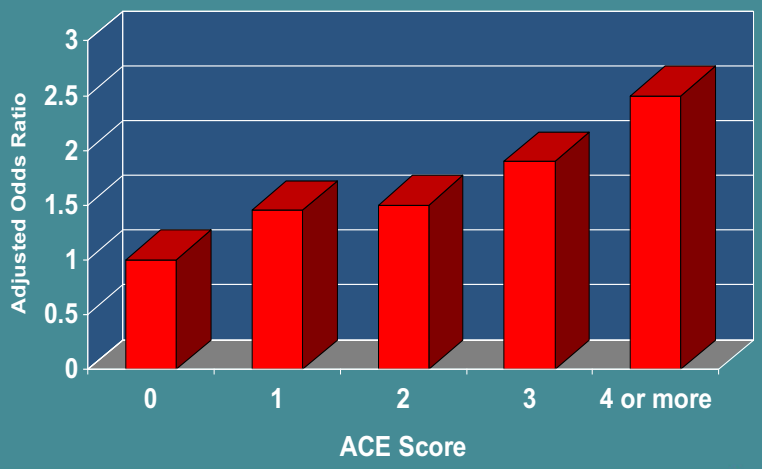
ACE Scores and Likelihood of > 50 Sexual Partners



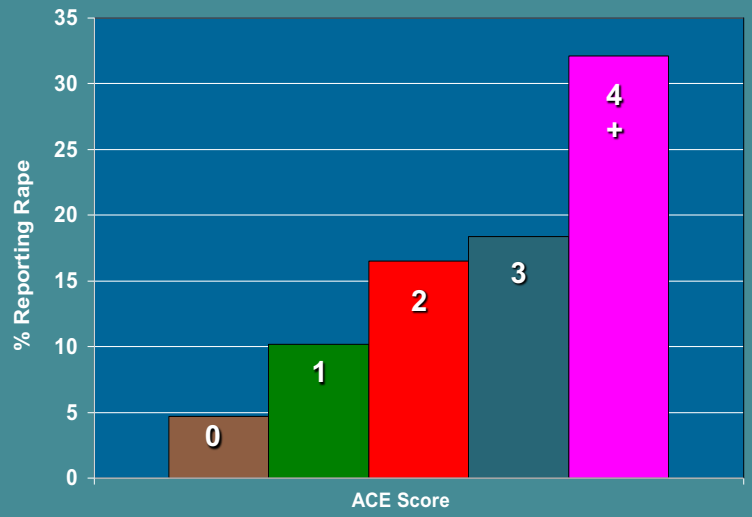
Sexual Abuse of Male Children and Their Likelihood of Impregnating a Teenage Girl

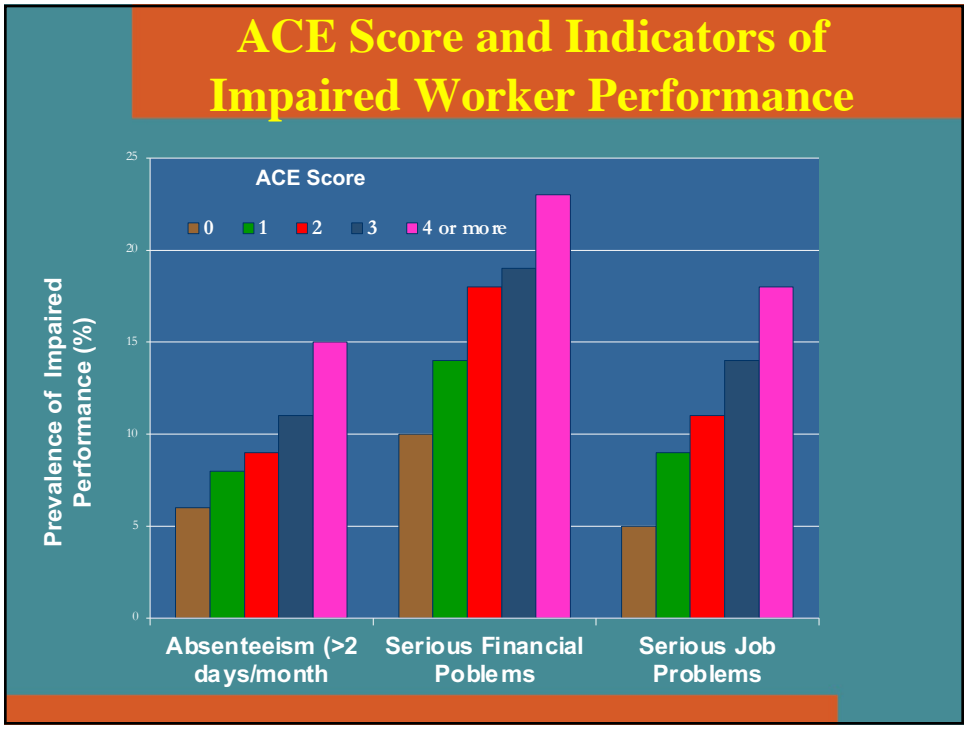


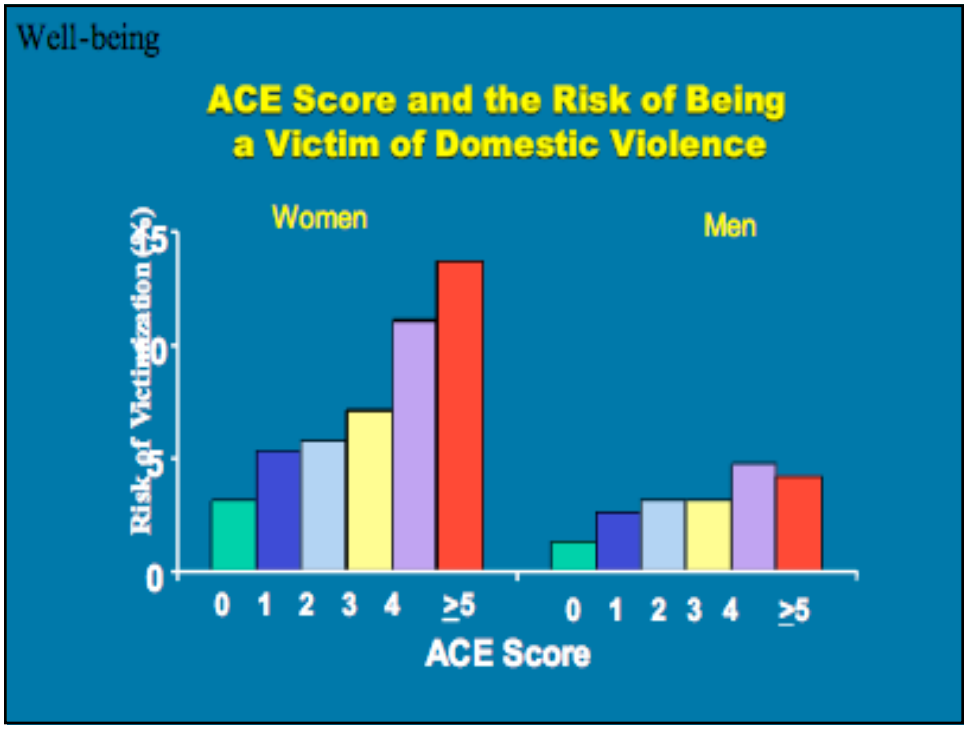
ACE Scores and History of STDs

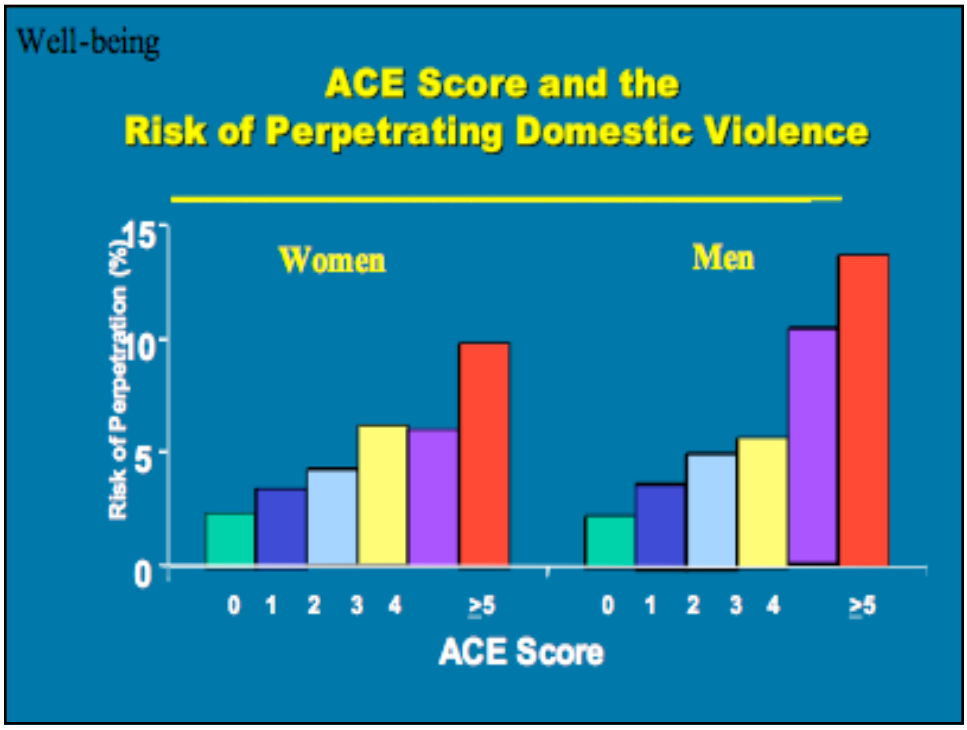


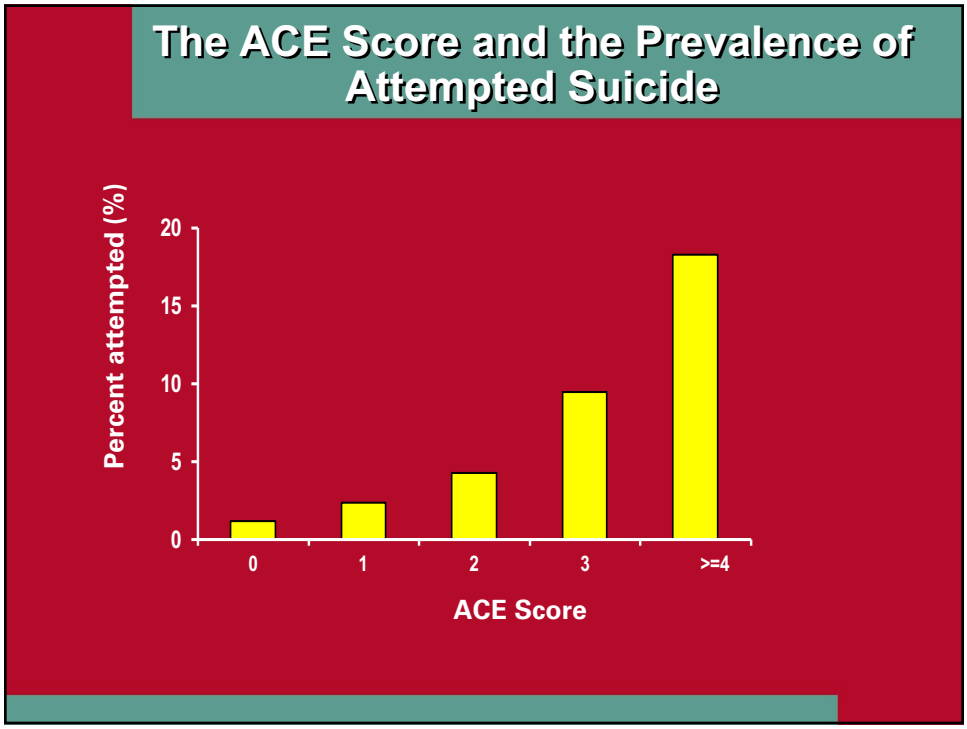
Childhood Experiences Underlie Later Being Raped



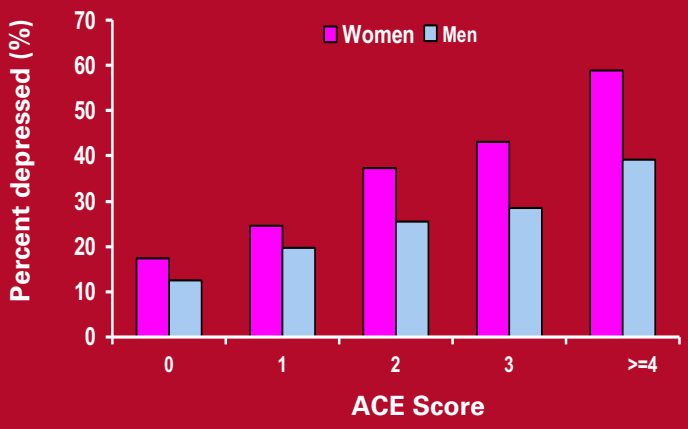

ACE Score and Indicators of Impaired Worker Performance
ACE Score
0
1
2
3
4 or more
Prevalence of Impaired Performance (%)
25
20
15
10
5
0
Absenteeism (>2 days/month
Serious Financial Poblems
Serious Job Problems


Well-being
ACE Score and the Risk of Being a Victim of Domestic Violence
Women
Men
Risk of Victimization (%)
0
0 1 2 3 4 ≥5
0 1 2 3 4 ≥5
ACE Score

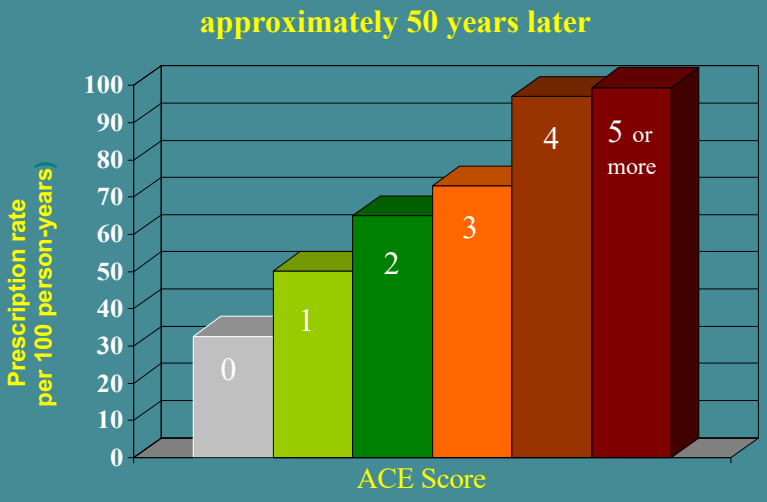

Well-being
ACE Score and the
Risk of Perpetrating Domestic Violence
Women
Men
Risk of Perpetration (%)
15
10
5
0
0 1 2 3 4 ≥5
0 1 2 3 4 ≥5
ACE Score


The ACE Score and the Prevalence of Attempted Suicide
Percent attempted (%)
20
15
10
5
0
0
1
2
3
>=4
ACE Score

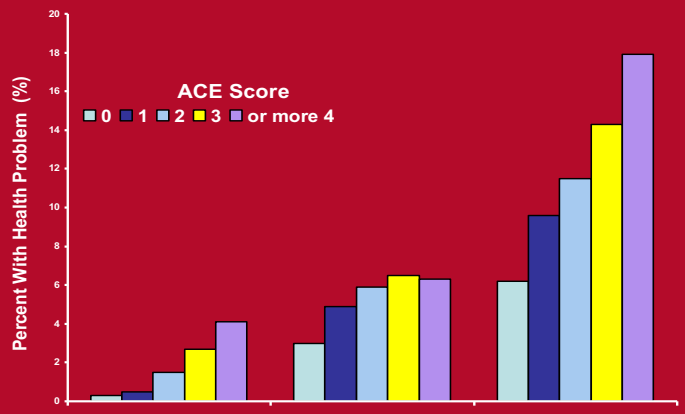
The ACE Score and a History of Lifetime Depression



ACE Score and Rates of Antidepressant Prescriptions

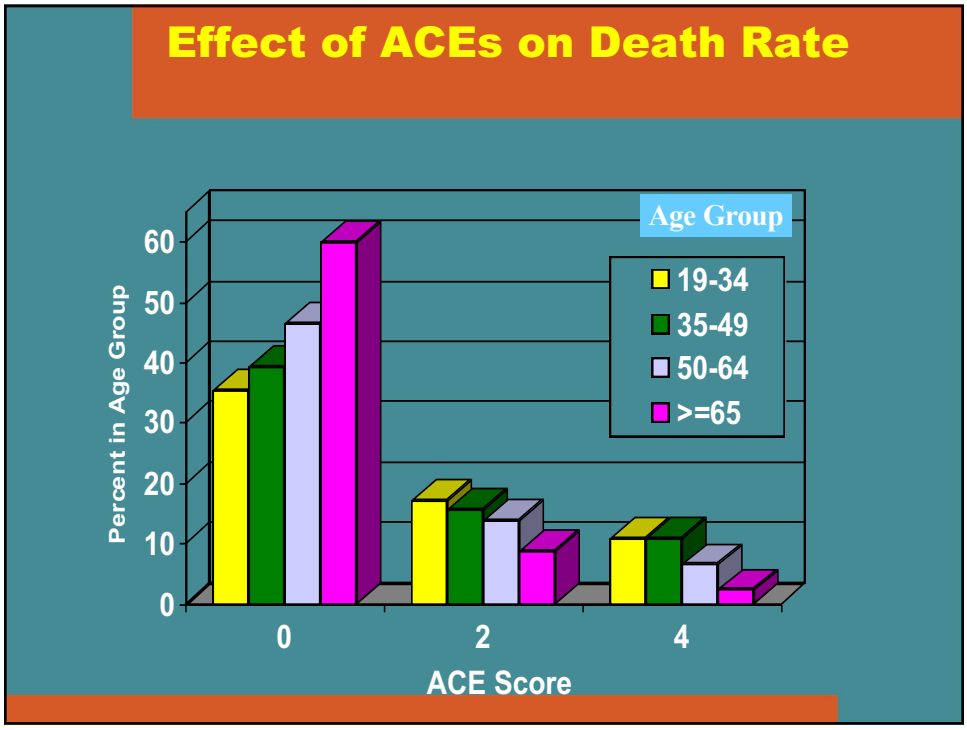


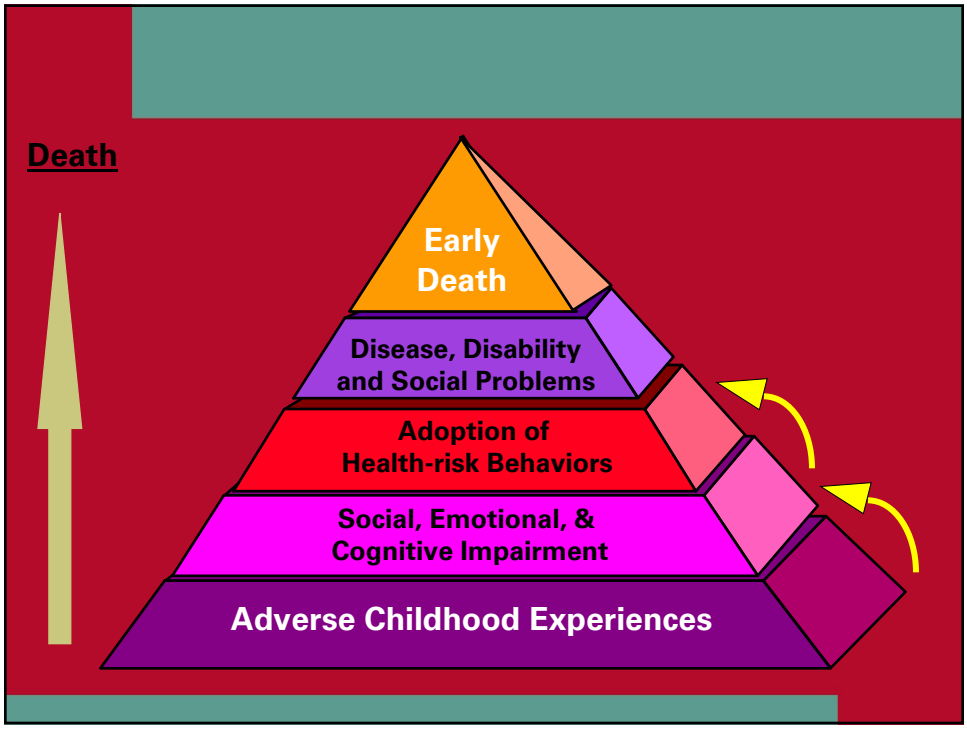
ACE Score and HIV Risks



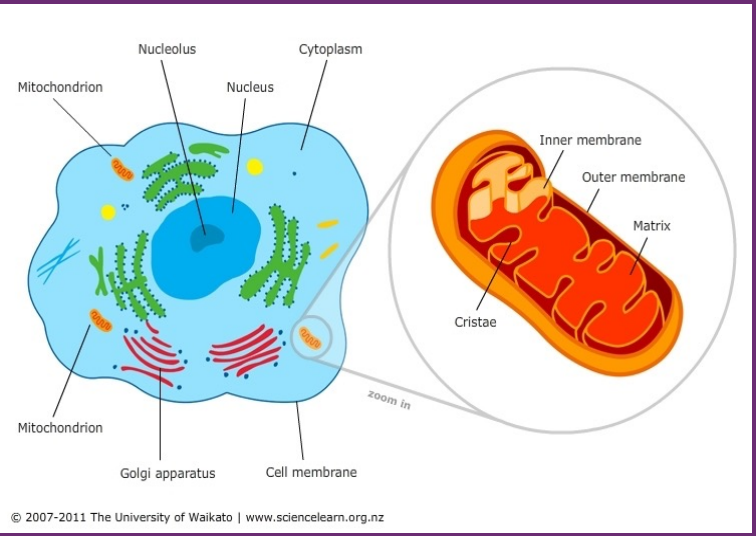
A Connection with Homelessness

- Psychological disorders and substance abuse are more common among homeless people
- ACEs connection to substance abuse and psychological disorders
- Over 50% of homeless with ACE Score of 4 or higher


Effect of ACEs on Death Rate
Age Group
19-34
35-49
50-64
>=65
Percent in Age Group
60
50
40
30
20
10
0
0
2
4
ACE Score


Death
Early Death
Disease, Disability and Social Problems
Adoption of Health-risk Behaviors
Social, Emotional, & Cognitive Impairment
Adverse Childhood Experiences

Cells and Their Energy Factories



Numbers of Mitochondria

- On average each of our cells host 500 mitos.
  - Roughly 10 percent of our total body weight.
- Energy needs: our heart and brain cells contain the greatest number of number of mitos.
  - There are approximately 10 million billion mitos in an adult human brain.

The Energy Generating Metaphor

Mitochondria, just like a dam, uses pressure in each step so that energy is released from electrons within the pump.

The biochemical reactions culminate with the final product, the synthesis of ***adenosine triphosphate*** *(ATP).*

Client Education

Because your energy generators are mighty: Call them ***Mitos***

They produce your principal energy: ATP for: ***All That Power***

Metabolic Energy = Life

- Energy production and use is called ***metabolism:***
  - Everyday a person's metabolism makes two hundred trillion trillion ATP molecules.
  - The rate at which the total number of ATPs are produced is a measure of your ***metabolic rate***.

Metabolic Rate

The metabolic rate is determined by how efficiently fuel is delivered to cells through our circulating system.

- Uses the right combination of oxygen, glucose, fatty acids, and sometimes amino acids to our mitochondria to produce ATP.

Energy Production

- ↑ food intake + Oxygen = ATP (energy)
  But with ↓ exercise --no demand for ATP
  And with regular oxygen ↑ free radicals

- When not enough antioxidants available:
  - Oxidation of lipids
  - Electron flow stops
  - More free radicals attack mtDNA
  - Cells fail to produce ATP and die

Anaerobic & Aerobic Metabolism

- ***Anaerobic metabolism*** is the creation of energy through the combustion of carbohydrates in the *absence* of oxygen

- ***Aerobic metabolism*** is the way your body creates energy through the combustion of carbohydrates, amino acids, and fats in the *presence* of oxygen.

Anaerobic Metabolism

- Early in our life anaerobic metabolism is critical for the growth of our body.
- Once we reach adulthood the emphasis on anaerobic metabolism shifts and the aerobic capacity declines.
  - we run the risk of building the wrong type of cells such as extra fat cells -- with less energy to burn it off.

Cellular Reactive Oxygen Species (ROS)

- Like a flooding a dam endures the risk of leaks, so too can mitos excessively leak:
  - ROS, a type of free radical.
- When in excess, ROS can damage cells, including the mitos that produced it.
  - But, low levels of ROS can lead to gene expression of anti-oxidant enzymes which protect from cells damage.

Free Radicals

- Highly reactive molecules that contribute to oxidative stress
- They lost an electron and are on the prowl to steal one from neighboring molecules.
  - –Cells malfunction
  - –Cells age (zombie cells)
  - –Cells are more vulnerable to disease
  - –DNA and mDNA more vulnerable to inaccurate gene expression

The Life Cycle of Mitochondria

- Mitos shelf life -- few days to a few weeks.
- They are recycled so that weak mitos are disposed of to insure quality of those that remain.
  - Removed by **"*mitophagy*"** ---killing off damaged mitos by mild ROS.
- Clears the way for mito ***"biogenesis."***

- **Poor self-care and ill health**
- **↑ flood of free radicals**

- Excessive fat cells ↑ ROS making all cells vulnerable to damage.
  - ROS and fat cells -- more likely with simple carbohydrates as fuel.
- The buildup of fat near mitos damages energy production.
  - Oxidative damage to the mitos spirals out of control.

Free Radicals—the Good and Bad

- We must use energy for:
  - maintenance and repair of cells
  - growth of new ones
  - engage in daily activities.
- When not used because of:
  - physical inactivity
  - overeating
    - there is a high rate of “oxidation.”

Client Education

- **Use it or lose it:**
  - **No exercise and overeating:**
  - **the dam leaks**
  - **↑ flood of free radicals**

Mobile Mitos

- Brain uses 20% of our body's energy, and our synapses use of 80% of that energy.
  - But, mitos at the synapses can only tolerate 25% drop in ATP before cognitive, emotional, and movement deficits.
- The energy fuels neuroplasticity by:
  - Mitos traveling on microtubules within our neurons to the synapses.

Mitochondria Burnout

- Mitos can burn out if the input and output is not balanced
  - Oxidative damage to:
    - Proteins
    - Lipids
    - mDNA
    - mito dysfunction.

Exercise and Biogenesis

- Aerobic exercise increases mitos in muscle cells by to 50% in 6 weeks.
  - ↑ ATP and ↓ ROS.
- ↑ biogenesis when ATP used up,
  - Number and size of healthy mitos increase to enhance energy production.

Diabetes of the Brain" - "Type 3 Diabetes."

- Insulin resistance and type 2 diabetes increase the risk of Alzheimer's and Parkinson's diseases.
  - "Insulin resistance in the brain leads to wide spectrum of neurogenerative impairments.
    - increases in free radicals, i.e superoxide,
    - low energy (ATP),
    - inflammation,
    - cell death,
    - neurotransmitter dysregulations.

Fat Cells and ROS

- Poor self-care and ill health leads to a flood of free radicals—a nonlinear tsunami.
  - Excessive fat cells, ↑ROS
    - makes all cells vulnerable.
  - Buildup of fat located near mitos causes damage to energy production.

Client Education

- Supply and demand is different for a athlete than it does for a couch potato.
  - Don't assume that consuming more calories will give you energy
    - The reverse is true.
      - Overeating *decreases* energy.

Free Radicals

- Highly reactive molecules that contribute to oxidative stress
- They lost an electron and are on the prowl to steal one from neighboring molecules.
  - Cells malfunction
  - Cells age
  - Cells are more vulnerable to disease
  - DNA more vulnerable to inaccurate gene expression

Anaerobic Metabolism -- Shift

- Childhood-- for the growth our body.
- Adulthood – to no growth just but maintenance
  - Along with less aerobic capacity
  - We risk of building the wrong type of cells:
    - extra fat cells and less energy to burn it off.

Exercise & Biogenesis

- Using ATP up:
  - Prevents excessive free radicals.
  - Expands the number and size of healthy mitos
  - Increases biogenesis
    - All for more ATP!

Client Education

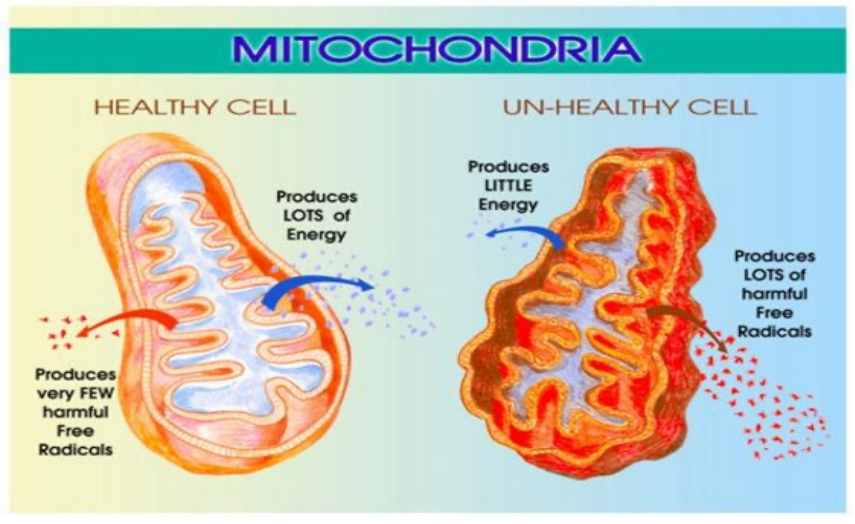
An Inflammatory Diet includes:

- Simple carbohydrates
- Saturated fats
- Trans fatty acids
- Processed foods

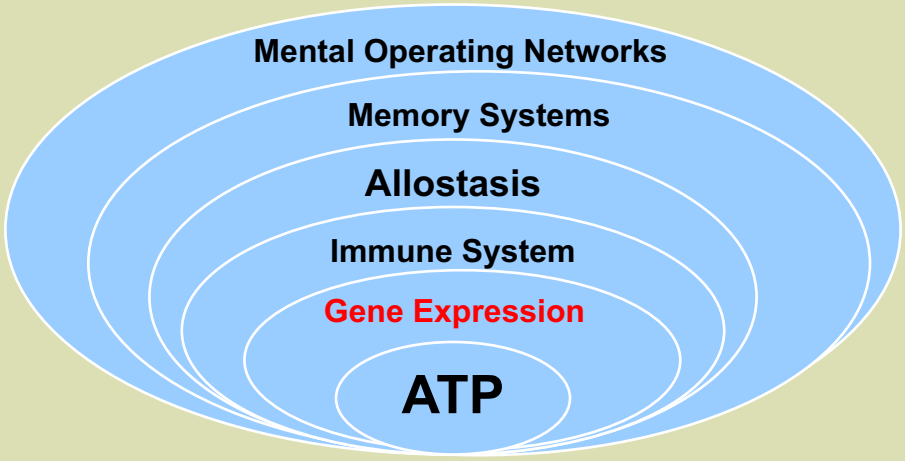
Resulting in a greater risk for:

- Metabolic syndrome
- Diabetes
- Dementia
- Cancer.

Free Radical Damage

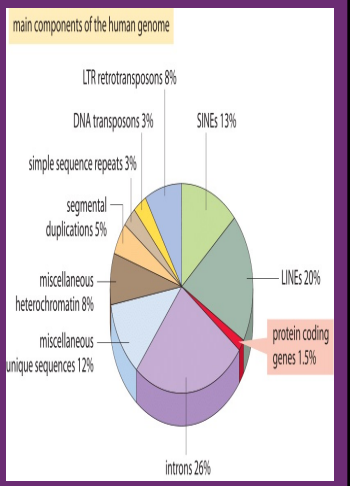


"Self"-Organization

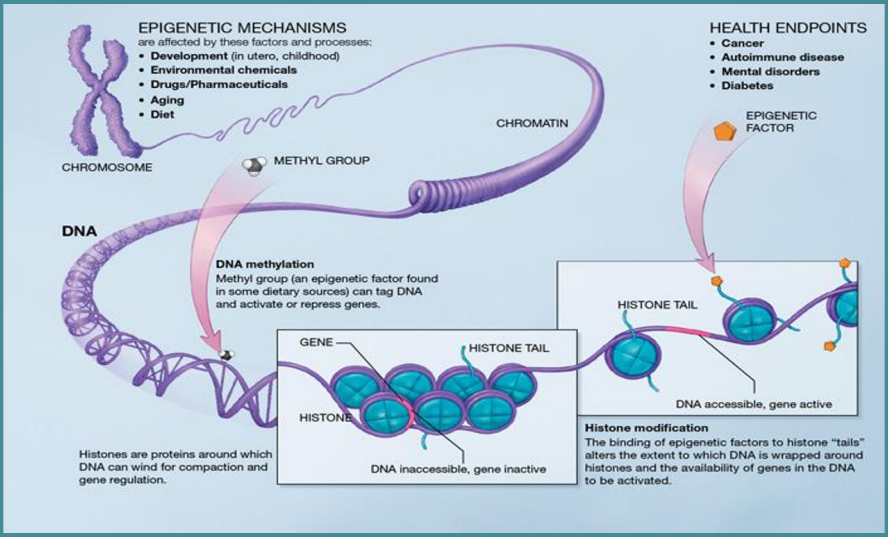


Epigenetics

- 24,00 genes (that code for protein)
  - Worm and human
- 2% (the rest—"junk DNA")
- As the complexity of the species increases so does the amount of "junk DNA"



Epigenetics



Epigenetics in Gene Expression

- Histones are proteins wrapped tightly into ball like shapes with floppy tails
- Acetylation of histones allows transcription—unwrapping genes for expression
- Methylation of histones keeps them in place—suppressing gene expression

Cell – DNA Interactions

- Cells can use RNAs and proteins as epigenetic:
  - –Highlighters that establish and maintain a pattern of information
  - –Erasers that remove it when necessary
  - –Decoders that use the information into useable instructions

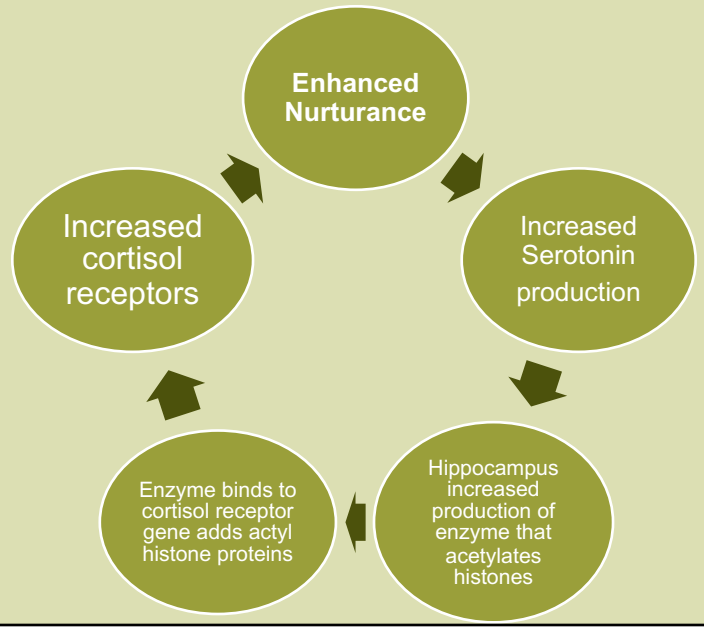
Epigenetics and Decreased Stress

- Decreased methylation levels of cortisol receptor gene:
  - In offspring who had good nurturing produces more cortisol receptors on the hippocampus
    - Lower levels of CRH, ACTH, and cortisol
    - More 5-HT
    - Stress tolerance (Good thermostat)

Infant experiences nurturing

- Her serotonin levels increase:
  - signals her hippocampus to increase the production of an enzyme called acetylates histones.
  - This enzyme binds to the cortisol receptor gene and adds acetyl groups to histone proteins.
- The histone acetylation creates a more relaxed environment so that DNA methylation is removed.
  - leads to higher expression of the cortisol receptor gene and consequently better ability to turn off the HPA axis— the stress response system.

Epigenetics of Stress Tolerance



Epigentics and parenting

- Good parenting produces kids with less methylation of the cortisol receptor gene
- The kids have a better thermostat for cortisol and can turn of the stress response system more easily

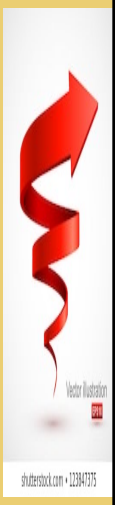
Cortisol level

SEVERE NEGLECT: Persistent Neurobiological Changes

- **Decreased serotonin**
  irritability; reduced emotional control
- **Increased CRF:** ↓ deep sleep; agitated depression; anxiety
- **Decreased Oxytocin:** attachment problems

Epigenetics and Increased Stress

- With methylation of the cortisol receptor gene, fewer cortisol receptors
  - it is difficult to turn off the stress response.
- Increased methylation levels of cortisol receptor gene:
  - In suicide victims with a family history of abuse and/or neglect
  - In preemies:



Epigenetics and Increased Stress

- Maternal separation;
  - leads to decreased DNA methylation of the arginine vaseopressin and CRH genes.
  - This results in the increased production of arginine vaseopressin and CRH, which stimulates the HPA axis— the stress response system.

Epigenetics and Neuroscience of Early Experience

- **Early secure attachment experiences regulate the opioid and GABA systems to generate feelings of comfort and buffer stress.** (Curley, 2011).
  - **Feeling soothed with less pain occurs through opioid release into the anterior cingulate cortex.**
  - **Increased GABA receptors dampen anxiety**
- • **Maternal nurturance stimulates the expansion of BDNF.**
  - **BDNF and NMDA expression as well as increased cholinergic innervation of the hippocampus enhance cognition** (Liu et al., 2002).
  - **BDNF buffers cortisol in the hippocampus from stress and promotes ongoing plasticity** (Redicki et al., 2005).
  - **The brains of suicide victims --lower mRNA levels of the genes for BDNF and receptor tyrosine kinase B** (Dwivedi et al., 2003).

Epigenetics: For Better or Worse

- The serotonin- transporter gene differentiates those people with the "short version" from the "long version" (eg S/S, L/S, or L/L).
  - Short version - mistaken for the "depression gene."
  - Yes, carriers of the short version may become depressed if they experienced ACEs, **but** those with supportive early environment and positive experiences can have the fewest symptoms.
- The genetic polymorphism BDNF alone does not operate as a plasticity factor, but the environment and multigene interactions together do.

Epigenetics: For Better or Worse

- Infants with a variant of the dopamine receptor gene (DRD4) have been linked to lower receptor efficiency and greater risk for disorganization and externalizing behaviors if exposed to maternal loss or trauma.
- Yet, when children with this supposed "vulnerability gene" were raised by mothers who had no unresolved loss they displayed significantly less disorganization. With nurturing mothers, they show the lowest levels of externalizing problem behavior.
- This variant of the DRD4 gene can afford the carrier to benefit disproportionally from supportive environments.

Epigenetics: For Better or Worse

- Carriers of a specific mutation of the catechol-O-methyltransferase (COMT) gene, --who use of cannabis during adolescence -- more likely to develop psychotic symptoms
- The COMT gene protein is of particular importance in regions such as the PFC, which is typically dysregulated in schizophrenia.
- The COMT gene is NOT a "schizophrenia gene" but is an enzyme that breaks down dopamine, norepinephrine, and epinephrine.

Cell Aging: Telomeres Length

- "Psychobiomarker": Linked to social status, perceived stress, depression, predictive of mortality and genetic impairment (Epel, 2009, Current Directions)
- •Telomeres: non-coding sequences (AKA "junk DNA") capping ends, serving as a
- "senescence clock" (Blackburn, 1978)
- •Telomerase: enzyme that prevents telomere shortening, promotes cell resilience.

- Psychobiomarker": Linked to social status, perceived stress,
- depression, predictive of mortality (Epel, 2009, Current Directions)

Factors that Impair DNA and Cells

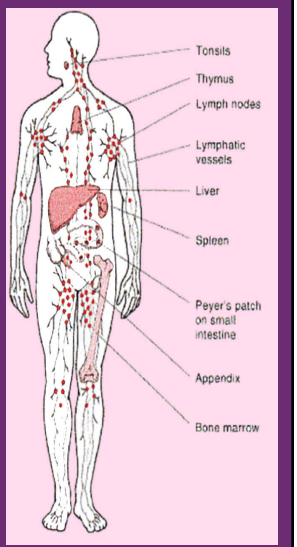
- When cells divide
- Telemeres shorten
- Gene expression changes
- Impairs cellular repair
- Recycling of cells slows
- Errors accumulate
- Cells fail
- Cells die

Factors that Shorten Telemeres

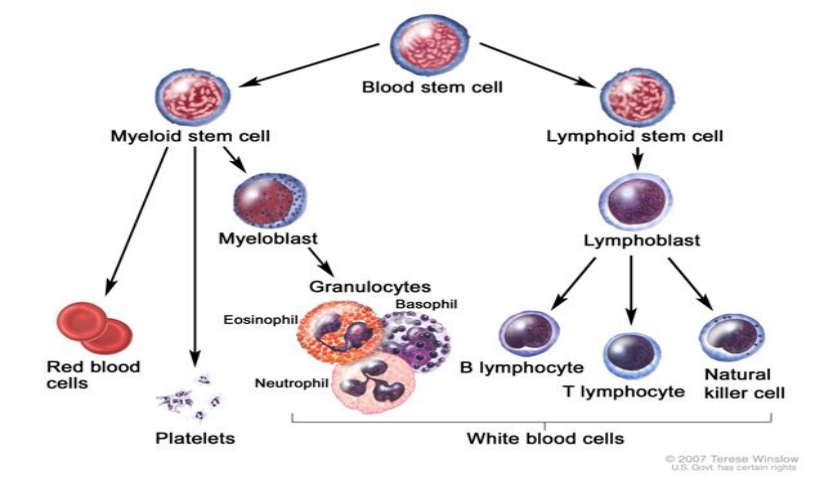
- Aging
- Cardiovascular disease
- Smoking
- Obesity (more than smoking!)
- Type 2 Diabetes
- Social isolation
- Poor diet
- No exercise
- Poor sleep
- Alcohol and other drugs
  - **All rendering DNA vulnerable to damage**

Components of the Immune System

- **Lymph vessels and lymph nodes — filtering system for the lymph. WBCs lie in wait for foreign substance to destroy**
- **Bone marrow — origin of WBCs**
- **Thymus — where T cells differentiate into functioning cells from precursors**
- **Spleen — filtering system for the blood**
- **Other organs — gastrointestinal tract has Peyer's patches with high density of WBCs, respiratory tract has tonsils, skin, etc.**



Me not Me Detection System



B and T "true" memory cells

Short Term Stress Can Suppress Immune System

Increased stress: (Kiecolt-Glaser/Glaser):

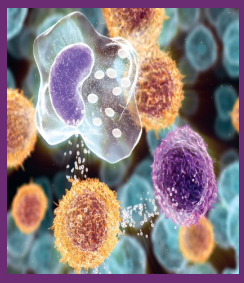
- Suppress T cell function
- Suppress natural killer cell function
- Suppress lymphocyte proliferation
- Reactivate latent viruses (herpes simplex virus; Epstein Barr virus)
- decreased ability of cell to repair broken DNA.
- Lower antibody response when vaccinated.

T cells attack a virus

*effects also seen in bereavement, divorce, and other stressors

Communication in the immune system happens via chemicals

- *Cytokines:* Proteins released by immune cells that act on target cells to regulate immunity, and signal the brain
- *Proinflammatory cytokines:* coordinate inflammatory responses in the body; in response to microbes; mediates acute inflammation (e.g. IL-1, TNFa, IL-6)
- *Anti-inflammatory cytokines*: controls the pro-inflammatory response (e.g. IL-10)
- *Chemokines*: recruit cells to affected tissues
- *Prostaglandins*: recruit immune cells, and *signal the brain*



Stress

Activation of corticotropin releasing hormone (CRH):

- Contributes to delayed gastric emptying
- Increased colonic activity
- Functional bowel disease (IBS)
- Increase in gut permeability
- Leaky gut – antigens leaking out
- Toxic liver overload
- Systemic disease

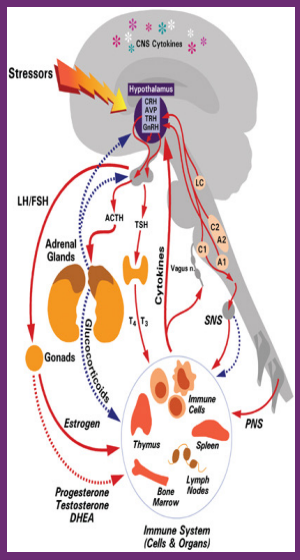
The Brain Controls the Stress Pathways

Distress, via the cortex and amygdala signal to the hypothalamus.

The hippocampus (memory) also has inputs to the hypothalamus.

The hypothalamus maintains homeostasis by regulating visceral activities: heart rate, blood pressure, body temperature, thirst, hunger, weight, sleep/wakefulness.

The hypothalamus also controls HPA stress response system



The Immune System Can Affect Your Emotions:

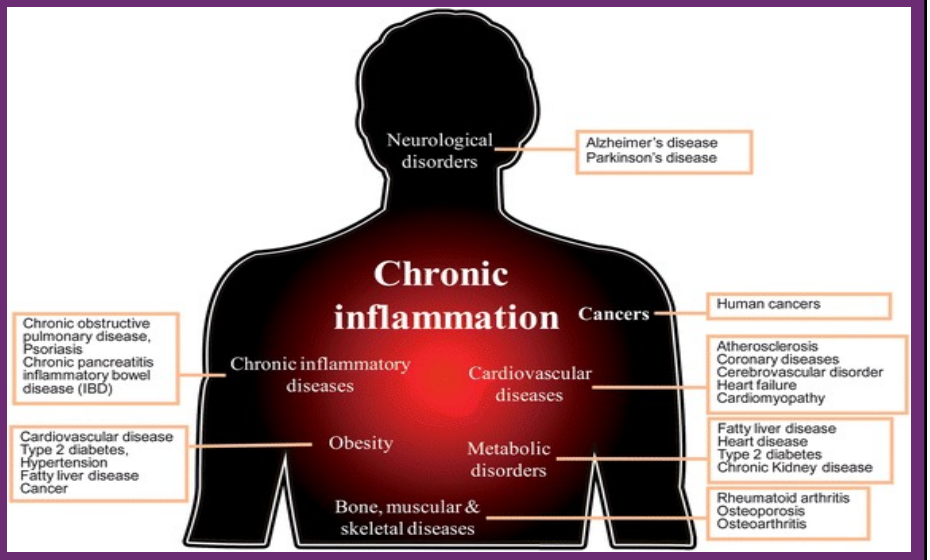
- PICs contributes to depression as underlying inflammatory conditions
- Stressors may contribute to depression or exacerbate it via PICs
- Depression linked to medical conditions-- involves PICs
- Strong link between depression and vulnerability to medical diseases (CVD, autoimmune)

Inflammatory pathways in the brain adversely affect memory and mood.

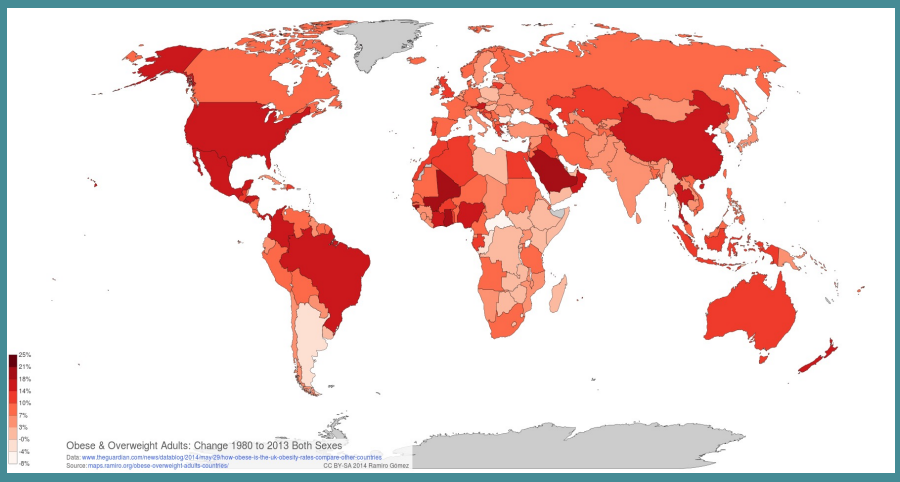
- PICs cause cognitive deficits that disturb synaptic strength.
  - High concentrations of receptors for PICs in the PFC and hippocampus, potentiating cognitive impairments,-- i.e. working memory, episodic memory, and executive functions
  - IL- 1 in the hippocampus impairs memory by interfering with BDNF, which is involved in neural plasticity, neurogenesis, memory, energy balance, and mood.

Pro-inflammatory Cytokines

- Stress can increase PICs levels
- High PICs can lower the concentration of serotonin and DA
  - Cognitive dysfunction, anxiety, fearfulness, depression, thoughts about suicide
- "Sickness behavior"---fatigue, social withdrawal, and immobility--depression (Hickie and Lloyd 1995).

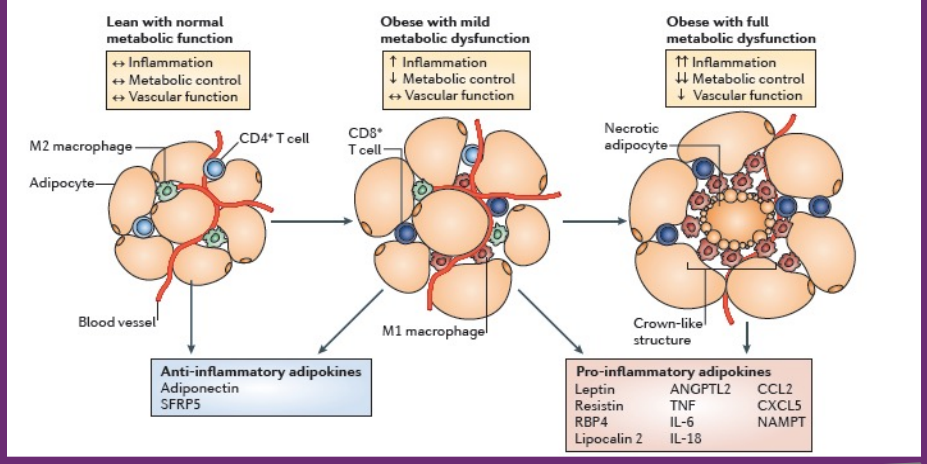


The Pandemic



Obese people over 40 will die 6-7 years earlier

Obesity-Associated Adipose Tissue Inflammation

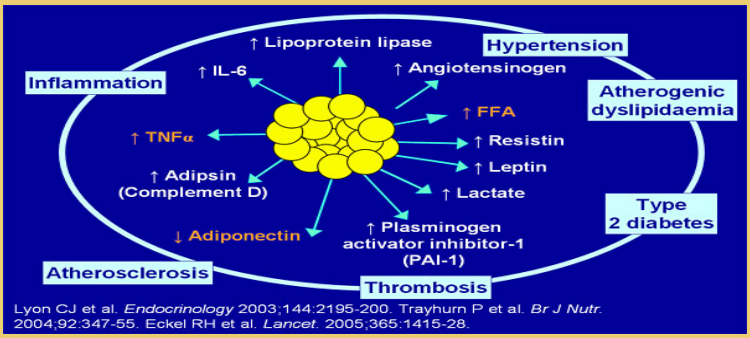


INFLAMMATION

Obesity, Inflammation, and Diabetes

- Fat cells secrete IL-6
- IL-6 can induce insulin resistance

Higher IL-6 may predict diabetes type 2

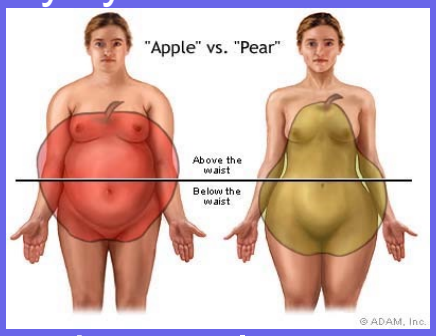


Lyon CJ et al. *Endocrinology* 2003;144:2195-200. Trayhurn P et al. *Br J Nutr.* 2004;92:347-55. Eckel RH et al. *Lancet.* 2005;365:1415-28.

Belly fat

Belly fat generates inflammation by releasing proinflammatory cytokines

- Lowers BDNF
- ↑ risk of dementia
- If you're going to gain weight go for the pear not the apple shape



Client Education

If you have extra weight, hope for the pear not the apple shape. Better yet, lose the body fat for the sake of your brain.

Fat cells leak out toxins that go to the brain causing inflammation, clouding thinking, and increasing depression.

WHO—World Population 7,505,257,673

- 4.7% with diabetes in 1980
- 8.5% with diabetes in 2014
- 10% forecast 2035

- Obesity Population: 774,000,000

Pre-diabetes

- Occurs when blood glucose levels higher than normal but not yet high enough for dx of diabetes
- According to the CDC-- 86 million
- Most develop type 2 diabetes in 10 years unless:
  - Lose 5 to 7 % of body weight
  - Make major changes to diet
  - Increase exercise diet

Diabetes and Psychological Disorders

- Depression 38%
- Anxiety 20%
- PTSD predicts the onset of type 2 diabetes
- Increases of cognitive impairment
  - –Memory impairment
  - –dementia

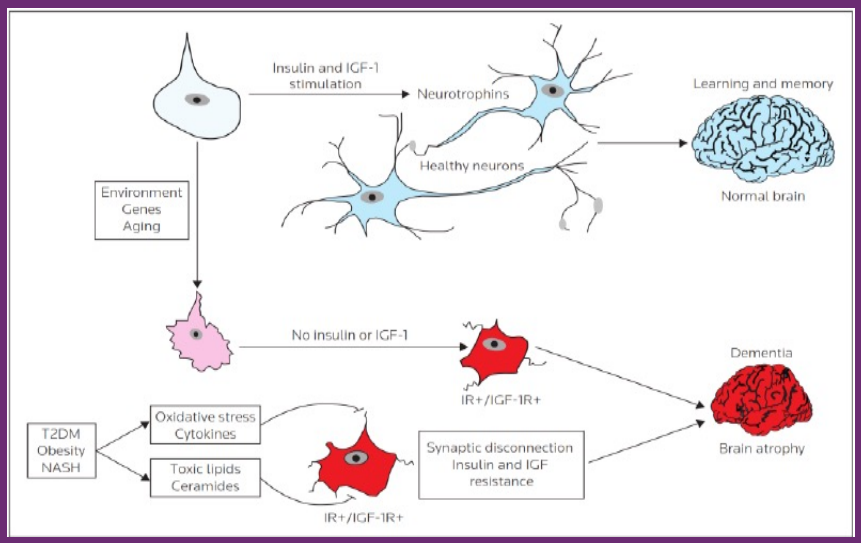
Stress and Diabetes

- **Cells need glucose for fuel—This is insulin's principal job**
- **The body needs more fuel when stressed**
- **↑ adrenaline and cortisol ↑ blood glucose**
- **↑ cortisol triggers the breakdown of protein to glucose**
- **Excessive cortisol results in too much glucose floating around**
- **Thus, ↑ risk of insulin resistance –Diabetes II**

Diabetes and Neuropathology

- Grey matter volume reduction in multiple brain regions (i.e. frontal temporal)
- Microstructral changes in white matter
  - –↓ connectivity and lesions
- Microvascular complications
- Metabolic impairment
  - –↓ insulin receptors

Diabetes and Brain Shrinkage



Diet, inflammation and Pre-diabetes

- -increased markers of inflammation e.g. cytokines, CRP
- -increased fasting blood glucose, elevated
- -weight loss improves inflammation and metabolic markers
- -dietary changes can help:
- Fruits and nuts, berries, fish, whole grains, omega-3 polyunsaturated fatty acids
- -avoiding trans-fat and saturated fats, sugary foods, red meat

Diabesity

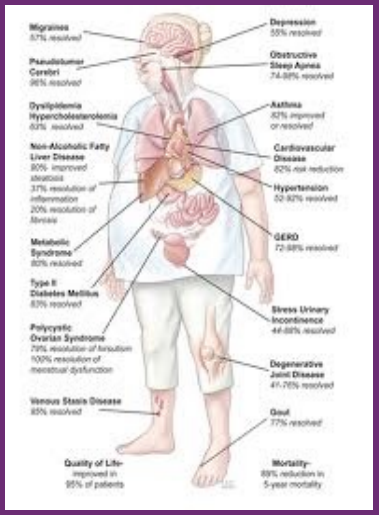
- Increased leptin and insulin resistance
- Increased blood pressure
- Increased cardiovascular disease
- Increased depression
- Chronic inflammation
- Neurocognitive impairment

Diabesity

Rank	Countries	Amount
#1	United States:	2,989 deaths
#2	Mexico:	807 deaths
#3	Brazil:	729 deaths
#4	Germany:	654 deaths
#5	Spain:	316 deaths
#6	Austria:	219 deaths
#7	Canada:	187 deaths
#8	Australia:	115 deaths
#9	South Africa:	114 deaths
#10	Denmark:	104 deaths

Cardo-Metabolic Syndrome

- Diabetes, cardiovascular disease, obesity
- Reduced microbial diversity
- Leptin resistance
- Mood disorders
- Inflammation



Metabolic Syndrome

- Increasing risk factors for:
  - Heart disease
  - Diabetes
  - Obesity
  - Low HDL, high LDL
  - High blood pressure
- All lead to depression

What drives inflammation in cardio-metabolic syndrome?

- Obesity- fat releases pro-inflammatory immune cells
- Gut barrier dysfunction
- Dysbiosis
- Inflammatory diet (high intake of saturated fats, refined sugar, processed foods, additives, lack of anti-oxidants)
- Advanced Glycation End Products
- Pro-inflammatory cytokines

Depression Has a Relationship to Inflammation

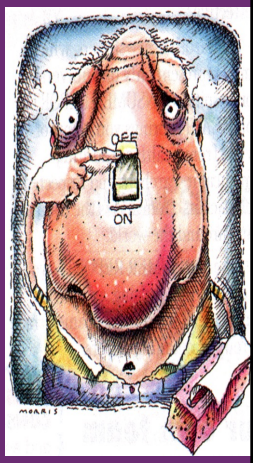
- Depressed patients -- increased levels of *proinflammatory cytokines* (PIC)—strong finding
- -Chronic inflammatory diseases are often associated with depressive symptoms
- --Depression is associated with inflammation in the brain
- So- does depression *cause* the increase in these cytokines or do these cytokines *cause* depression?
- Both: It is a nasty positive-feedback loop!

➢PICs cause a depression-like Sickness Behavior

- Stress can increase PICs levels
- High PICs can lower the concentration of serotonin and DA
  - –Cognitive dysfunction, anxiety, fearfulness, depression, thoughts about suicide
- "Sickness behavior"---fatigue, social withdrawal, and immobility--depression (Hickie and Lloyd 1995).

How does inflammation affect the brain: *Sickness behavior*

- *A symptom cluster also seen in chronic stress
  - Depressed and/or anxious mood
- * increased sensitivity to pain
- *loss of interest in food
- * social withdrawal
- * disordered sleep
- *fatigue, “cognitive fuzziness”

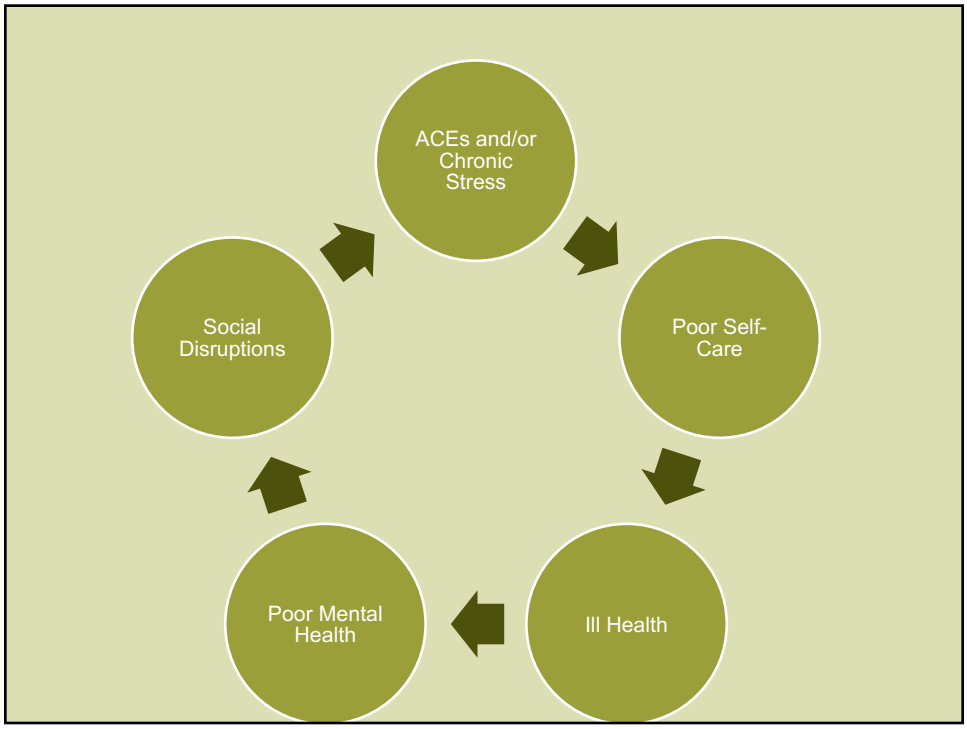


Depression and fatigue in illness

- Common symptoms of both acute and chronic illnesses
- Both caused by inflammation
- Involves suppression of brain arousal systems

Client Education

- Feeling ill makes you act ill and if you do, the feelings of depression will increase.

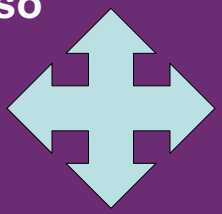


Hypocortisol vs. Hypercortisol Activity

- Chronic stress (especially uncontrollable) alters the cortisol system
- Early on there can be *higher* cortisol
  - Can lead to agitated depression
  - Kills white blood cells
  - Metabolic syndrome
- More distant traumas may result in an inadequate cortisol response
  - Autoimmune disease
  - Inflammation
  - depression

Stress Can Enhance Inflammation

- **Brief stresses can *increase* production of *pro-inflammatory cytokines***
  - ***Study of tandem parachuters***
- **Chronic stressors (i.e caregiving for a child with cancer) can also have this effect-prolonged**
- **Stressors with depression**



How does stress affect inflammation?

- Chronic stress- leads to increased inflammation (via cortisol resistance- immune cells –e.g. the microglia)
- Stress can disrupt balance within the immune system
- Chronic stress cause epigenetic changes in the expression of pro-inflammatory cytokine genes in immune cells
- -Peripheral inflammation induces neuroinflammation

Developmental Programming of stress responses

- Experiencing trauma or stress in infancy or childhood leads to impaired regulation of HPA axis
- Elevated inflammation, especially in gut
- Increased pain conditions including fibromyalgia & irritable bowel syndrome
- Epigenetic changes to genes involved in inflammation

Immune Dysregulation and Hopelessness

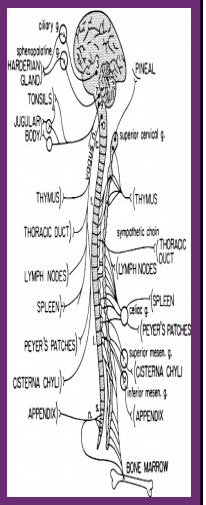
- Ability to meet challenges is key- stress from not meeting them dysregulates immune system, increases inflammation and impairs brain function
- Acute or chronic: stress can impair immune responses
- Controllable vs. uncontrollable
- Social stress and loneliness

Inflammation and Dementia

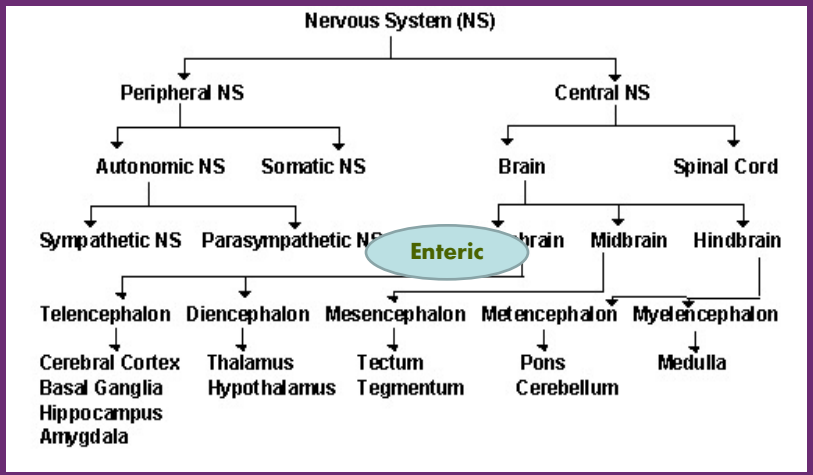
- Dementia exacerbated by chronic inflammation.
- Obesity and diabetes as risk factors
- Small strokes may be caused by inflammation.
- Inflammation plays a role in deterioration of brain cells, formation of plaques.
  - Some of the protein in plaques are products of inflammation.
- Inflammatory mediators can cross into the brain and influence learning and memory.
- Stress may influence the onset and course of dementia via these inflammatory pathways

Peripheral nerves are also involved in inflammation

- Bidirectional: nerves sense inflammation, contributing to it
- There are both pro-inflammatory and anti-inflammatory effects
- C-fibers modulate pain and inflammation
- Parasympathetic nerves reduce inflammation (especially vagus)

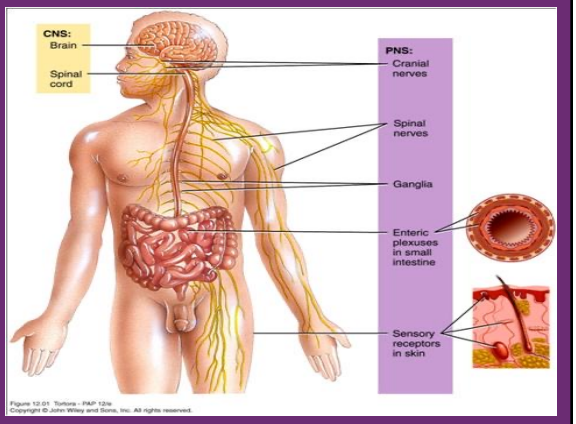


The Gut Brain



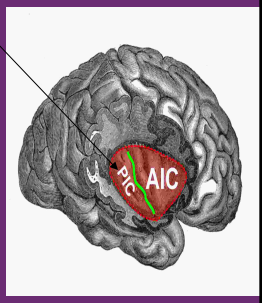
Enteric Nervous System

- ***Enteric*** **– meshwork of nerve fibers that innervate the viscera (gastrointestinal tract, pancreas, gall bladder)**

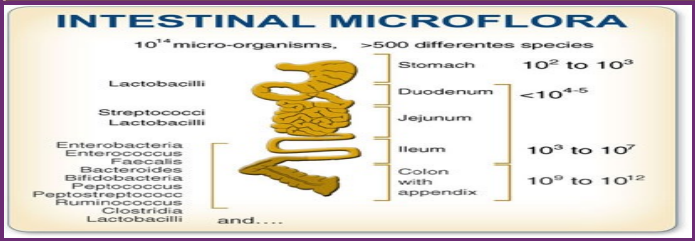


Language of Gut

- **Visceral sensations include: nausea, bloating**
- **All arrive at Insular Cortex in brain**
  - **Part of the Salience Network**
- **Plays role in emotions & body homeostasis**
- **Regulates the immune system**
- **Conscious desires – food, drugs**



Microbiome



- The GOOD: helps digest certain foods the stomach/small intestine doesn't, can combat invading microorganisms. Microbes generally do not cause disease unless they grow abnormally; they exist in harmony with us.
- The BAD: may have a role in auto-immune diseases (e.g., diabetes, rheumatoid arthritis, multiple sclerosis, fibromyalgia) and possibly some cancers. A poor mix of microbes in the gut may also aggravate obesity.

Our microbes are like an organ

- Control each other's behavior
- Collaborate with our immune system in host defense
- Program phenotypes/activity states of immune cells
- Diet influence our microbial populations
- Link of inflammation and disease
- Influence brain development
- Influence our behavior

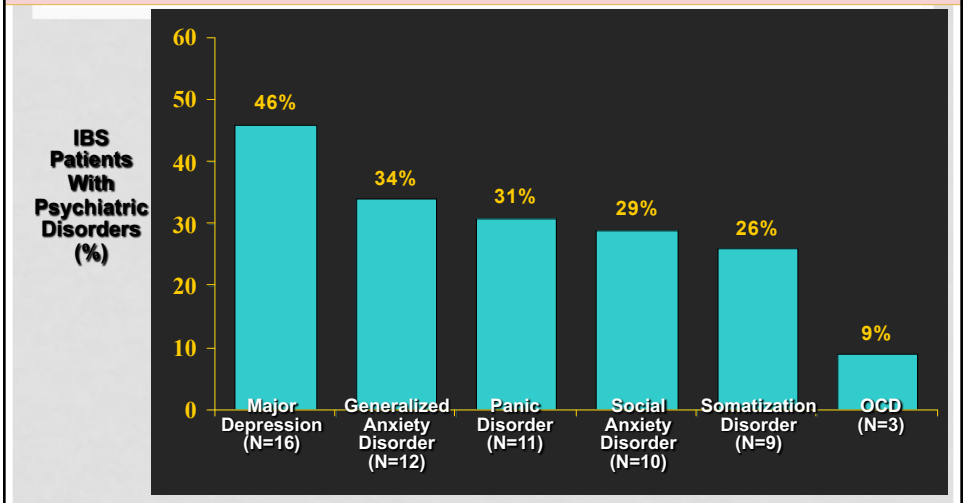
Gut bacteria

- Play a key role in nutrition
- Production of neurotransmitters
- Synthesize: vitamins such as thiamine (B_1), folic acid (B_9), pyridoxine (B_6), and vitamin K
- Produce digestive enzymes to absorption calcium, magnesium, and iron.

Gut Bacteria

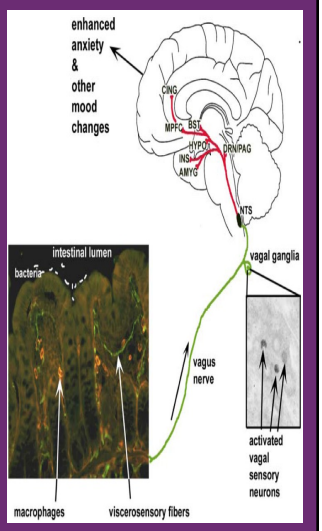
- 90% of bacteria in the colon F/B ratio:
- Firmicutes
  - Fat loving—increases fat absorption
  - Efficient at extracting calories from carbs
  - Turns on genes that increase the risk for obesity, diabetes, and CVD
- Bacteroidetes
  - More dominant in lean people

LIFETIME PSYCHIATRIC DISORDERS IN PATIENTS WITH IBS



Inflammation, microbes and anxiety

- Anxiety is common in illness, and inflammatory signals from the body contribute, e.g. TNF, vagal activation
- A signal that something is not right
- Destructive role of dysbiosis (imbalance in microbes)

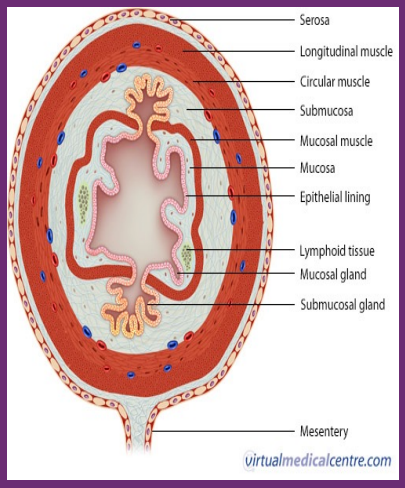


Stress/Depression and the Gut Microbiome

- Stress can induce increased permeability of the gut allowing bacteria to cross the epithelial barrier and activate a mucosal immune response, which alters the microbiome and leads to enhanced HPA activity.
- In irritable bowel syndrome (IBS; cramping, abdominal pain, bloating etc) and depression there can be an alteration of the HPA axis induced by increased gut permeability

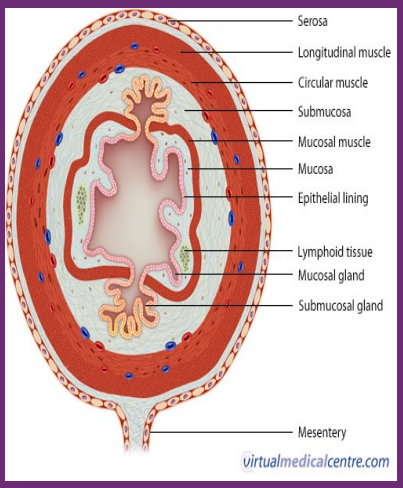
"Leaky gut": the consequences of stress and inflammation and link between diet and health

- AKA "increased intestinal permeability"
- Is associated with many disorders (diabetes, metabolic syndrome allergies, neurological etc.)
- Allows more absorption of toxins and lets fluid out e.g. during inflammation and infection (diarrhea)
- Many factor regulate this: immune cells and molecules, microbes, stress



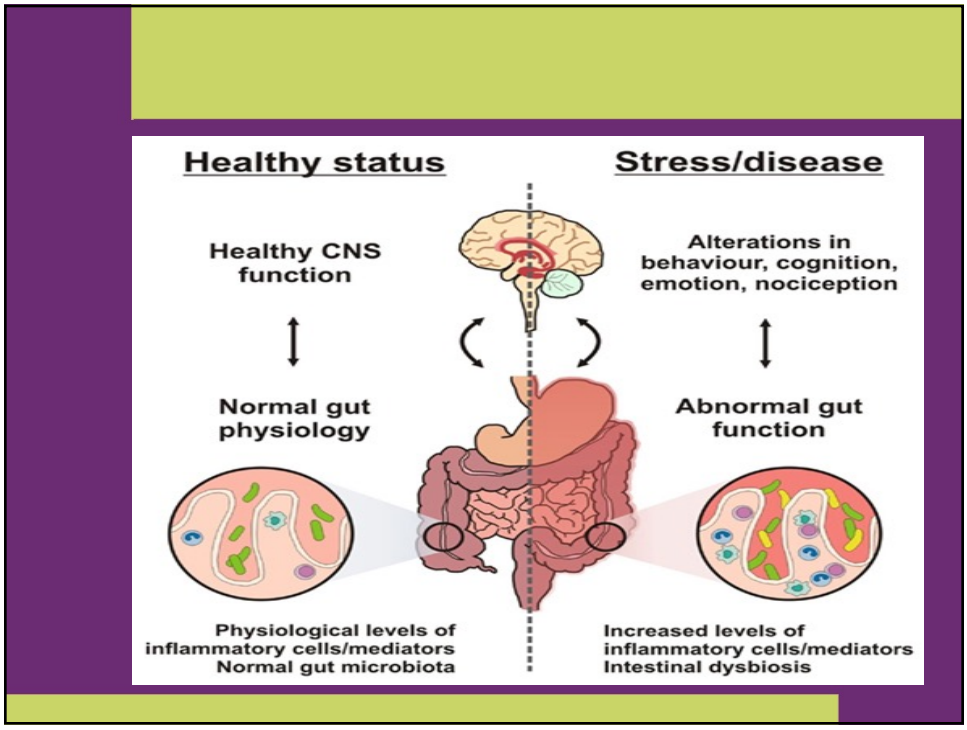
"Leaky gut": the consequences of stress and inflammation and link between diet and health

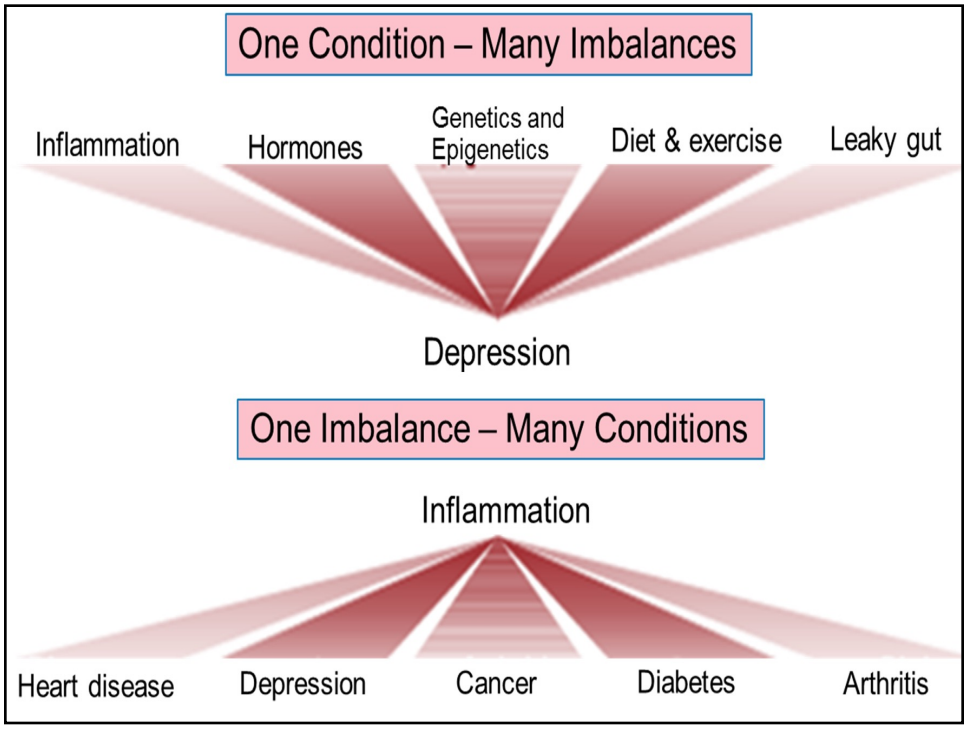
- **intestinal permeability**
- **Firmacutes + LPS**
- Lipopolysaccharide (LPS), a cell wall component of Gram-negative bacteria, induces neuronal death, decreases neurogenesis, and impairs synaptic plasticity and memory,



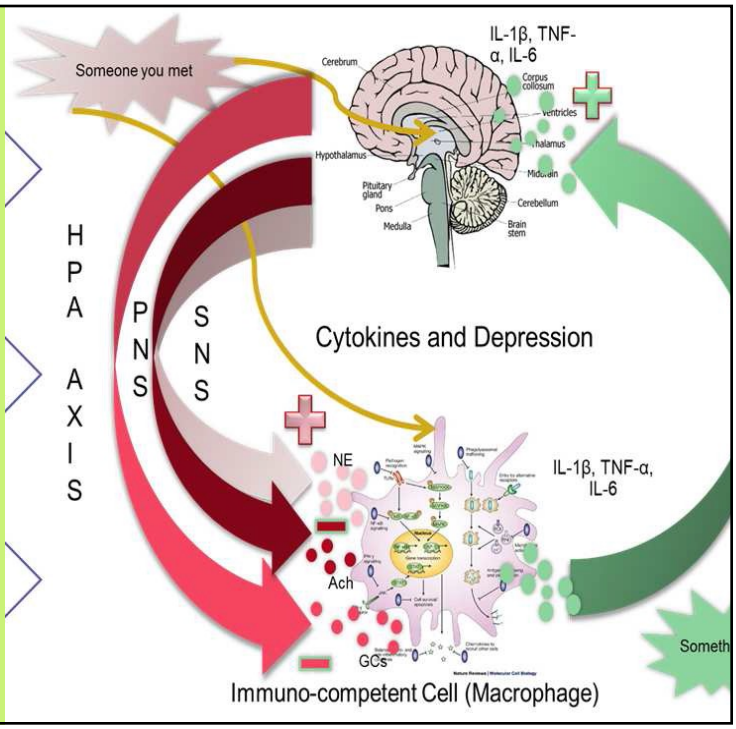
Dysbiosis and Microbial Diversity: the Importance of Balance

- **Diversity is good- a hallmark of disease is reduced microbial diversity**
- **Low diversity is associated with DYSBIOSIS**
- ***Dysbiosis* is when there is an imbalance in microbes, leading to overgrowth of some species**
- **Dysbiosis with inflammation--**↓5-HT


Healthy status
Stress/disease
Healthy CNS function
Alterations in behaviour, cognition, emotion, nociception
Normal gut physiology
Abnormal gut function
Physiological levels of inflammatory cells/mediators
Normal gut microbiota
Increased levels of inflammatory cells/mediators
Intestinal dysbiosis


One Condition – Many Imbalances
Inflammation
Hormones
Genetics and Epigenetics
Diet & exercise
Leaky gut
Depression
One Imbalance – Many Conditions
Inflammation
Heart disease
Depression
Cancer
Diabetes
Arthritis

- Bad Diet
  - Simple carbs
  - Transfatty acids
  - Saturated fats
  - Food allergies
  - Bad oils
  - High dairy
  - High gluten
- No exercise
- Chronic illnesses
- Autoimmune disorders
- Chronic pain
- Chronic stress
- Being overweight
  - Apple shape
- Leaky gut



Affect Asymmetry

Set points

Left Hemisphere

Positive emotions
Approach behaviors
Feeling engaged

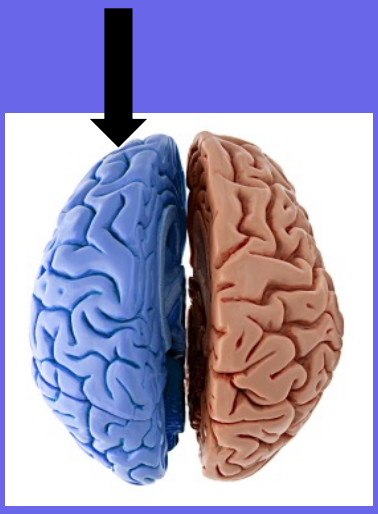
Right Hemisphere

Negative emotions
Withdrawal and Avoidance
Feeling overwhelmed

Left PFC:

Suppressing Sadness

Activating Positive Emotions

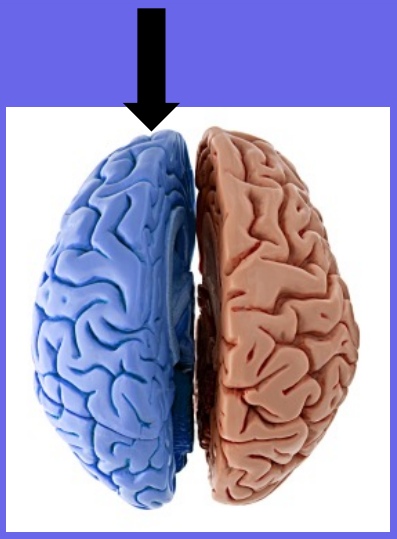


Client Education

- When you are overwhelmed with anxiety or depression it is best to shift from the big picture to the small, and do something that approaches a goal in a piecemeal and incremental manner.

Left PFC more DA:

Activation
&
Approach
Behaviors
(curiosity; assertion)



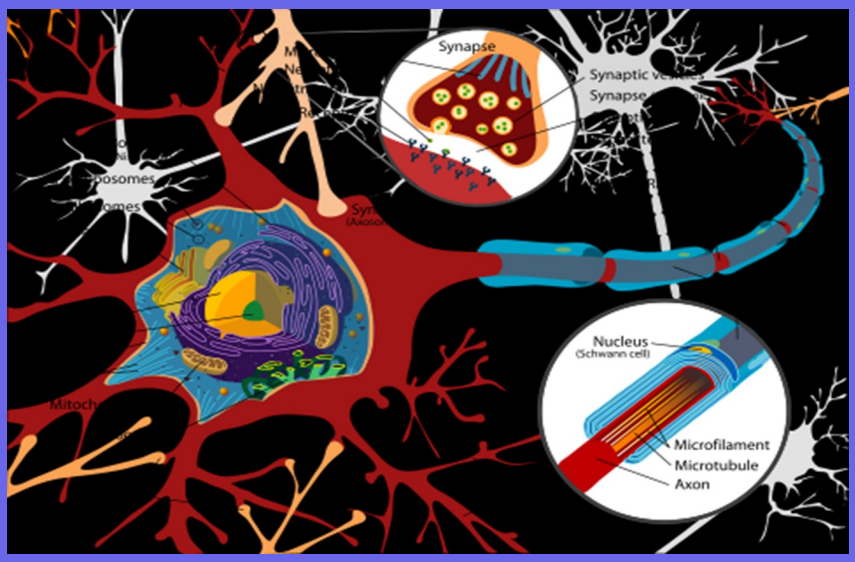
Right PFC more NE:

Activating
Behavioral
Inhibition

Associated
With negative
Emotions

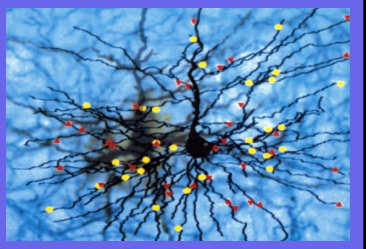
100 Billion Neurons

Each with 10,000 synaptic connections



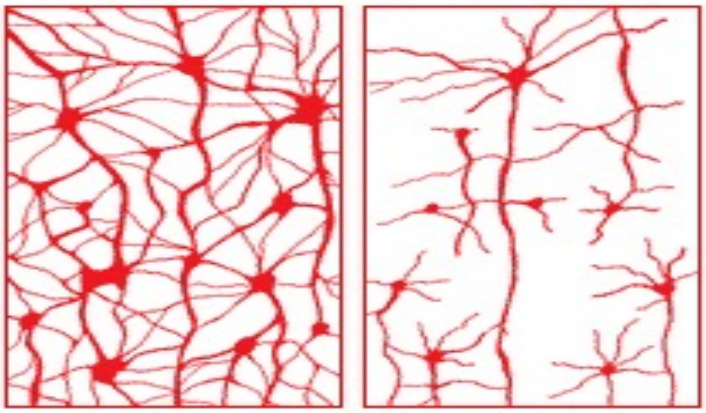
Neuroplasticity

- Increases in:
  - synaptic efficacy
  - receptor density



  - Up-regulating their activity
  - Glial cell availability
  - Changes in the shape and structure of synapses

Brain cell connections



section of a stimulated brain

section of an unstimulated brain

Neurons that fire together, wire together

- *Neuroplasticity* is a general term that describes changes in the brain as you experience and learn (Buonomano & Merzenich, 1998)
- Neuroplasticity involves many changes to the brain including:
  - New synaptic connections
  - Strengthening of connections through LTP
  - The growth of new dendrites (dendritogenesis)
  - Neurogenesis (the growth of new neurons)

Client Education

- Your brain is not hardwired but soft-wired.
- Our job together is to rewire your brain so that you no longer suffer from anxiety and depression.

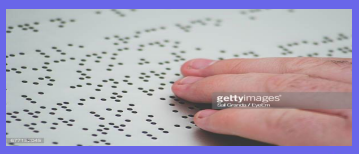
Examples of Neuroplasticity

- London cabdrivers - larger right posterior hippocampus. The longer they were on the job, the larger the size of their hippocampus. (Maguire, et al, 2000)
- Adults who juggled three balls for 3 months increased grey matter in the midtemporal area and left posterior intraparietal sulcus. - 3 months of little or no juggling, -- grey matter decreased and approached baseline values. (Draginski, et al, 2003)

Examples of Neuroplasticity

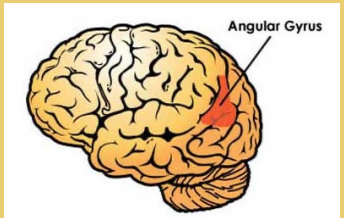
- Musicians using specific fingers to play their instruments showed enlarged areas of their somatosensory strips associated with those fingers. (Pantev, et al, 2001)

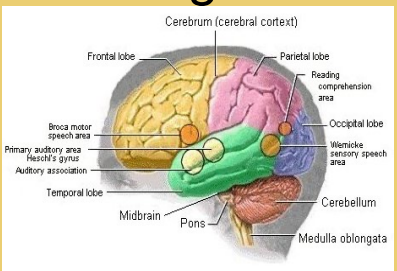
- Blind Braille readers showed enlarged cortical areas associated with their reading finger compared to blind non-Braille readers and to sighted people. (Pascul-Leone & Torres, 1993)



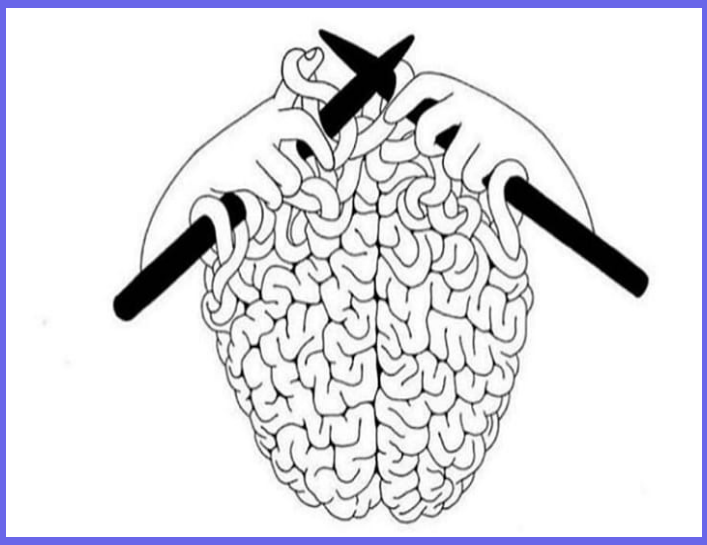
Neuroplasticity Examples

- Bilingual people have a larger angular gyrus (Green, et. al. 2007)
- Professional musicians have a Heschl's gyrus -2xs larger than non-musicians

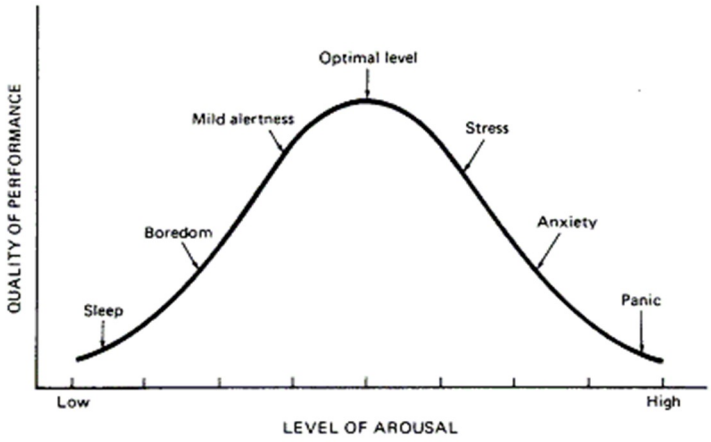




Mind/Brain Causality



Yerkes Dodson arousal curve



Client Education

You have to do what you don't feel like doing so that eventually you will feel like doing it.

Increasing Neuroplasticity

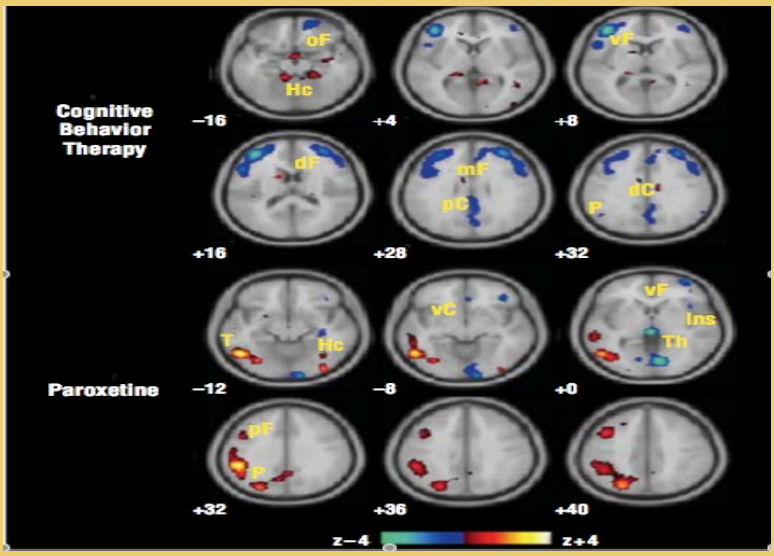
- Tasks are of sufficient difficulty
  - Increased difficulty as you master each level
- Sufficient intensity
  - A few learning sessions each day
  - At least 3 learning sessions each week
  - Done for several weeks
- Like body building
  - Lift more than you can easily
  - 3 reps of 10
  - 3 xs per week
  - Several weeks

Client Education

- Though you feel like you're not ready to take the first step, actually it is not feeling ready that provides the brain chemistry necessary to rewire your brain.

Don't wait to feel ready!

Brain Change: Two Perspectives



Psychotherapy and the Brain

Direct, observable links between successful CBT/IPT and brain changes

- **Reduced amygdalar activity in:**
  - **phobics** (Straube, *et al.*, 2006),
  - **panickers** (Prasko *et al.*, 2004),
  - **social phobics** (Furmark *et.al*, 2002)
- **Increased ACC activation in PTSD** clients (Felmingham *et al.*, 2007)
- **Increased hippocampal activity in depressives** (Goldapple *et al.*, 2004)
- **Decreased caudate activity in OCD** (Baxter, *et al.*, 1992)

A Mnemonic "Recipe" for Neuroplasticity

- **F**ocus—activating the PFC
- **E**ffort—for neuroplasticity
- **E**ffortlessness—learned
- **D**etermination—to keep it

Brain-Based Therapy

- BBT changes how we think about the relationship and change:
  - Need a "Safe emergency."
  - Experience *creates* brain biology
  - Brain biology effects experience (e.g. depression)

Brain Derived Neurotropic Factor

- BDNF plays a crucial role in reinforcing neuroplasticity and neurogenesis. It helps:
  - Consolidate the connections between neurons.
  - Promotes the growth of myelin to make neurons fire more efficiently
  - Act on stem cells in the hippocampus and PFC to grow into new neurons

Factors that Decrease Neurogenesis

Aging

Chronically high cortisol

Chronic stress

Recurrent depression

Marijuana

Obesity

Factors that Increase Neurogenesis

Exercise

- play induces BDNF gene expression

Fasting

Fewer calories consumed

Food content --(Omega—3)

Profound new experience

Client Education

You can grow new neurons in the area of your brain that gives you the capacity for memory. The first steps include maintaining a healthy diet, aerobic and cognitive exercise.

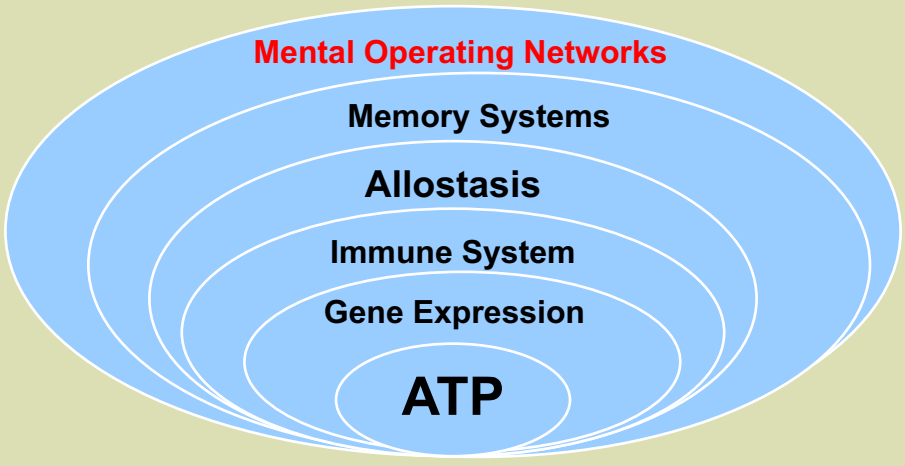
Neurotrophic Factors: "Brain Fertilizers"

- Insulin-like growth factor (IGF), is associated with energy utilization, brain growth, and maturation and can be epigenetically facilitated by prosocial circuits in the brain
- Nerve growth factor (NGF), promotes myelin and neuron differentiation
- Nurturing increases NGF which binds to the cortisol receptor gene to increase cortisol receptors:
  - However, when the cortisol receptor is suppressed, as occurs with neglect or child abuse, NGF does not bind well and fewer cortisol receptors are produced in the hippocampus

Neurotrophic Factors: Brain Fertilizers

- Decreased methylation of the glial cell-derived neurotrophic factor (GDNF) gene is associated with greater stress tolerance
- Increased methylation of the GDNF gene is associated with decreased stress tolerance. GDNF is essential for regulating dopamine release in the nucleus accumbens and for the survival of dopaminergic neurons.
- Chronic unpredictable stress alters dopaminergic functions, reshaping circuits in the prefrontal cortex, impairing decision making, and un-inhibiting maladaptive habits and working memory.

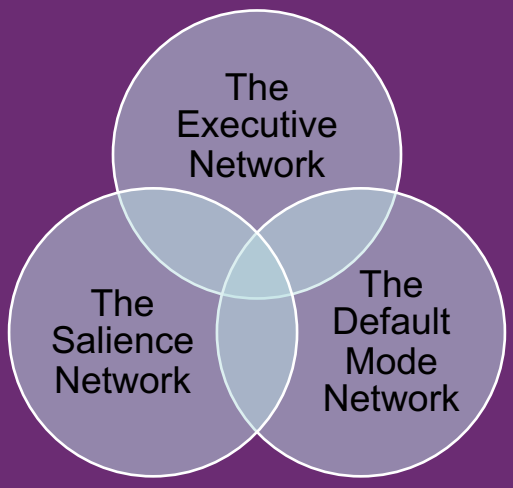
"Self"-Organization



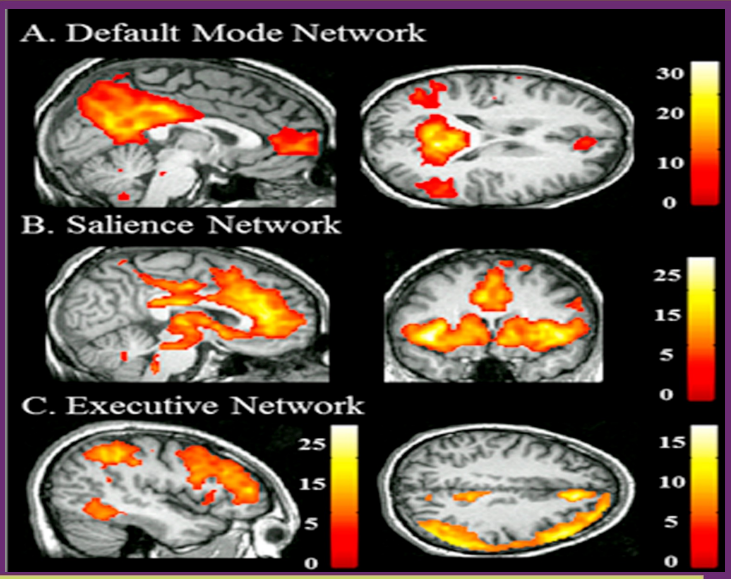
The Mind's Operating Networks:

- **Salience Network:**
- the material "me"
- emotional and reward saliency;
- **Default Mode Network:**
- mind-wandering; fantasying, ruminating
- mentalizing, projecting to the future or past;
- **Central Executive Network:**
- moment to moment monitoring of experience
- selection, planning, toward goals;

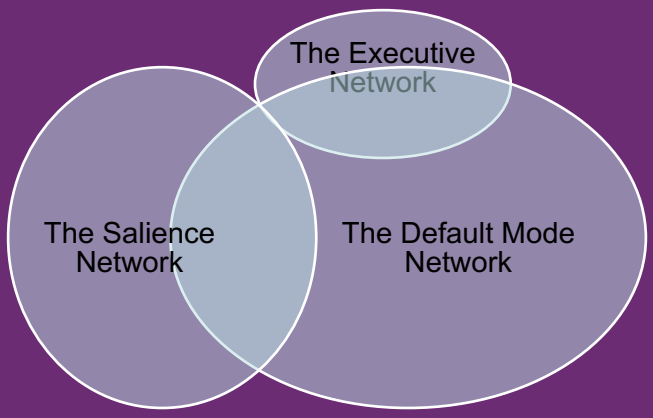
Balancing the Mental Networks



The Mental Networks



Imbalanced Mental Networks

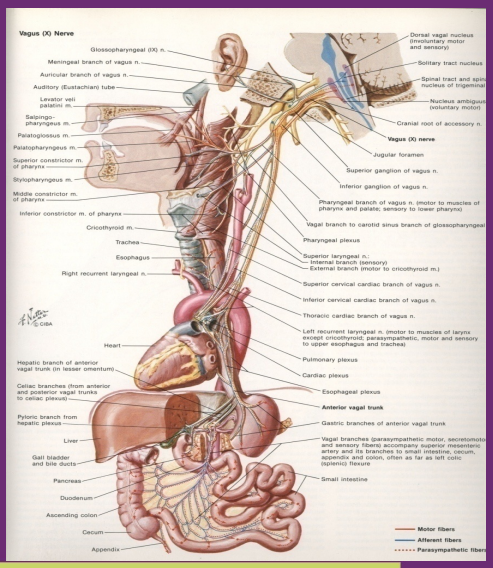


Salience Network:

- referred to as the 'sentient self' (the material "me")
- detecting emotional and reward saliency;
- detecting and orienting toward external events in bottom-up fashion;
- bilateral anterior insula, dorsal anterior cingulate, amygdala

The Vagus Nerve System

- Tenth Cranial Nerve --a complex of sensory and motor nerve fibers.
- *Vagal tone*- the ability to modulate target organs without sympathetic arousal
- allows attachment and sustained relationships.

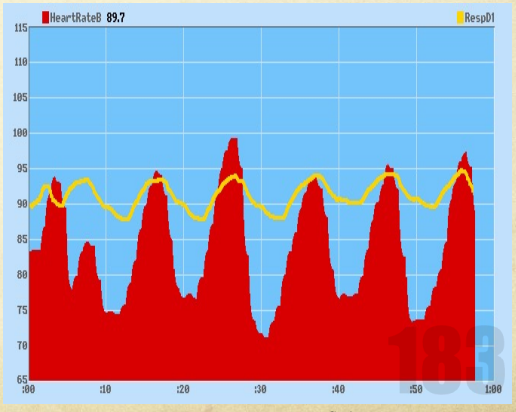


Variability is good

Peak/valley differences
= vagal tone ***when resp is in normal range***

Heart rate increases with inhale.

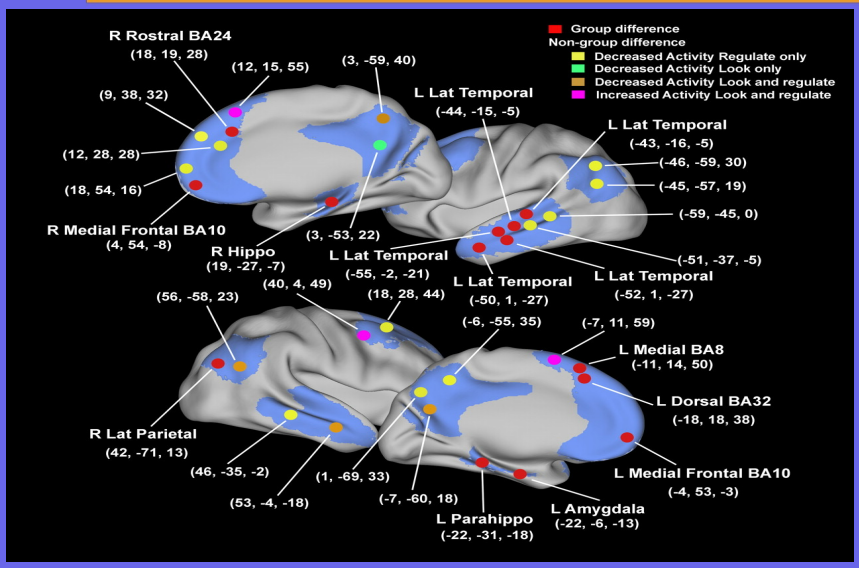
Heart rate decreases with exhale. This pattern shows high vagal tone (high PSNS activity) and a high amount of heart rate variability.



Default Mode Network:

- reflecting, spontaneous thoughts or mind-wandering;
- activated during tasks of mentalizing, projecting oneself into the future or past;
- activation when reflecting on social relationships;
- anterior and posterior midline and cingulate cortex

Activity in the default mode network



Sheline Y I et al. (2009)

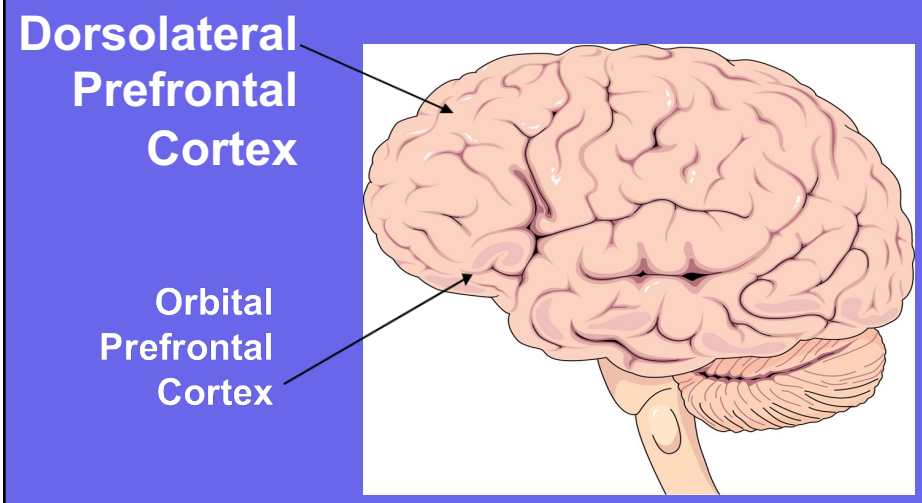
DMN Variations

- Increases when DLPFC is not engaged:
  - Stressed, bored, no novelty, or tired
- Social and self-referential –needed for sense of self
- Malfunctions in the DMN:
  - Schizophrenia—impaired self reflection—not sure where thoughts come from
  - Depression—negative ruminations

Central Executive Network:

- moment to moment monitoring of experience (meta-cognition)
- responsible for selection, planning, and decision-making toward goals;
- working memory that helps select, orient, and maintain an object in the mind;
- bilateral dorsolateral prefrontal cortex

DLPFC and the OFC



Pre-Frontal Cortex

- **Dorsolateral pre-frontal cortex (DLPFC)--- working memory: 7, plus or minus 2, …….or 20-30 seconds of information**
- **Orbital frontal cortex (OFC)**
  - **Social brain**
  - **Affect regulator**
  - **Empathy**
  - **Attachment, warmth, and love**
  - **Connections with limbic area, i.e., amygdala**
  - **Phineas Gage**

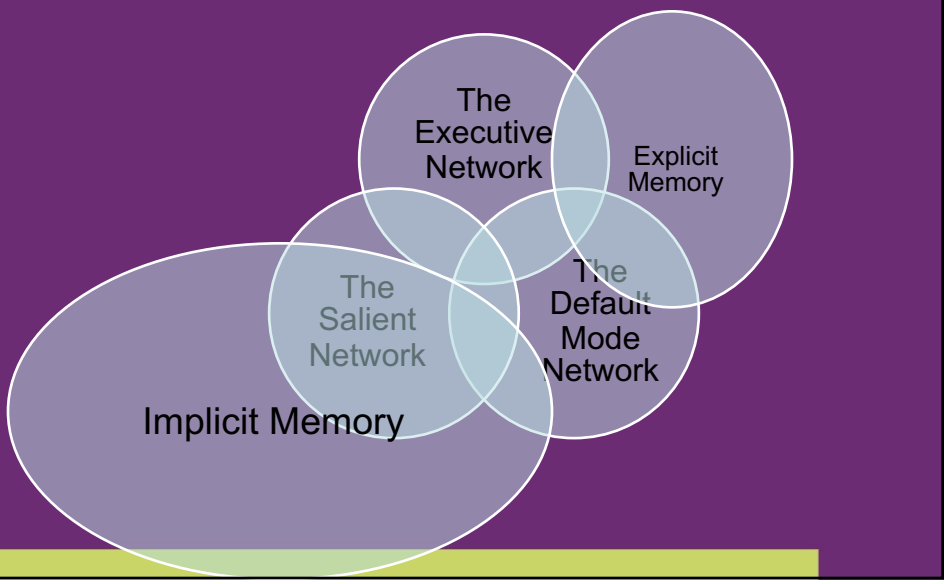
Underdevelopment and underactivity in the Executive Network can contribute to:

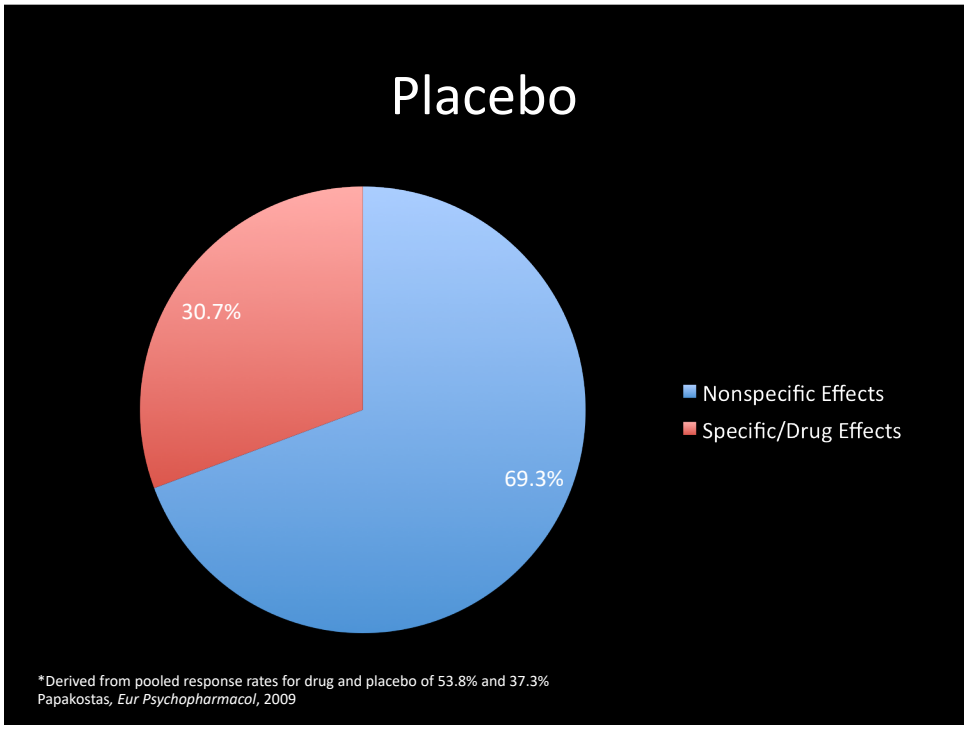
- Attentional disorders
- Paradoxical syndrome known as ”pseudo-depression,”
  - marked by a lack of spontaneity and affect, rather than negative affect. In other words, he looks depressed but denies depression when asked.

Symphony of Wellbeing

- mPFC involved in the representation and evaluation of self-referential information
- pCC involved in the integration of self-referential
- Together they support self-evaluation
- Increased connectivity within parts of the DMN

The Mental Neworks & the Long-Term Memory Systems

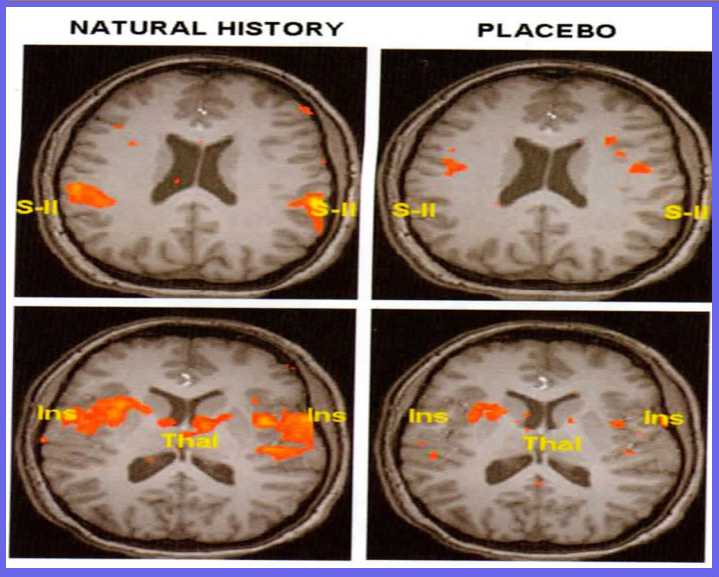




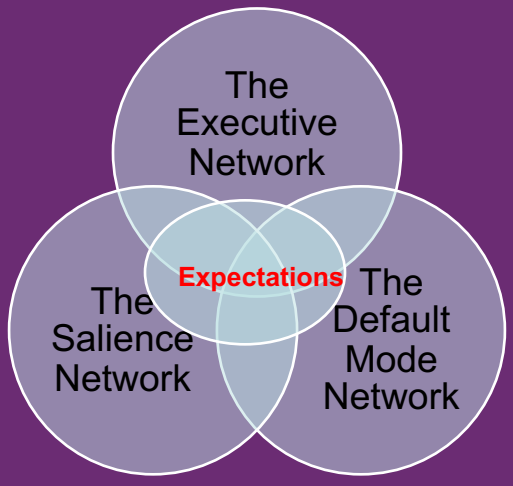
Incidence of Placebo Response

- 10% to 70%
- Average 35% across studies and diseases as well as psych disorders
- Works best for subjective outcomes like pain and psychological disorders
- Half as effective as morphine
- Quite effective with depression and anxiety

IBS and Pain vs. Placebo



Balancing the Mental Networks



Outcome Data

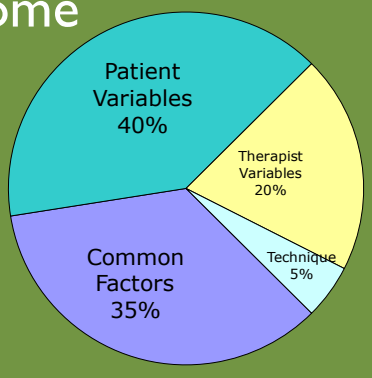
- 43% of patients recover without therapy
- Therapists are poor judges, not just of the outcome of a complete therapy, but even of a single session
- We overvalue our own competence and undervalue that of our colleagues:
  - 80% of the therapists consider themselves "better than the average" therapist
- Psychotherapy can produce enduring adverse effects

The Modern Era: 2000-2011

Psychotherapy Research

Factors affecting outcome

- Common factors: 40%
- Patient factors: 40%
- Therapist factors: 15%
- Technique: 5%



After Lambert and Ogles, 2004

Mind-Brain-Gene Feedback Loops

Regulatory Networks of the Social Brain

- Bonding/Attachment
- Cognitive capacity
- Affect Regulation
- Safety
- Mental and physical health

Developmental Programming of stress responses

- Experiencing trauma or stress in infancy or childhood leads to:
  - Impaired regulation of HPA axis
  - Epigenetic changes to genes involved in inflammation
    - Elevated inflammation, especially in gut
    - Increased incidence of pain conditions including fibromyalgia & irritable bowel syndrome

The Effects of Social Medicine

- ↓ Cardiovascular reactivity (Lepore, et al, 1993)
- ↓ Blood pressure (Spitzer, et al, 1992)
- ↓ Cortisol levels (Kiecolt-Glaser, et al, 1984)
- ↓ Serum cholesterol (Thomes, et al, 1985)
- ↓ Vulnerability to catching a cold (Cohen, et al, 2003)
- ↓ Depression (Russell & Cutrona, 1991)
- ↓ Anxiety (Cohen, 2004)
- ↓ Natural killer cells (Kiecolt-Glaser, et al, 1984)
- ↑ Slows cognitive decline (Bassuk, et al 1999)
- Improves sleep (Cohen, 2004)

Client Education

Your health will suffer without positive social connections

Cell Aging: Telomeres Length

- "Psychobiomarker": Linked to social status, perceived stress, depression, loneliness: predictive of mortality (Epel, 2009, Current Directions)
- •Telomeres: non-coding sequences capping ends, serving as a:
  - "senescence clock" (Blackburn, 1978)
- •Telomerase: enzyme that prevents telomere shortening, promotes cell resilience.

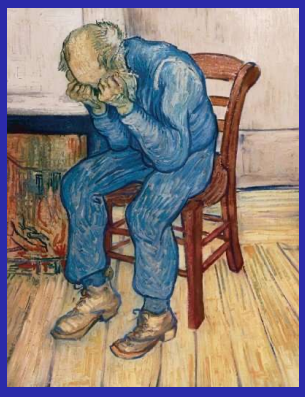
- Psychobiomarker": Linked to social status, perceived stress,
- depression, predictive of mortality (Epel, 2009, Current Directions)

Client Education

You will live longer with positive relationships

Loneliness

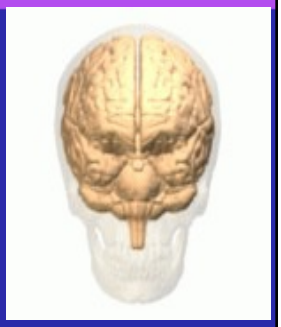
- **In Portugal 1000 people 65> assessed:**
  - **Loneliness was the single most important predictor of depression** (Paul, et al, 2006)
- **In London 2600 people 65>**
  - **More than 15% were at risk for social isolation and depression** (Illife et al., 2007)



The Cost of Loneliness

- In the long-run as detrimental as smoking to longevity (Cacippo & Hawley, 2009)
- The temporal-parietal junction (TPJ)—associated with cognitive empathy is much less activated and can atrophy
  - Creates a downward spiral → less successful → less successful
- Less activity of the ventral tegmental area (VTA) and the nucleus accumbuns
  - Less of a sense of pleasure

The Cost of Loneliness



- As detrimental as smoking to longevity
- The temporal-parietal junction - cognitive empathy less activated and can atrophy
- Demished ventral tegmental area (VTA) and nucleus accumbuns
  - Less of a sense of pleasure

Hungry Social Networks

- Brain development involves many forms:
  - the establishment of synaptic connections
  - the pruning of others
  - changes to the behavior of a single ion channel
  - dendritic outgrowth
  - changes to the shape and number of sprouting new axons
  - modifying their dendritic surfaces

(Kolb & Gibb, 2001)

Client Education

You have brain networks that need social activity or they will shrink

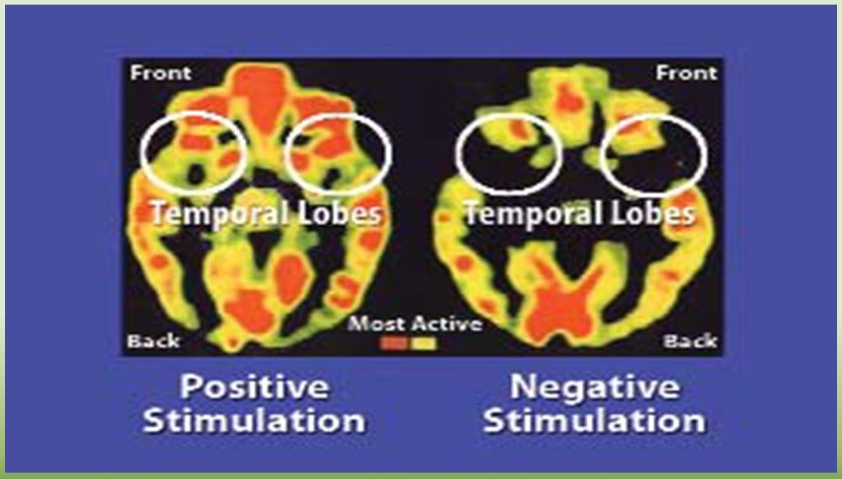
Deprived Social Brain Networks

- 150,000 children found languishing in Romanian orphanages. They were emotionally neglected.
- They missed human contact during critical periods (Kuhn & Schanberg, 1998).

Sustained impairment if over one year

- Increased Cortisol
- Impaired OFC
- Cognitive impairments (i.e. ADD)
- Shorter Telemeres

"Normal" vs Deprived

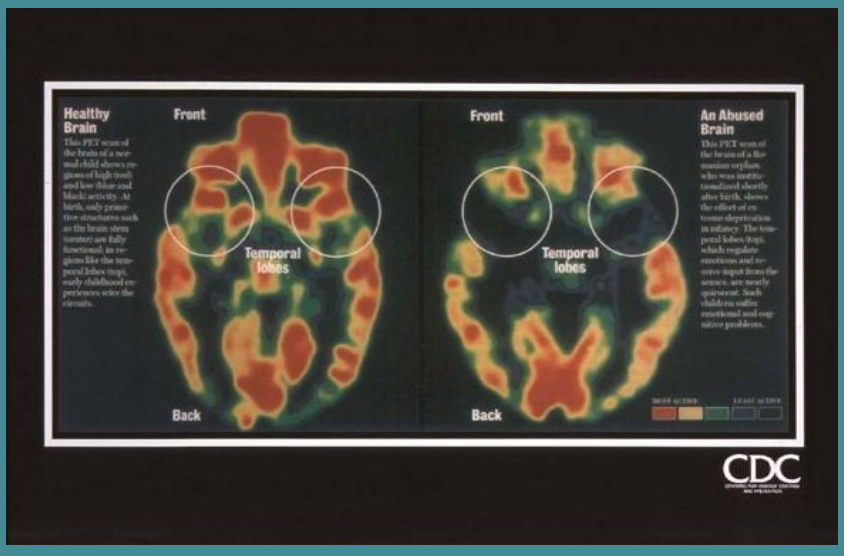


Brain activity of a normal five-year-old child (left) and a five-year-old institutionalized orphan neglected in infancy (right).

Child Abuse and Neuropathology

- Diminished left hemisphere and left hippocampal volume (Bremner et al., 1997).
- Accelerated loss of neurons (Simantov, et. al., 1996)
- Delays myelination (Dunlap, et. al., 1997)
- Abnormalities in developmentally appropriate pruning (Todd, 1992)
- Inhibition of neurogenesis (Gould, et. al., 1997)
- Adults who were physically or sexually abused as children – high IL-6 & CRP
  - diminished left hippocampal development (Howe, Roth, & Cicchetti, 2006).

"Normal" vs Abused Brains



Maternal separation leads to the following:

- ↓ development of inhibitory neurons and changes in the connections of serotonin and dopamine neurons in the mPFC
- Downregulation of gene expression for GABA receptors in the locus ceruleus, resulting in more norepinephrine
- Upregulation of gene regulating glutamate receptors, which contributes to anxiety and depression.
- Abnormally programmed gene expression in the amygdala, hippocampus, and PFC, priming the stress system
- Plasticity between the PFC and amygdala skewing toward the amygdala and the rest of the stress system

Epigenetic changes to the developing child's stress response system

Still Face and Visual Cliff

- **Visual Cliff paradigm** (Source, 1985)
  - Mother shows fear – child won't cross
  - Mother smiles 80% will cross
- **Still Face paradigm** (Tronick, Cohn, Field)
  - 9 months old no longer approach novel toys—imagination shuts down
  - s/he becomes agitated and distressed

Amygdala activation adults vs. children

- The amygdala involved in disambiguation of social situation—helps an individual disregard irrelevant information
- Fearful faces provoke more amygdala activity in adults than children
- Neutral faces (ie. Still Face Paradigm) provoke more amygdala activity in children than adults
  (Tottenham, et. al., 2009 for review)
- With maturation: neutral faces and ambiguity are tolerated due to increased cortical processing
  (Casey, et. al., 2005)

Gender Differences

- Boys more likely to likely to orient towards mothers' facial expression of joy, vocalizations, and gestures
- Girls more object oriented with sustained attention
  - Girls show more self-regulatory behaviors
  - Greater PFC—amygdala development
- The slower development of boys makes them more reliant on caregivers for help with their emotional regulation.
  - More at risk for suffering from abuse and neglect
  - More reactive to maternal emotions
  - More hostile attribution bias to ambiguous social situations

Infants of depressed mothers

- Display more aversion and helplessness, and vocalize less
- Higher heart rates, decreased vagal tone, and more developmental delays at 12 months of age (Field, 2005)
- Maternal depression during the first two years of a child's life is the best predictor of cortisol production in children at age 7 (Ashman, et al., 2002)

Intergenerational Transmission

Infants of depressed mothers have:

- Over-active right frontal lobes
- Under-active left frontal lobes
- Lower levels of DA and 5-HT
- Higher levels of stress hormones (Field et al., 1998)

- Treating the mother's depression contributes to the child's improvement

D.W. Winnicott

- Analysand of Melanie Klein
- *Good-enough parenting*
- The *holding environment*
- *Impingements mirroring*
- *transitional object*

"Good Enough" Parents

- Perfect *isn't* good enough
- High levels of affective matching correlate with insecure attachment
- Low levels also correlate with insecurity
- Moderate matching is optimum

Good-enough parenting and frustration tolerance

- If the baby is matched by instantaneous soothing s/he will not develop the PNS and the brakes to the SNS and HPA axis
- Good enough parenting factors in time before the baby is soothed
  - To anticipate being soothed and activate the parasympathetic nervous system
  - builds in frustration tolerance

John Bowlby (1907 – 1990)

- *Supervised by M. Klein*
- *Safe haven*
- *Attachment figures*
- *Proximity seeking*
  - infants seek proximity to the attachment figure for safety.

"Like a thermostat"

ISS/ Maternal Behaviors

Child Categorization	*Maternal Behavior*
(Secure)	emotionally available, perceptive & effective
(Avoidant)	distant & rejecting
(Anxious/Ambivalent)	inconsistent availability
(Disorganized)	conflictual behavior

Boys Respond Differently

- Given that fathers excite and set limits, the research paradigm referred to as the Risky Situation (RS) serves as a measure of the father and boys activation relationship.
  - the father's caregiving behavior tends to focus on arousal and excitement as well limit setting (Paquette & Bigras, 2010).
- Rough- and-Tumble Play (RTP) paradigm, the father activates but also sets limits. When fathers do not exercise dominance in the RTP with preschoolers they are more likely five years later to have poor emotional control and high levels of physical aggression, especially boys (Flanders, et al, 2009).
  - **RTP trains the child's prefrontal cortex to learn to set limits on affect.**

The Neuroscience of Attachment

- Balance Between the two branches of the Autonomic Nervous System
- Endorphin & Benzodiazepine receptors
- Cortisol Regulation
- Positive Immunological Functioning
- Neural Growth and Plasticity

Thermostat of Attachment

- **Secure attachment limits elevations of cortisol in stressful situations because the parent perceives and responds to the inner state of the child** (Fonagy & Target, 1997).
- **Early positive maternal care protects the hippocampus from high levels of cortisol** (Meaney et al., 1989).
- **Insecurely attached toddlers in the face of stranger and separation situations show elevated cortisol levels** (Nachmia, et al, 1996).

Insecure Attachment Longitudinally

- **Anxious/ambivalent and avoidant attachment styles associated with the development of depression.**
  - **Avoidant style leads to depression based on a sense of alienation**
  - **Anxious /ambivalent style leads to depression based on an internalized sense of helplessness and self-doubt.**

Client Education

- Though the stress thermostat function in your brain is not working, we will work <u>together</u> to rebuild it so that you will no longer react to normal situations as if they are dangerous.

Correspondence between Child & Adult Attachment Categories

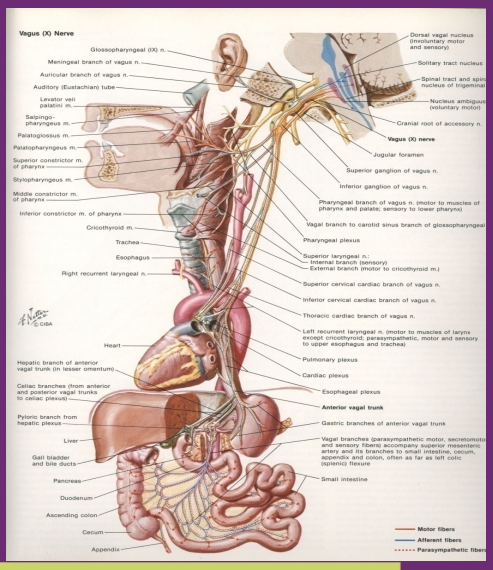
Child (ISS)	• *Adult (AAI)*
- secure	• - free/autonomous
- avoidant	• - dismissing
- ambivalent	• - preoccupied
- disorganized	• - unresolved

Social Brain and the PSN

- **Neurochemistry includes:**
  - **Oxytocin**
    - **Turns down cortisol**
- **Central Parasympathetic Nerves**
  - **"Smart" Vagus Nerve**

The Vagus Nerve System

- Tenth Cranial Nerve --a complex of sensory and motor nerve fibers.
- *Vagal tone*- the ability to modulate target organs without sympathetic arousal
- allows attachment and sustained relationships.

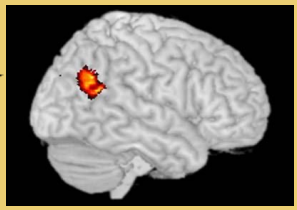


Vagal Brake (Porges)

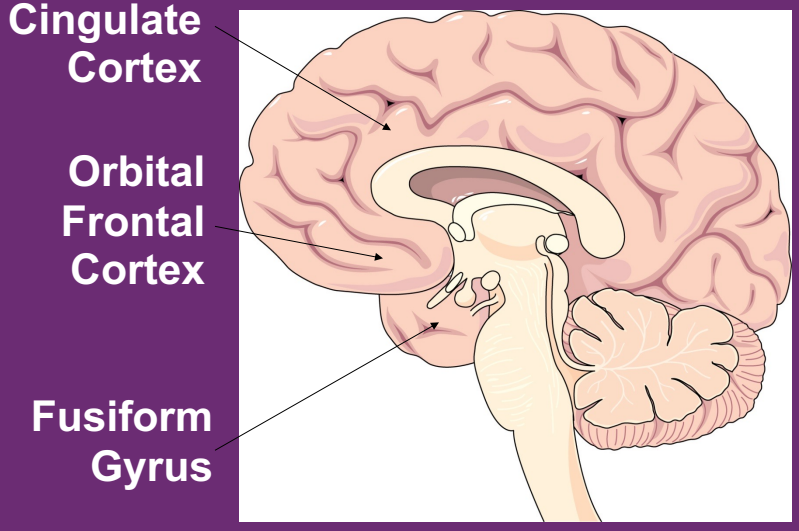
- *Higher vagal tone* correlates with:
  - Self-Soothing capacity
  - Quality of caretaking and attachment
  - More reliable autonomic responses
  - The range and control of emotional states
- *Lower vagal tone* correlates with:
  - -- Anxiety
  - Impulse Control problems
  - Hyperactivity, Attention deficit and distractibility
  - Avoidant & Disorganized Attachment
  - Irritability

Theory of Mind

- Amygdala
- Insula
- Right TPJ
- Anterior cingulate (Siegal & Varley, 2002)



- The R-OFC -- decoding mental states
- The L-OFC -- reasoning about those states (Sabbagh, 2004).
- There may be major nodes:
  - the medial prefrontal cortex for self-related mental states;
  - the superior temporal sulcus for goals and outcomes

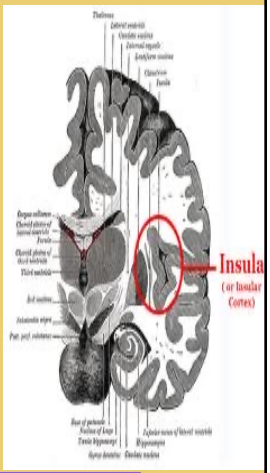


Anterior Cingulate Cortex

- ACC integrates cognitive and emotional information (Bush, et al, 2000)
- Active when detecting emotional signals from self and others (Critchley, et al., 2004)
  - The ACC is involved in both physical pain and social rejection (Eisenberger & Lieberman, 2005)
  - The dorsal ACC activates when fear of rejection occurs (Lieberman, 2005)
  - Activated when someone we love experiences pain or social ridicule (Botvinick, et al, 2005)
- Part of neural basis for cooperation (Pilling, et al, 2002)
- Damage results in reduced empathy and/or maternal behavior (Brothers, et al., 1996)

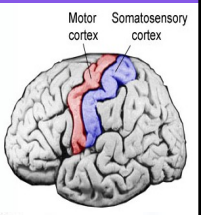
Insula and Empathy

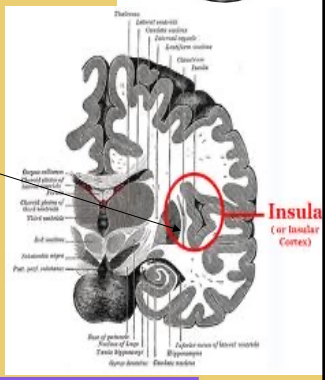
- Conduit between subcortical areas and cortex
- Draws on information from body areas, and input from amygdala and hippocampus
- Works with medial PFC to interpret and regulate emotional experiences
- Links mirror neuron systems with body states "Insula Hypothesis of empathy (Carr, et al, 2003)



Insula and Touch

- Soft touch: C—Tactile fibers (CT)
  - Unmyelinated—thus slower, tracks to the:
    - **insula** (part of the Salience Network
    - Emotional touch
    - Oxytocin
    - Impaired in people struggling with forming relationships





Spindle Cells

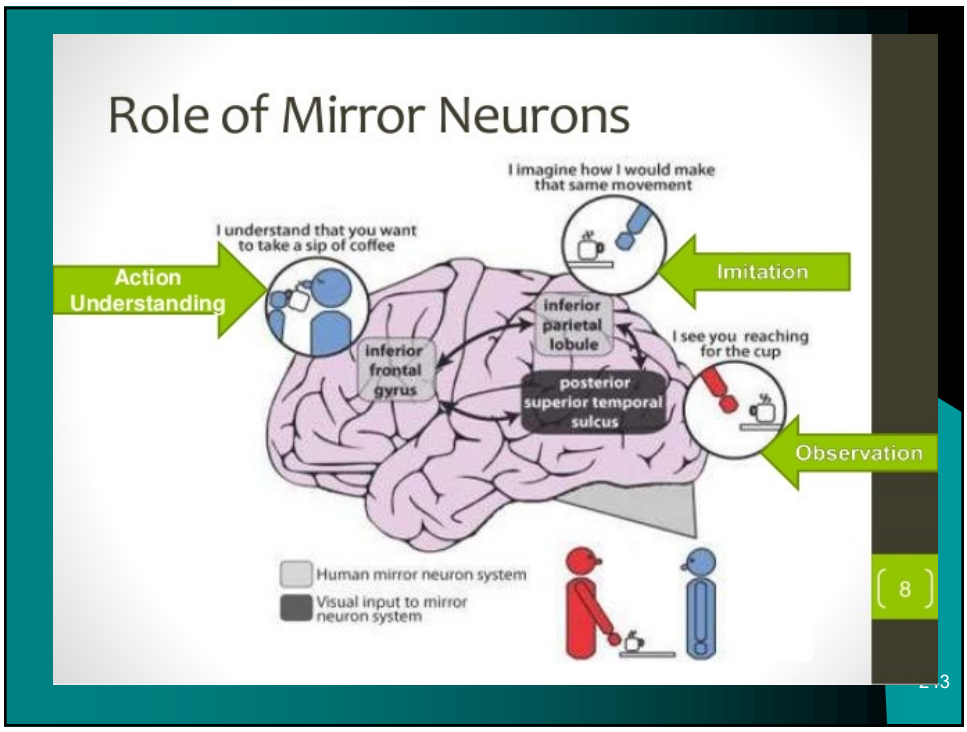
- Found in abundance in the OFC, AIC, and ACC---transmitting salience info
- Four times larger than other neurons, with a long extension
- At birth humans have approximately 28,000 spindle cells,
  - growing to 184,000 by age four,
  - 193,000 by adulthood.
- By comparison an adult ape has 7,000.

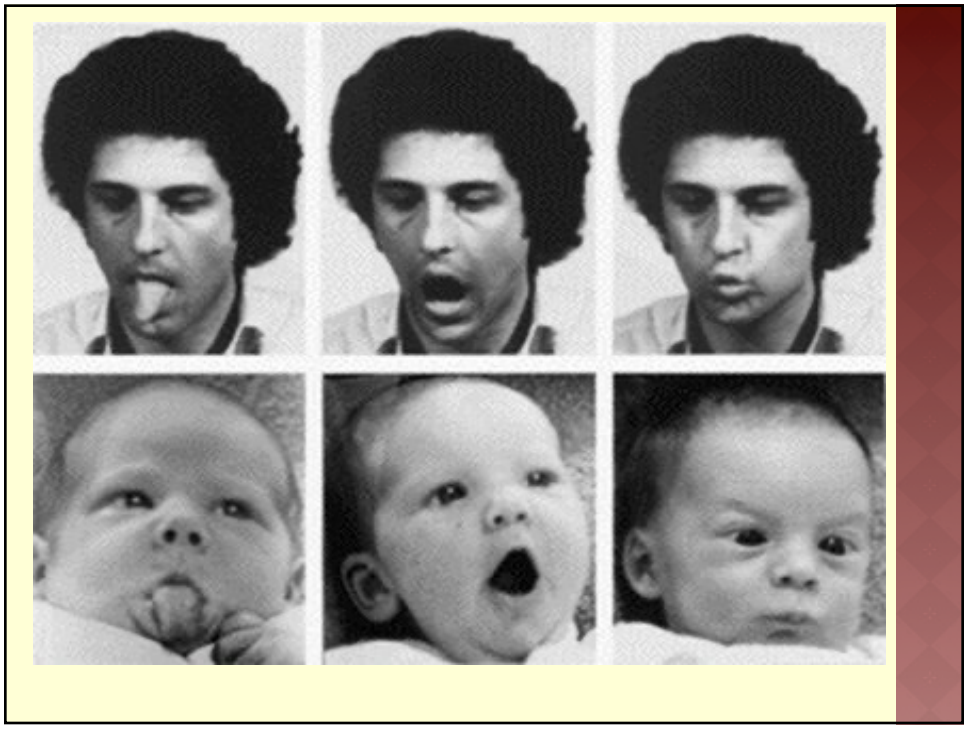
Spindle Cells

- Respond extremely quickly— "Behavioral Flexibility"
- Involved in making snap judgments, but also in solving complex problems in emotionally stirring situations
- Rich receptors of dopamine, serotonin, and vasopressin, important for generating mood and bonding
- Vulnerable to neglect, abuse, and trauma

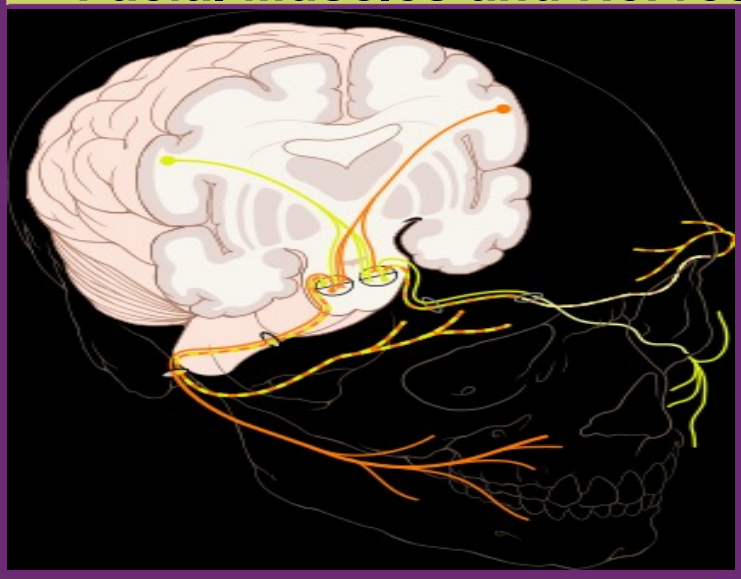
Mirror Neurons

- Originally found in monkeys (Rizzolati & Arbib, 1998)
- Critical for evolutionary development of social skills
  - Associated with anticipating goal-directed behavior
- Associated with empathy (Iacobini; Miller, 2005)
- Found in PFC, posterior parietal lobe, superior temporal sulcus, insula, and cingulate cortex


Role of Mirror Neurons
I imagine how I would make that same movement
I understand that you want to take a sip of coffee
Action Understanding
Imitation
inferior parietal lobule
inferior frontal gyrus
I see you reaching for the cup
posterior superior temporal sulcus
Observation
Human mirror neuron system
Visual input to mirror neuron system
8



Contralateral Facial Muscles and Nerves



Facial Expressions

Left Hemisphere

Controls expression on the lower right side of face

- Is NOT adept at reading facial emotion expression (e.g. alexithymics)

Right Hemisphere

Controls expression on the lower left side of face

- Is adept at reading facial emotion expression

Facial Expressions

- We view objects and faces with different systems
- Facial-reading systems --amygdala, fusiform gyrus, and supertemporal gyrus (Gauthier, et al, 2000)
- Reading of faces when faces are right-side up, but not when faces are upside-down (Kilts, et al, 2003)
- When we view faces upside-down, we view them as objects, unable to read their emotional content
- ASD patients read faces as if they were viewing objects

D Smiles

- Guillaume Duchenne (1806-1875) identified the orbicularis oculi muscles around the eyes
- Non-D smiles, possibly masking negative states and are more likely to be asymmetrical
- D smiles -- L-PFC activation
- Non-D smiles -- R-PFC activation (Ekman, et al, 1996)

Feedforward Expressions

- Therapists can model and influence the client's facial expressions and mood via feedforward and feedback:
  - Contracting muscles on the right side activates LH and positive emotions
  - Contracting muscles on the left side activates RH and negative bias--e.g., a "smirk" (Schiff, et al, 1992)

Smiling Kindles Positive Moods

- Perceiving the smiles of others triggers the release of DA (Depue & Morrone-Strupinsky)
- Presenting smiles for a fraction of a second followed by neutral stimulus increases the positive reaction to that stimulus (Dimburg & Ohman, 1996)
- Bilateral smiles ↑L-PFC positive moods
- Smiling during periods of stress ↓ cardiovascular arousal back to baseline (Fredrickson & Levenson, 1998)

Psychological Boost of Humor

- ↓ Anxiety (Yovetich, et al, 1990)
- ↓ Stress (Wooten, 1996)
- ↓ Depression (Deaner & McConatha, 1993)
- ↑ Self esteem (Martin, etal, 1993)
- ↑ Energy and hope (Bellert, 1989)
- ↑ A sense of empowerment (Wooten, 1996)

Laughter is Good Medicine

- Improves cognitive functions (Fry, 1992)
- Exercises and relaxes the muscles (Kuhn, 1994)
- Increases heart rate and blood pressure (Pearce, 2004)
- Decreases cortisol levels (Berk, et al, 1988)
- Increases natural killer cell activity (Takahashi, et al, 2001)
- Altering gene expression (Hayashi, et al, 2006)
- Stimulates the dopamine reward system (Mobbs, et al, 2003)
- Increased longevity (Yoder & Haude, 1995)

Client Education

- The saying ‘laughter is good medicine’ is true.
- The more you practice laughing, the more likely you will feel good and feel like laughing.

Cultural Framing

Race -- Ethnicity

- An integrated constellation of practices, symbols, values, and ideals as well as humor
- Shared by a community
- Transmitted from one generation to the next
- Constantly renegotiated and subject to change
- Operating at the individual and societal level
  - Producing outcomes
    - Socialization
    - Identity
    - Healing

Maximizing the Placebo Effect

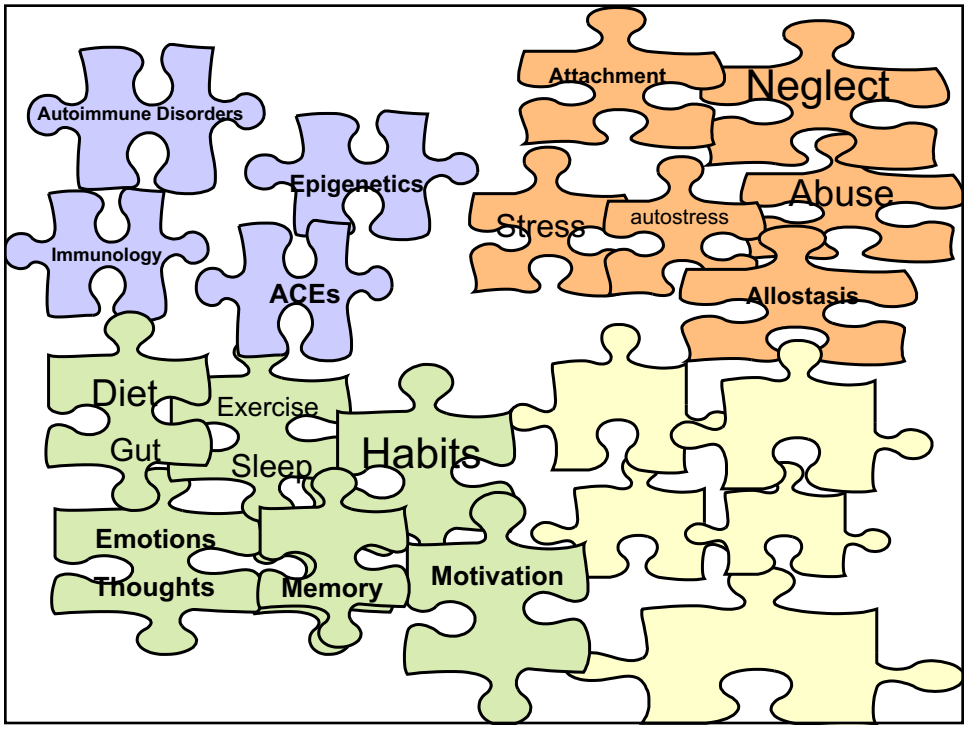
- Good listening skills
- Empathetic Attention
- Gaze Attunement
- Appropriate Touch
- Communication style (language and prosody)
- Welcoming physical appearance
- Physical Proximity
- Asymmetrical power dynamics between therapist/client (Kradin, 2008)

Therapeutic Frames of Reference

- The expectancy set
- Degrees on the wall
- Confidentiality explained
- Empathy—Compassion
- 50 minute hour
- Problem/symptom focus
- Solution focus

Social Summary

- Social brain networks need activation
- Health related costs without activation
- Neurochemistry of social connection
- Non conscious facial expressions
- The emotional and cognitive costs of loneliness
- Social medicine for stress reduction



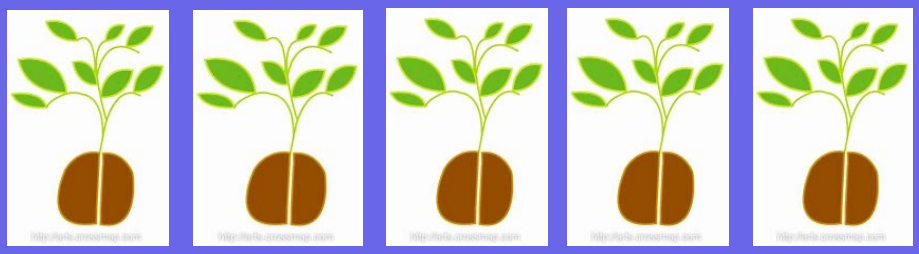
Mind-Brain-Gene Feedback Loops

Self-Regulation Factors

- Social
- Exercise
- Education
- Diet
- Sleep

SEEDS

It is an evolutionary imperative to nurture our SEEDS (Heather Lowndes)



Socialise
Calms nervous system
↑ Oxytocin (feel good)
↓ Cortisol (less stressed)
↑ Sense of connection
↑ Problem solving
↑ Attention
↑ Humour and fun
↑ Energy

Exercise
Calms nervous system
↑ Serotonin & Dopamine
↑ GABA (calm)
↑ Energy levels
↑ Growth new brain cells
↑ Sleep
↑ Alertness and thinking
↑ Attention
↑ Chance to socialise
↑ Cardiovascular strength
↑ Physical strength
↑ Flexibility & endurance

Education
↑ Brain power
↑ Serotonin & Dopamine
↑ Growth of new brain cells
↑ Thinking ability
↑ Working memory
↑ Challenge to learn
↑ Novelty – try new things
↑ Social connection
↑ Interest in life
↑ Ability to focus
↑ Sense of achievement

Diet
Calms nervous system
↑Brain chemistry
↑ Brain clarity
↑ Mood
↑ Sleep
↑ Energy
↑ Alertness
↑ Concentration
↑ Ability to focus

Sleep
↑ Hippocampus activity
↑ Memory
↑ Brain cell growth
↑ Serotonin
↑ Immune system
↑ Mood
↑ Energy
↑ Alertness
↑ Concentration

…AND MUCH MORE…

Movement is an Evolutionary Imperative

- 5 million years as Hunter-gathers
- Activity level
- Walking 10 miles a day

Typical Activities of Hunter-Gatherer: Correlates in modern day forms of exercise

Slow Cardio: 5-10 miles/day of low intensity walking

- Hunter gatherers cover 5-15 miles per days. Persistence hunters cover in excess of 30 miles/day.

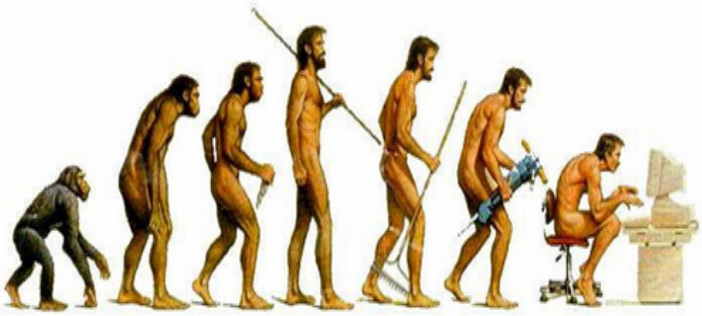
Resistance Training: Lifting, Throwing, and Carrying Objects

- Encompass functional movements such as pushing, pulling, sprinting, and jumping

Interval Training: Periodic bursts of high-intensity activity

- Brief bouts of sprinting alternating with walking or jogging in pursuit of prey

De-evolution



Beta-Endorphin and the High

Exercise, a form of voluntary stress, activates the hypothalamic-pituitary-adrenal axis

- Beta-endorphin is released from anterior pituitary

Subjective feelings of euphoria are mediated by rising levels of beta-endorphin

- Beta-endorphin increases in prefrontal and limbic regions of the brain after 2 hours of endurance running and levels correlate with euphoria

Exercise Increases Neurotransmitters

NE increases abruptly at exercise

- NE turnover is increased in the frontal cortex and is helpful to alleviate symptoms of ADHD

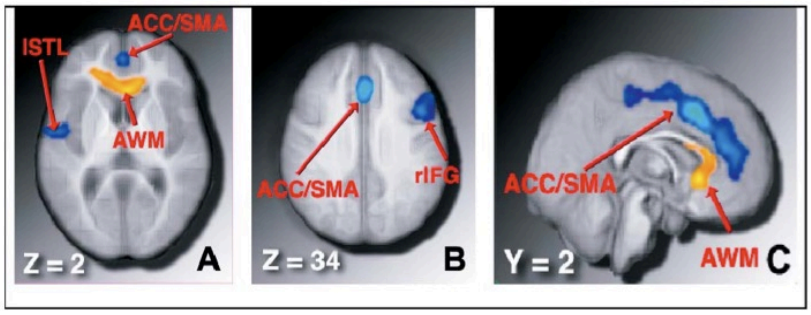
5-HT is modulated by exercise in specific brain regions and is also affected by intensity and duration of exercise.

- High-intensity interval training increases 5-HT synthesis in the hippocampus via interaction with BDNF.

DA is also increased in pathways involved in regulation and control of movement

- Higher levels of moderate to vigorous activities lowers the risk of developing Parkinson disease

Aerobic Exercise Training Increases Brain Volume in Aging Adults



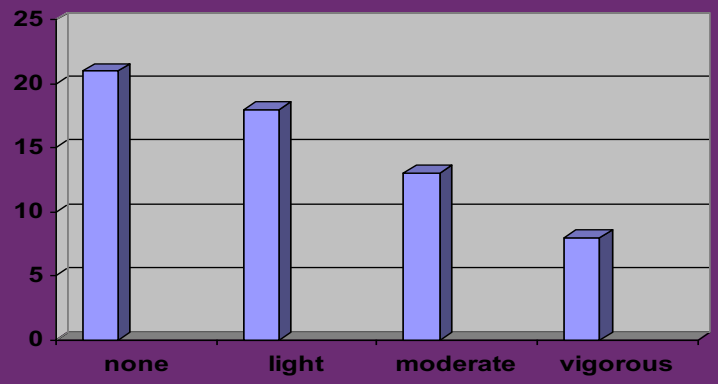
Blue regions: Gray matter volume was increased for aerobic exercisers

Yellow regions: White matter was increased for aerobic exercisers

Colcombe SJ, Erickson KI, Scalf PE, et al. Aerobic exercise training increases brain volume in aging humans. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. 2006;61(11):1166–1170.

Effect on C-Reactive Protein

- **The effect of exercise on C-Reactive Protein (inflammation chemical). Degree of physical activity by level of C-Reactive Protein Based on study of 13,748 people (Ford, 2002)**



Exercise and Depression

- Ohio State study---45 minutes of walking per day/ 5 days per week (heart rate at 60% to 70% of their maximum) lowered BDI mean scores from 14.81 to 3.27 compared to no change for controls (depressed non-walkers)
- Univ. of Wisconsin – exercise (jogging) as effective as psychotherapy for moderate depression
  - After one year 90% of exercise group were no longer depressed. 50% of psychotherapy group
- Duke Univ. – found that exercise was as effective as Zoloft
  - At 6 month follow-up exercise was 50% more effective in preventing relapse
  - Combining exercise and Zoloft added no benefit re: relapse (Babyak, et. al. 2000)
- NIMH panel concluded that long-term exercise reduces moderate depression.

Exercise and Depression

- **Alameda County study of 8,023 tracked for 26 years**
  - **Those that didn't exercise were 1.5 times more likely to be depressed**
- **Finnish study of 3.403**
  - **those that exercised 2 to 3 times per week were less depressed, angry, stressed and cynical**
- **Dutch study of 19,288 twins and their families –**
  - **those that exercised were less anxious, depressed, neurotic and more socially outgoing**
- **Columbia University study of 8,098**
  - **same inverse relationship between exercise and depression**

Exercise Improves Sleep

Exercise improves sleep quality and normalizes circadian rhythms.

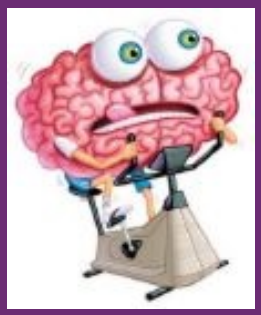
- increases slow wave sleep and total rest time
- decreases the amount of time to fall asleep
- decreases the amount of time spent in non-restorative sleep.

Lack of restorative sleep increases PICs and is associated with chronic disease

A single night of sleep deprivation results in higher levels of PICs

Exercise Optimizes

- **Mood**
  - **↑ neurotransmitters**
    - **Serotonin**
    - **Dopamine**
    - **norepinephrine**
  - **physical health**



Exercise Optimizes

- Cognition
  - –alertness
  - –attention
  - –motivation
  - –cognitive flexibility

Telomerase

An enzyme that adds nucleotides to protects telomeres:

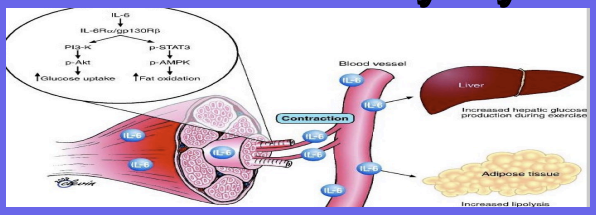
Insulin, IGF-1, VEGF, EGF upregulate telomerase activity.

All increased by aerobic exercise

Exercise and the Brain

Mechanism	Impact
Gene Expression	Neuroplasticity (Cottman & Blanchard, 2002)
Brain Derived Neurotrophic Factor (BDNF)	Neurogenesis & Neuroplasticity (Adlard, et al, 2005)
Insulin-like Growth Factor (IGF-1)	Energy Utilization (Carro. et al 200)
Nerve Growth Factor	Enhanced Neuroplasticity (Neeper, et al, 1996)
Vascular Endothelial Growth factor (VEGF)	Capillary Health (Fabel, et al, 2003)

Myokines:
Anti-inflammatory Cytokines



While inactive muscle could contribute to pathologies, myokines are candidates for treating metabolic diseases

Exercise-induced myokines are involved in mediating anti-inflammatory effects

Pedersen BK. The disease of physical inactivity - and the role of myokines in muscle-fat cross talk. The *Journal of Physiology*. 2009;587(23):5559-5568. doi:10.1113/jphysiol.2009.179515.

Mood Regulation Exercise:

- Must be aerobic
- Intensity in keeping with level of fitness
- 30 minutes 3-4 times a week

Or three 10 minute periods of exercise every day

Exercise Doses

- 10,000 steps per day (5 miles)
- Average: 6000
- 10 minute brisk walk: ↑ energy 60-120 minutes
- Mood: feel better than during any otherpart of the day (Gauvin, et al.., 2000)

Exercise Summary

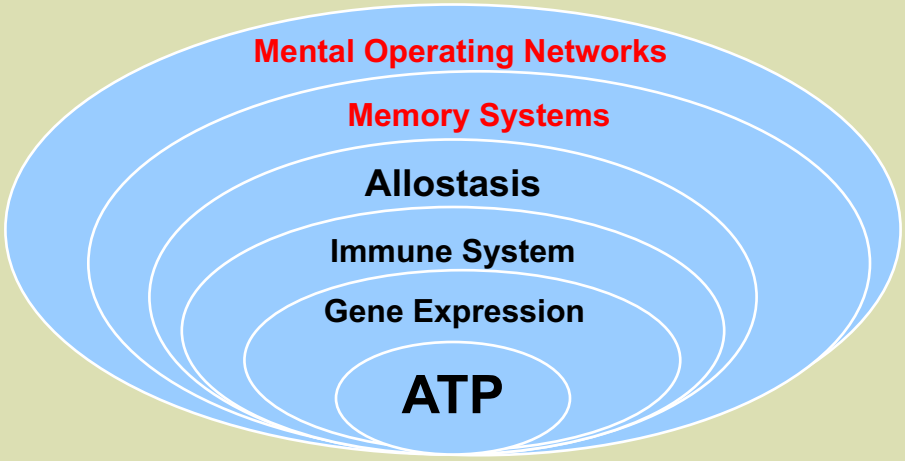
- Evolutionary imperative
- Not exercising is worst than "Smokadiabesity"
  - –WHO study of 200K—not exercising worse than smoking
- Exercise boosts mood
- Exercise boost cognition
- New neurons—neurogenesis

SEEDS

Education

Memory Improvement

“Self”-Organization



Working Memory

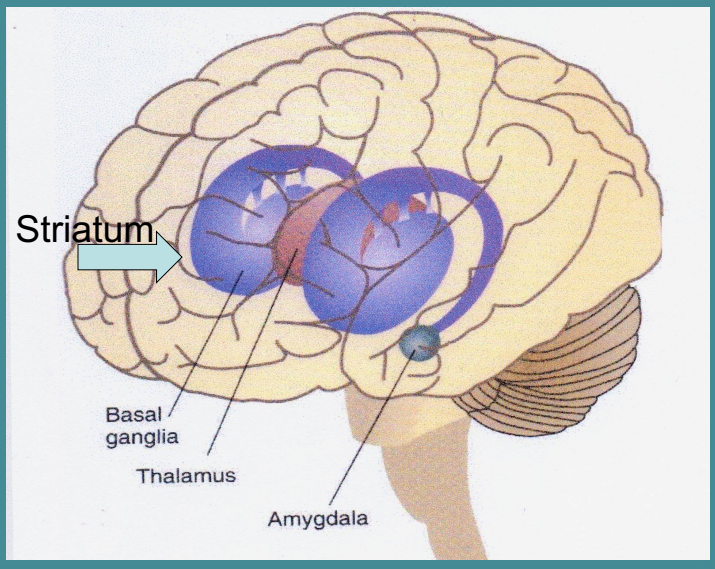
The Magic Number 7
+/- 2

- Telephone Number
- License Plate
- Days of the Week
- Colors of the Rainbow
- Deadly Sins
- 7 Dwarfs (Snow White)
- 7 wonders of the world
- Name Some Others….

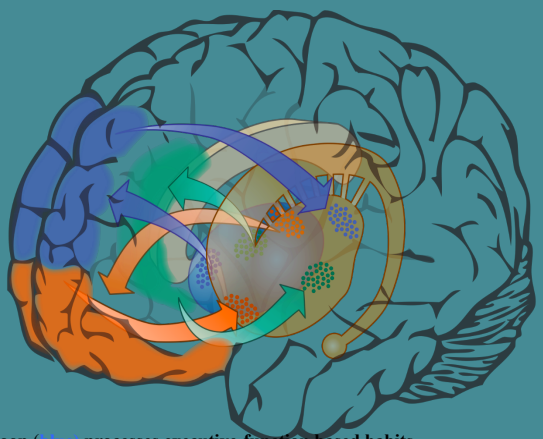
Two LT Memory Systems

Implicit	Explicit
Non-declarative	Declarative
• Procedural • Emotional • Generalized • Classical conditioning	• Episodic • Autobiographical • Semantic • Context Specific
Amygdala and BG-driven	Hippocampus-driven

The Habit Circuits



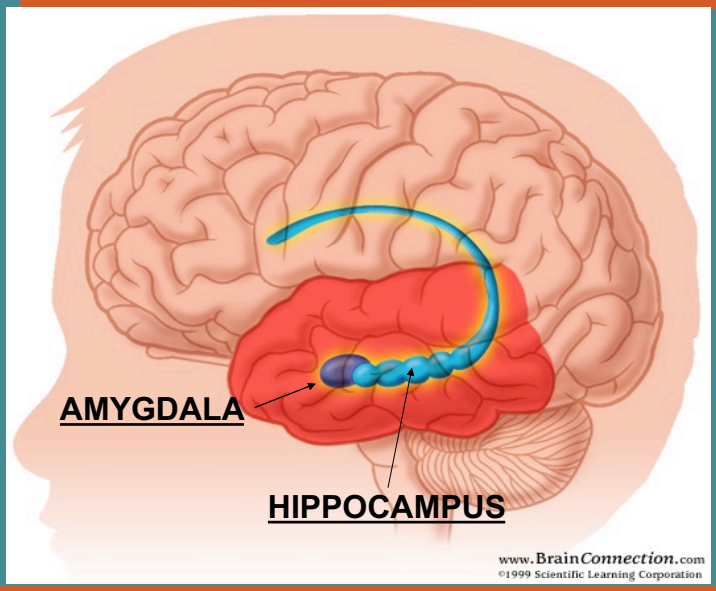
The Habit Circuits



The upper loop (blue) processes executive-function based habits.

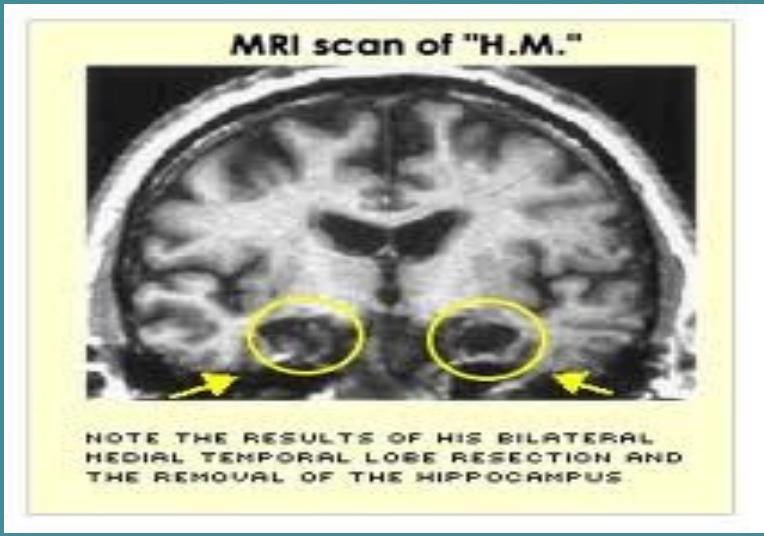
The middle loop (green) processes attention-based habits.

The lower loop (orange) processes social-emotional and reward-based habits



AMYGDALA *Implicit Memory System*	HIPPOCAMPUS *Explicit Memory System*
•Fear Conditioning •Emotional Valance •Generalized •Cortisol Heightened •Sensitivity • (Hypervigilence) •Matures Early •"Little Albert" •"LSMFT"	• Many Cortisol Receptors • Context Specific • Heightened Cortisol leads to atrophy • Matures Later • Vs. Infantile Amnesia • "H.M."

Henry's Brain

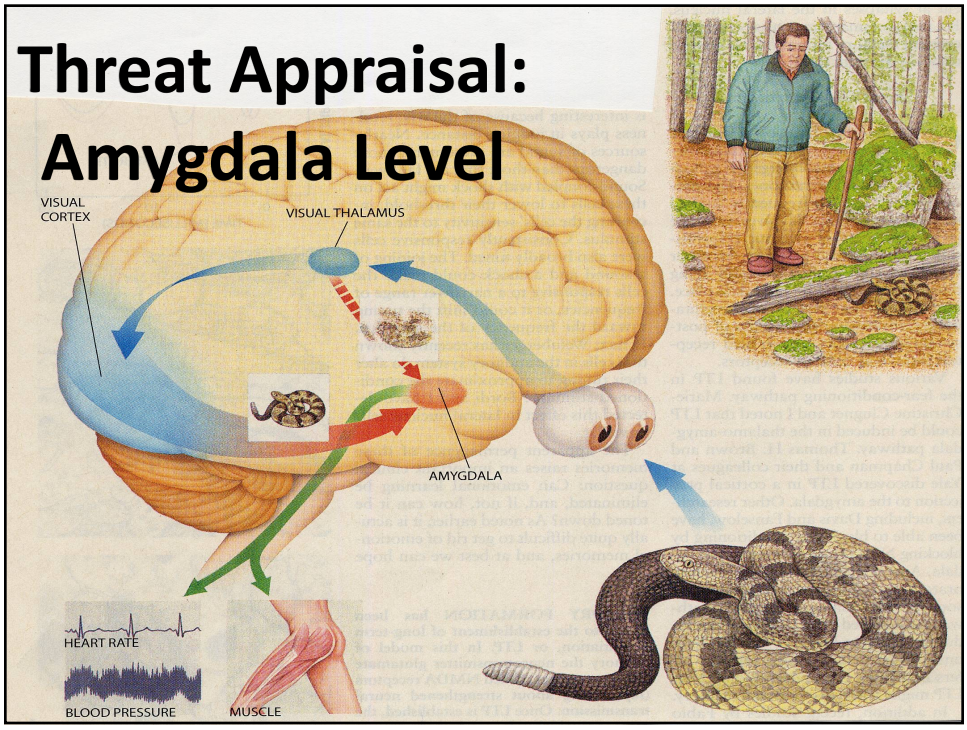


Amygdala and Hippocampus

- Amygdala contributes to emotional amplification of explicit memories
- Explicit memories can be state-based (e.g., when we are depressed, we remember depressing events)
- When the amygdala and hippocampus are activated together memories are more robust and durable
  - Make what you want the client to remember emotionally relevant

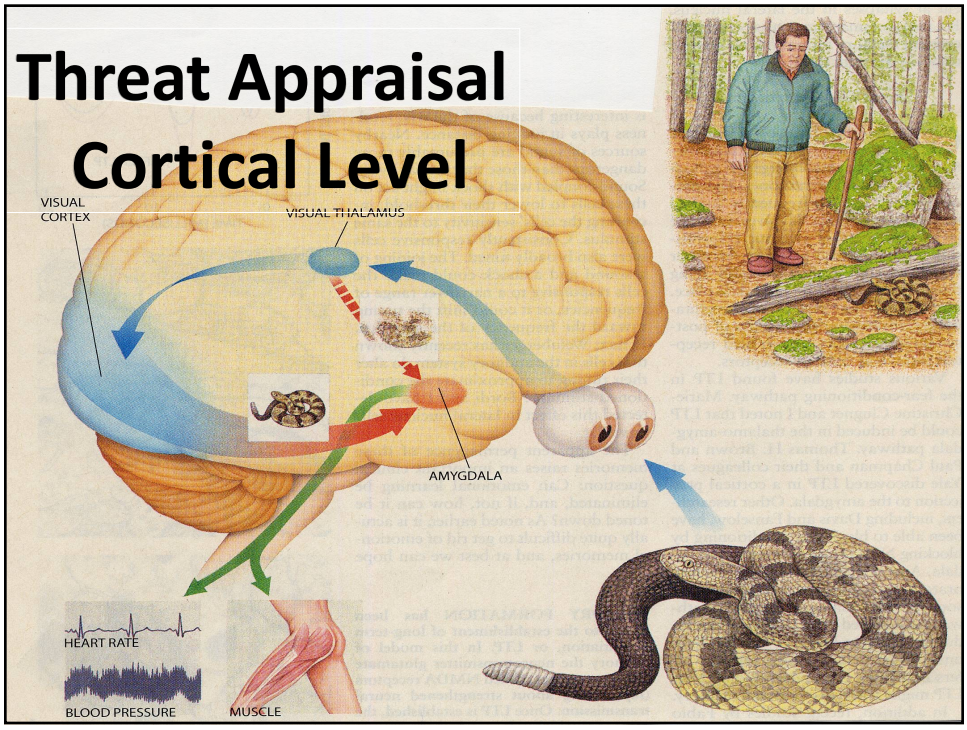
Hippocampal Coding

- Needed temporarily to bind together distributed sites in cortex that together represent a whole memory
  - Index to database of explicit memory
- Novelty detector: compares incoming info to stored knowledge; if difference, triggers dopamine increase
- Specialty is binding new to old information
  - Pattern completion (CA3)
  - Pattern separation—the ability to distinguish between similar experiences: (denate gyrus) ---**without it new safety memories cannot form and anxiety spreads**



The Fast Circuit to the Amygdala

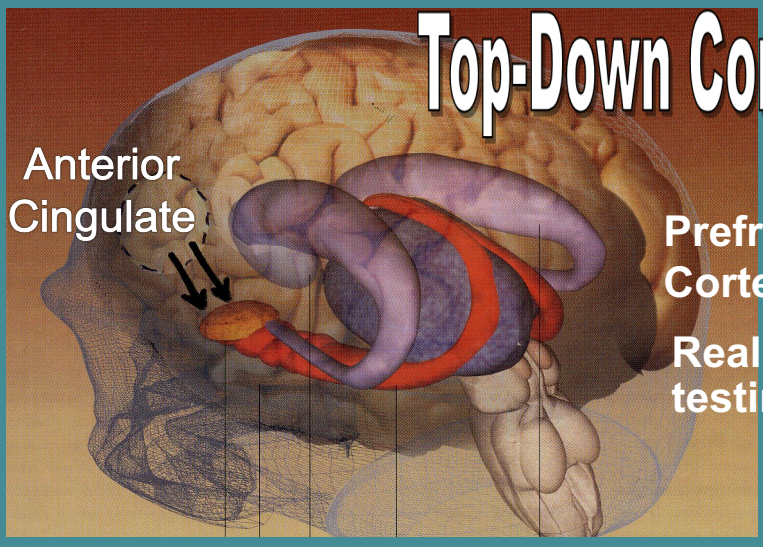
- Sensory info goes to the Thalamus then directly to the Amygdala:
- Fight or Flight: SNS and HPA activation
- Emotional Learning
- Fear Conditioning
- PTSD, panic, etc.
- Flashbacks
- "Bottom up"



The Slow Circuit to the Amygdala

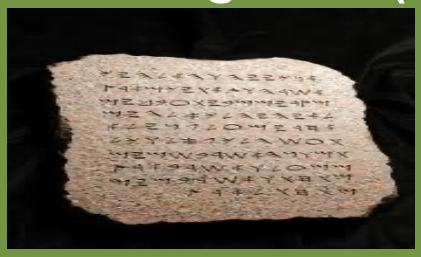
- Sensory info goes to the Thalamus through the Cortex and Hippocampus to the Amygdala
- Complications:
  - Worries and GAD
  - Fears and Phobias
- Benefits:
  - Tames the Amygdala
  - With exposure, New Thinking (cortex)
- "Top down"

Cortical-level Appraisal



The Dynamics of Fear

- Amygdala memories are hard to forget ("Stone tablet")



- Hippocampal circuits tell us what to fear and in what context ("Etch-a-Sketch")

Flashbulb Memories

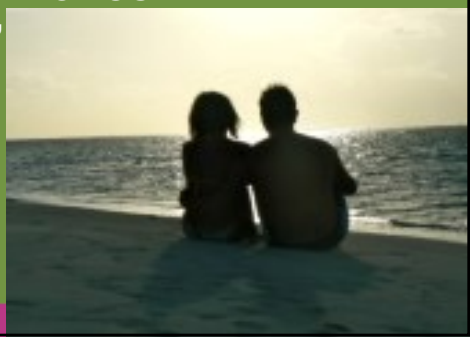
- A particular type of explicit memory
- During emotional peaks, NE dramatically sensitizes synapses
  - Increasing the ability of receptors to be recruited to synapses
  - Primes neurons by increasing their sensitivity

Negative Memories

- Fear and negative emotion narrows attention to threat:
  - **–"weapons focus"**
- Thus, less accuracy for peripheral memory of stimuli (i.e. color of the car or person's hair) more to the object of threat (gun, knife, etc.)

Positive Emotion and Memory

- Positive emotion promotes wide frame
- During positive experience we may want to "take it all in"
- Recalling positive memories -- "reminiscence bump"
- with increased
- positive memories
- (Bertsen & Rubin, 2002)



Memory Test

Memory Giants

- Homeric Bards
- Talmudic Scholars
- Muslim Scholars
- West African griots: genealogies
- Thomas Aquinas: dictated the Summa Theologica (3100 pp) from memory
- Akira Haraguchi, age 60, recited Pi to 100,000 decimal places from memory in 16 hours in 2006

Client Education

- Your brain is not like a computer, coding every program used or website visited.
- Your memories change in response to new experiences. That's what therapy does.

Memory (summary)

- **Attention is critical to the coding of new memory**
- **The power of mnemonics**
- **The "Inverted U": too little stimulation (e.g., boredom) or too much stimulation (e.g., trauma) conflict with the coding of new memory**
- **A moderate degree of anxiety works best to facilitate neuroplasticity and new memory**

Client Education

- A bad diet will deplete your brain chemistry, making your alarm system unnecessarily overactive.
- Just skipping breakfast will cause you to be depressed and have less energy and ability to deal with stress and anxiety.

Break a Fast

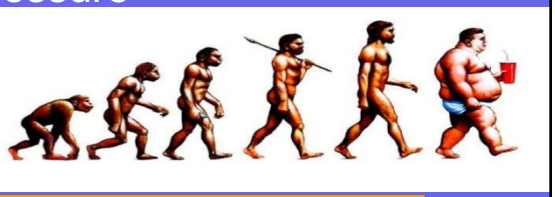
Skipping Breakfast contributes to:

↓ problem solving
↓ working memory
↓ attention
↓ concentration
↓ energy

↑ Mood swings
↑ depression
↑ stress reactivity
↑ anxiety

Perils of the Western Diet

- Fructose blunts the effects of leptin which normally tells us we are “full”
  - Fructose produces uric acid
  - Increased cardiovascular disease
- Increasing risk of metabolic syndrome
- **Shrinks the left hippocampus**
- Increased blood pressure
- LDL cholesterol
- Increased stroke
- Type 2 Diabetes

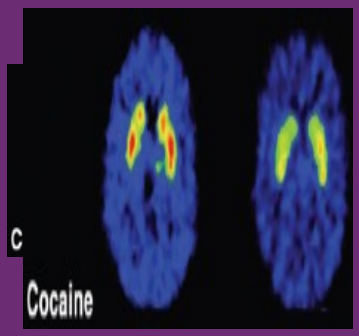


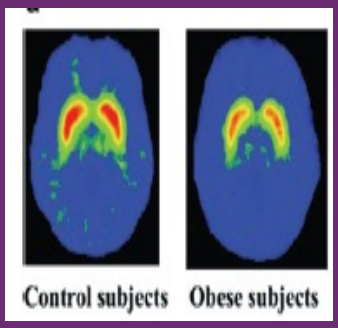
Client Education

- A bad diet will deplete your brain chemistry, making your alarm system unnecessarily overactive.
- Just skipping breakfast will cause you to be depressed and have less energy and ability to deal with stress and anxiety.

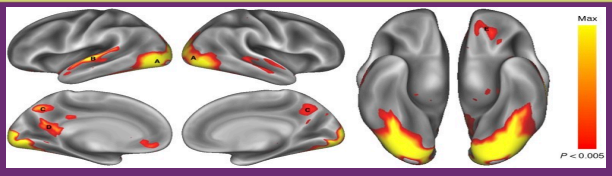
Dopamine D2 Receptors in Drug Users And Comfort Food Addiction

- Drug Addiction
- Obese
  - DA D2 (Dopamine Receptors)
  - In the brains of controls, drug abusers, and obese subjects





Priming Appetite and Obesity



Children can view 13 food ads per hour

The higher the BMI the greater the responsiveness to food commercials

Activity in the left OFC, Nacc, and right Insula

Priming Appetite for Bad Food

- Grey matter volume in two brain regions predicts selection of healthful food or tasty but unwholesome cuisine
- While the volume of grey matter in the DLPFC and the vmPFC predicts the choice of healthful food:
  - **Those people with less grey matter in these areas chose unhealthy foods**

Deficiencies of B Vitamins

Low B-1	Low B-2	Low B-6	Low B-12	Folic Acid
*Decreased Alertness *fatigue *Emotional Instability *Decreased reaction time	*Trembling *Sluggish *Tension *Depression *Eye problems *Stress	*Nervousness *Irritable *Depression *Muscle weakness *Headaches *Muscle Tingling	*Mental slowness *Confusion *Psychosis *Stammering *Limb weakness	*Memory problems *Irritable *Mental sluggishness

The OFC and Serotonin

- Large numbers of 5-HT receptors in the OFC
- ↓ 5-HT in OFC ↓ inhibition of the amygdala
- Tryptophan depletion impairs reverse learning tasks (Robbins & Everitt, 1995)
  - Ability to evaluate, integrate, and act on environmental cues
  - To stop responding to something when it becomes unhealthy and shift back to something healthier

Glycemic load (GL) – a measure of rise in blood sugar

The higher the GL of a food:

the greater the adverse insulin effects

Long-term consumption of foods with a high GL leads to a greater risk of:

Obesity

Diabetes

Inflammation

Depression

Client Education

- Eating a lot of simple carbohydrates, especially sugar, causes your brain to become stiff, rigid, and make you less able to rewire your brain.
- This means that you effort to think clearly, feel calm in the face of anxiety and lift out of depression will falter.

Omega 3

20% of the brain is made up of essential fatty acids (EFAs)

One third of myelin is EFAs

International Recommendations: 650 mg

Current American average consumption: 130 mg

The imbalanced ratio between Omega-6 and Omega-3.

Increased triglycerides (vegetable oil and animal fat) is correlated with depression (Glueck, 1998)

Glycation (excess glucose)

- The body's membranes become "gunked up"--slowing down neural communication
- Blocks protein from moving freely
- Interferes with synaptic transmission
- Causes structural damage to the mitochondria (the cells' energy factories)
- Lead to free radicals
- Causes inflammation.

Advanced glycation end products (AGEs)

- Acts as chemical glue that attaches molecules to one another
  - Causes *cross-linking*, (like overcooked meat)
- Associated with the formation of plaque, inflammation, atherosclerosis, particularly in diabetes

Fructose

- Unlike other sugars, it produces uric acid and blunts the effect of leptin, the hormone that tells the brain to stop eating.
- It flips a switch in the body, causing it to hoard fat, raise blood sugar and blood pressure.
- Can increase LPS by 40%.
  - With Firmicutes, LPS increases gut permeability and so inflammation.
- Triggers free radical products of damaged fatty acids, called isoprostanes, rising 34% just ninety minutes after consumption (↑ with AD)

Hyperglycemia

- Induces mitochondrial superoxide production in the cells that line the blood vessels
  - –Atherosclerosis
  - –Hypertension
  - –Heart failure
  - –Accelerated Aging
  - –Type 2 diabetes (who have smaller mitochondrial)
  - –AGE bind to mitochondria and complicate the functioning

Consuming 6000 calories a day doubles the risk of MCI

trans-fatty acids can:

1. Be absorbed directly by the nerve membranes
2. Block the body's ability to make its own essential fatty acids
3. Alter the synthesis of neurotransmitters such as dopamine
4. Negatively effect the brain's blood supply
5. Increase bad (LDL) cholesterol while decreasing good (HDL) cholesterol

trans-fatty acids

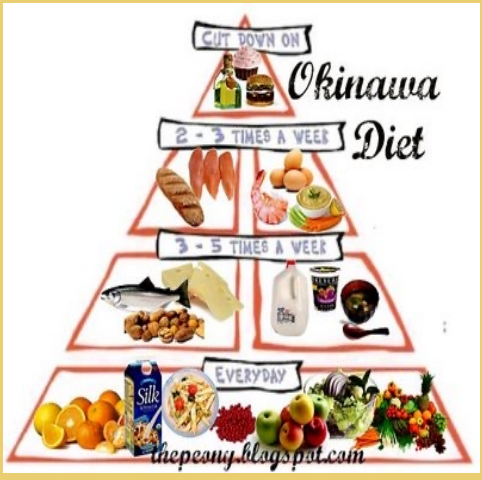
6. Increase plaque in the blood vessels
7. Increase blood clots
8. Increase triglycerides, which cause the blood to be sluggish and reduces the amount of oxygen to the brain
9. Cause excess body fat, which can have a destructive effective on the brain

    i.e. pro-inflammatory cytokines

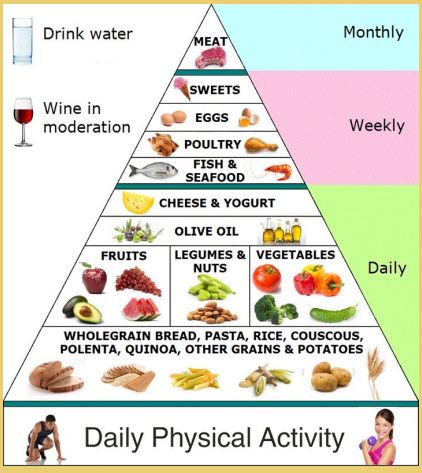
Protecting the Brain from Pre-Diabetes and Metabolic Syndrome

Diets styles for longevity:

Okinawan



Mediterranean



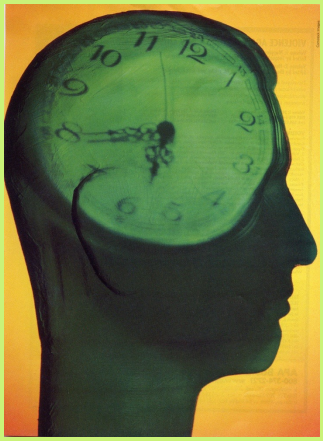
Diet Summary

- –The importance of breakfast
- –The perils of simple carbohydrates--↑ depression
- –Transfatty acids -↑ depression
- –Essential fatty acids
- –3-4 balanced meals
- –Vegetables 3xs per day
  - »↓ depression risk by 30%
    (Nurse's Health Study)

SEED**S**

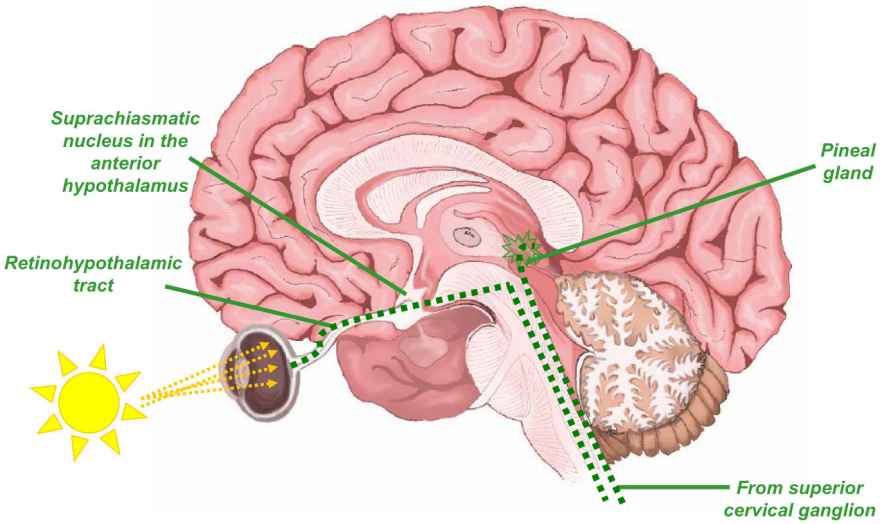
Sleep

Circadian Rhythm



- Wake and asleep times
- Body temperature
- Release of specific hormones
- Regulation of the immune system
- Recalibrating the brain

Circadian sleep drive is regulated by a "biological clock"



The Importance of Sleep for the Brain

- Protein synthesis (Ding, et al, 2004)
- Synthesis and transport of cholesterol (Cirelli, 2005)
- Expression of molecules associated with synaptic plasticity (Taishi, et al, 2005)
- Increase LTP (Cirelli, 2005)
- Gene expression (Cirelli, 2005)
- Memory consolidation

Medical Conditions - Insomnia

- Fibromyalgia
- Huntington's disease
- Kidney disease
- Hyperthyroidism
- Parkinson's disease
- Epilepsy
- Cancer
- Hypertension

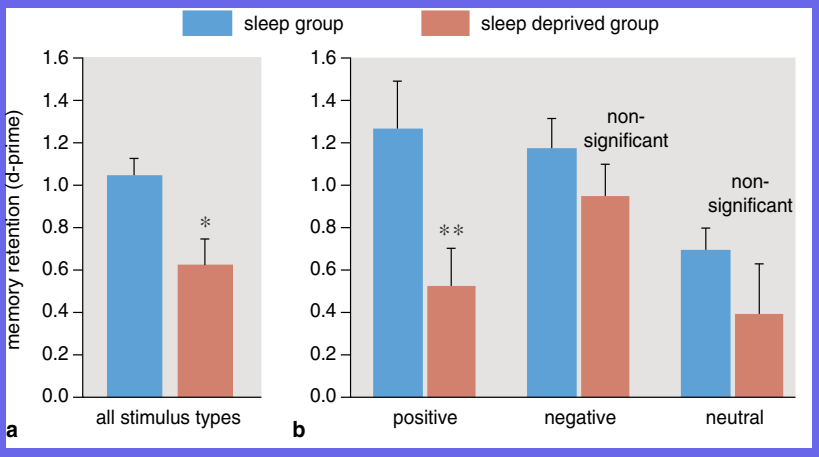
Poor Sleep Linked to Alzheimer's

Lack of sleep or waking up several times may increase the risk of Alzheimer's disease

Getting less sleep or sleeping poorly is tied to an increase in brain levels of beta-amyloid

Older adults, (average age 76); those who said they got under five hours a night, or who slept fitfully had higher levels of beta-amyloid in the brain than those who slept over seven hours a night

Sleep deprivation impairs memory

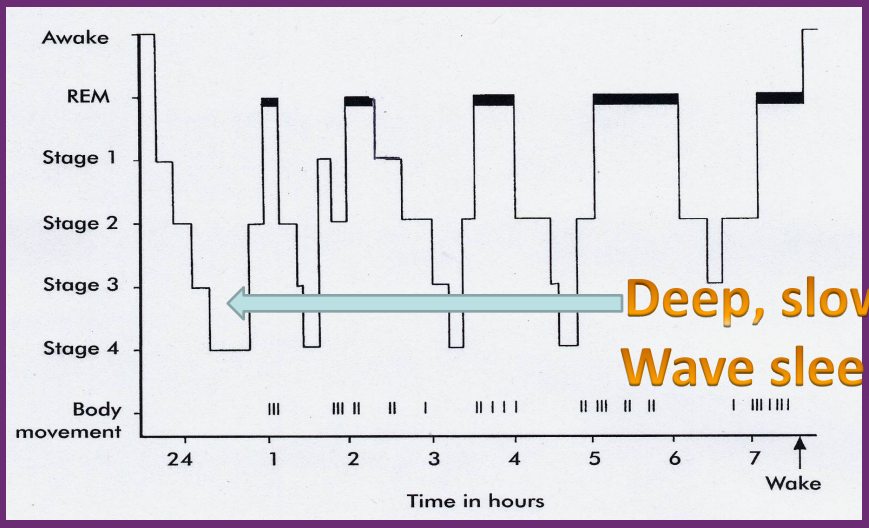


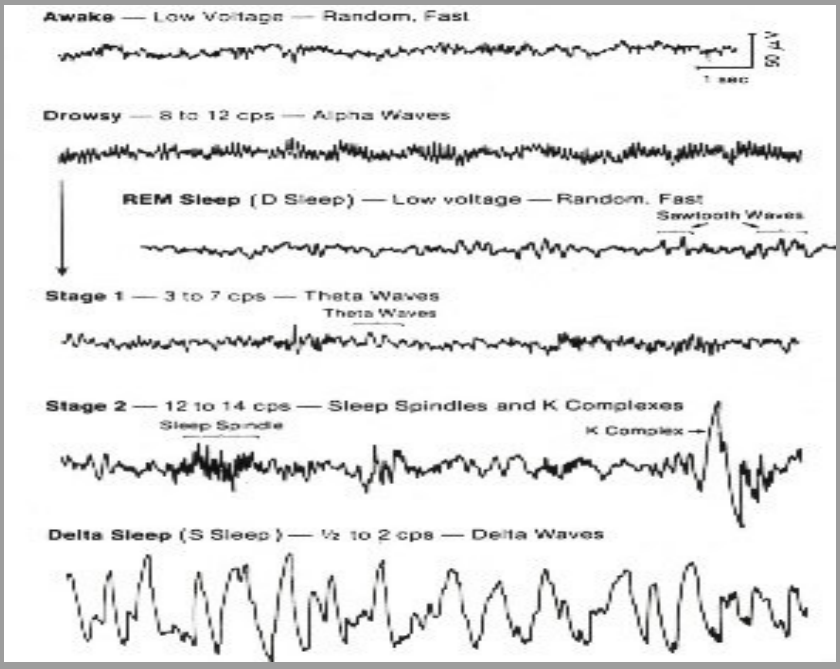
- 36 hours of sleep deprivation
- Word-pair test

Sleep Hygiene

- Don't do anything in your bed other than sleep (except for sex).
  - –Do not watch television, balance your checkbook, discuss finances with your spouse, or argue in bed. Make your bed carry only one association—*sleep*.
- If you can't sleep and find yourself tossing and turning, get up and go to another room.

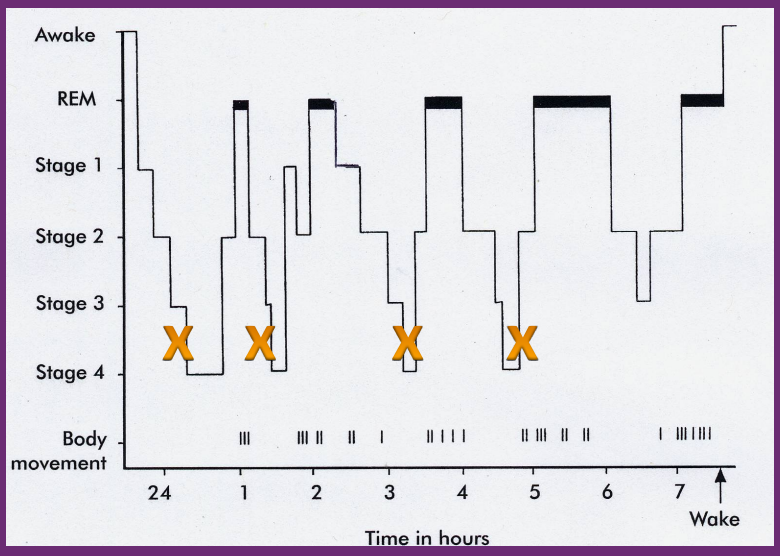
Normal Sleep Architecture





Pathologic Changes in Slow wave sleep

dep, anx, pain, apne, substance abuse



Slow wave sleep deprivation

- **> Fatigue**
- > Increases in cortisol
- **> Inflammation**
  - **> Trouble concentrating**
  - **> Impaired emotion regulation**

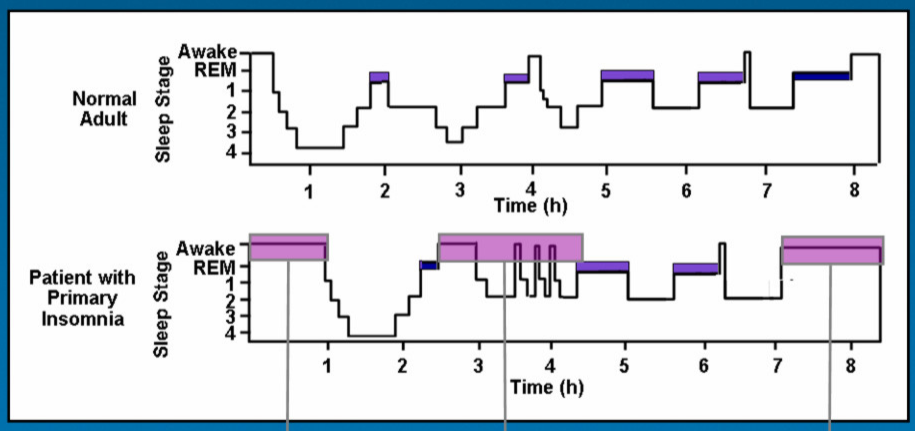
Increase in negative memories

–Increase in depression

Sleep deprivation

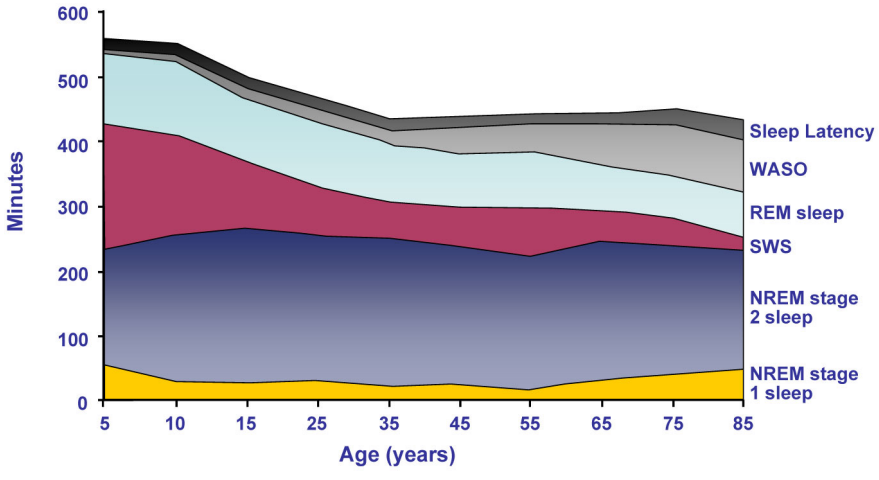
- **↓ ability to clear glucose**
- **↓ in leptin (which normally would inhibit hunger)**
- **↑ in ghrelin (increasing hunger)**
- **↑ in weight**
- **↑ vulnerability to type 2 diabetes**

Sleep Hypnogram for a Normal Night's Sleep versus Insomnia



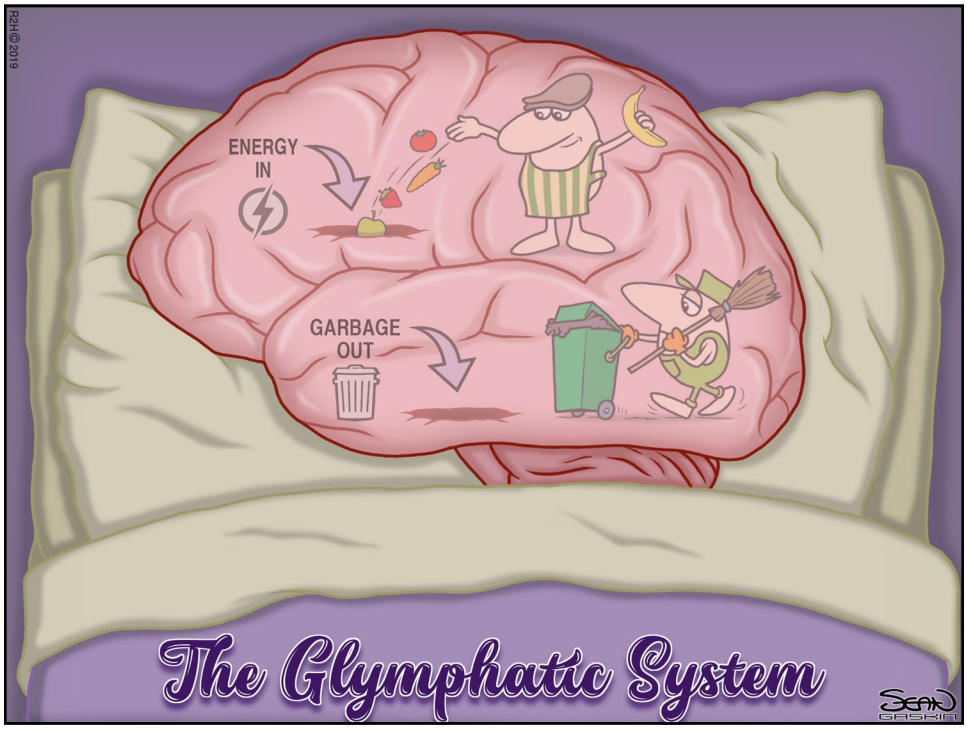
SEPRACOR

Sleep changes over the lifetime of an individual



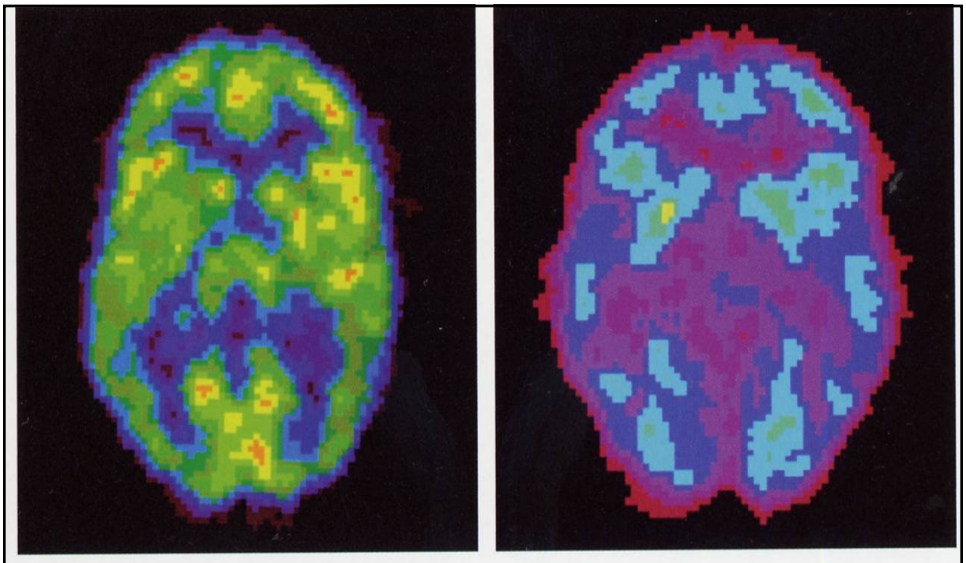
WASO: wake after sleep onset
REM: rapid eye movement
SWS: slow wave sleep (stage 3-4 sleep)
NREM: non–rapid eye movement

Ohayon MM, et al. *Sleep*. 2004;27:1255-1273.



Brain Clearing

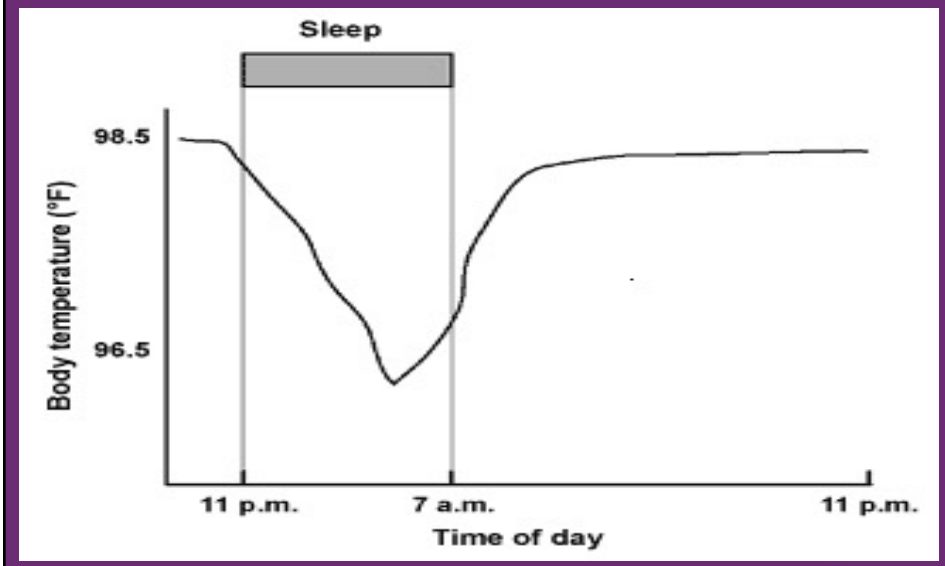
- "Glymphatic" system, a nod to both glial cells and its functional similarity to the lymphatic system
  - –Sleep as a dishwasher for your brain
- Sleep clears B-amyloid in the brain via increased CSF flow in interstitial space



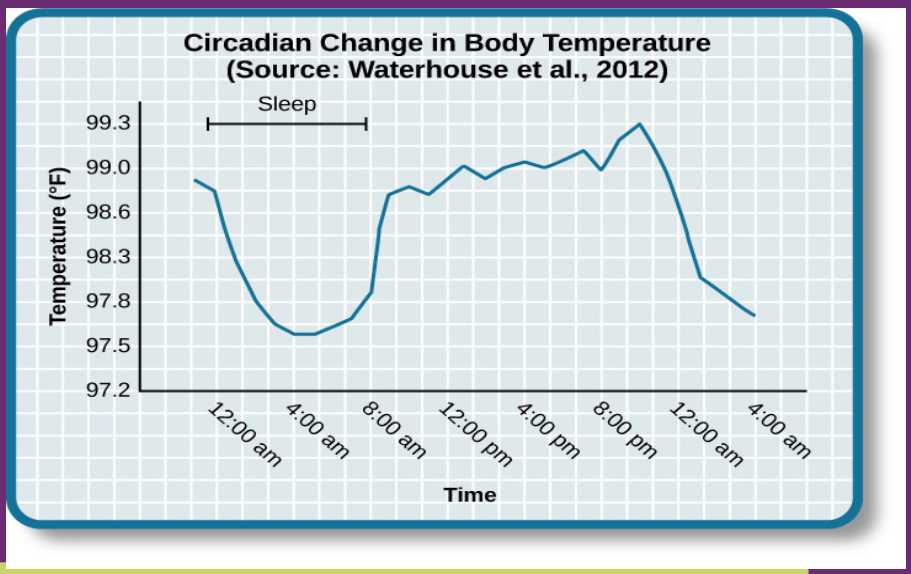
DEEP SLEEP
This PET scan shows that activity quiets down in many areas of the brain during deep sleep. The purple areas are the least active.

DRUGGED SLEEP
Most sleeping drugs induce a deeper sleep than normal. The purple areas on this PET scan show that much of the brain is inactive.

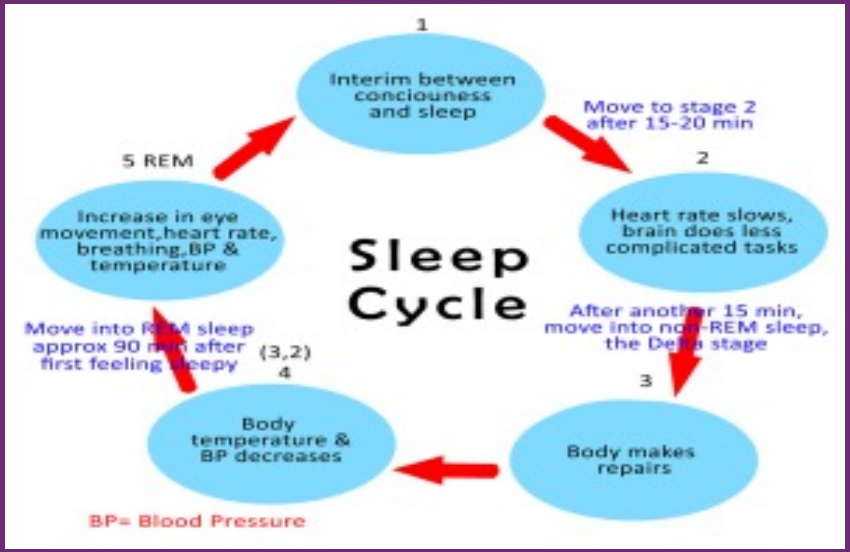
Body Temp and Sleep

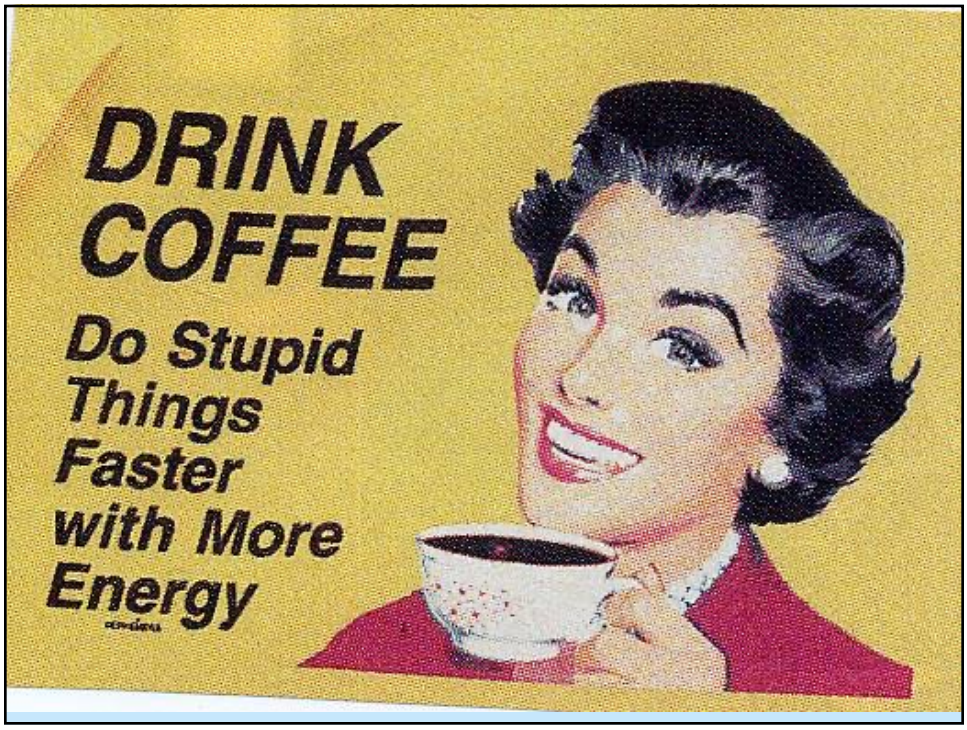


Body Temp per 24 Hours



Body Temp, Cortisol, and Melatonin



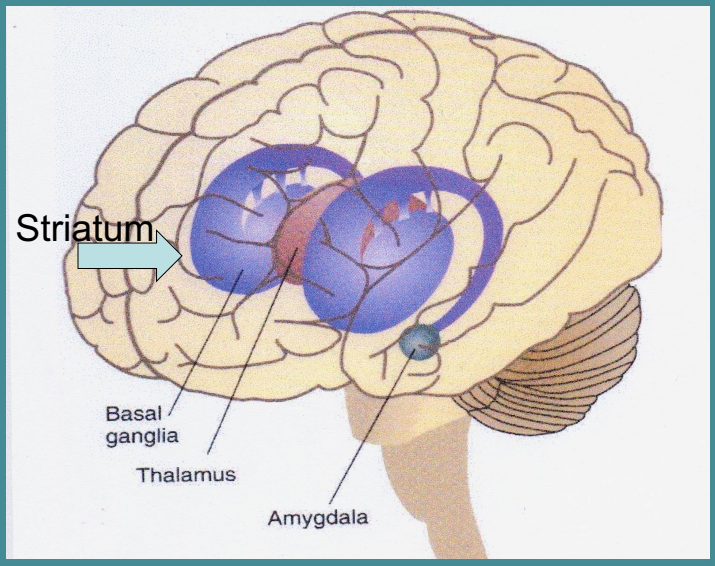


Sleep Summary

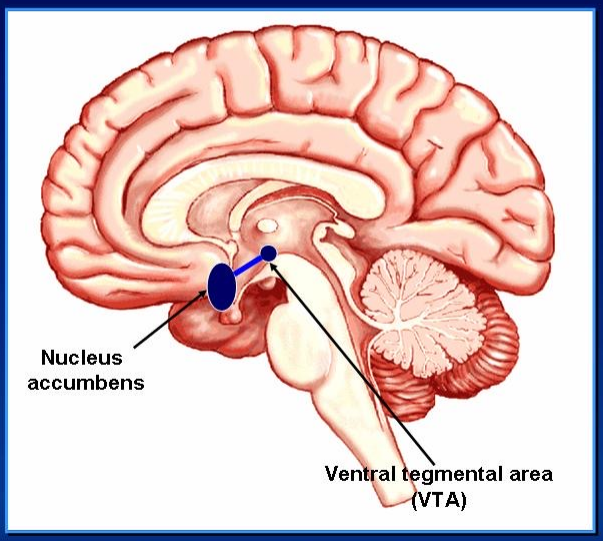
- Under 6 hours impairment
- Avoiding sleep depressors
- Negative sleep thoughts
- Body temperature
- Diet
- Exercise

Mind-Brain-Gene Feedback Loops

The Habit Circuits



Brain Reward Pathways



- The VTA-nucleus accumbens pathway is activated by all drugs of dependence including alcohol
- This pathway is important not only in drug dependence, but also in essential physiological behaviors such as eating, drinking, sleeping, and sex

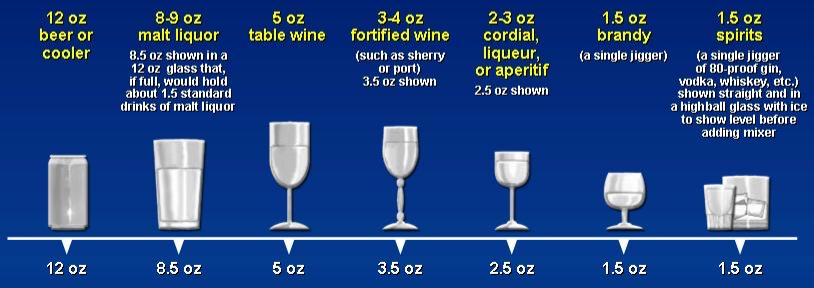
Source: Messing RO. In: Harrison's Principles of Internal Medicine. 2001:2557-2561.

Drugs Associated with Neurotransmitters

- Why do people have "drugs of choice"?
- Dopamine - amphets, cocaine, ETOH
- Serotonin - LSD, ETOH
- Endorphins - opioids, ETOH
- GABA - benzos, ETOH
- Glutamate -ETOH
- Acetylcholine - nicotine, ETOH

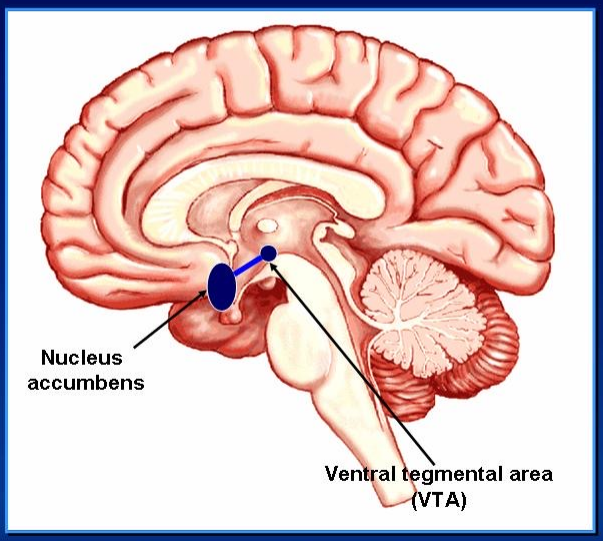
Defining the "Standard Drink"

- A **standard drink** = 14 g ethanol
  - 12 oz of regular beer or cooler (5% alcohol)
  - 5 oz of table wine (12% alcohol)
  - 1.5 oz of hard liquor (40% alcohol, 80 proof)
  - The average person metabolizes about 1 standard drink per hour



Source: National Institute on Alcohol Abuse and Alcoholism. Bethesda, Md: NIAAA; 2004. NIH Publication No. 04-3769.

Brain Reward Pathways



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Source: Messing RO. In: Harrison's Principles of Internal Medicine. 2001;2557-2561.

Effects of Acute Alcohol on Other Neural Circuits

GABA and Glutamate Systems

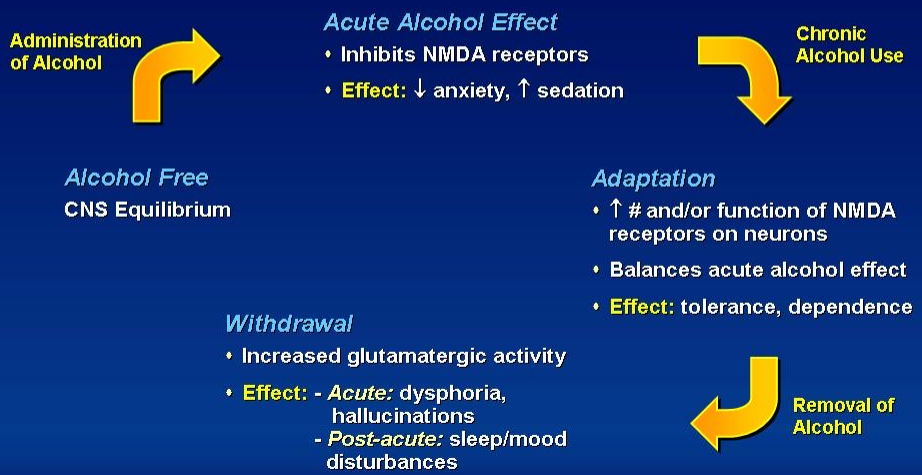
- Increases the effects of GABA, the major inhibitory neurotransmitter in the brain
- Inhibits the effects of glutamate, the major excitatory neurotransmitter in the brain
- Contributes to decreased anxiety and increased sedation during acute alcohol intake

GABA = gamma-aminobutyric acid.

Source: Littleton J. *Alcohol Health Res World.* 1998;22:13-24.

Effects of Alcohol on Neural Circuits

Glutamate System

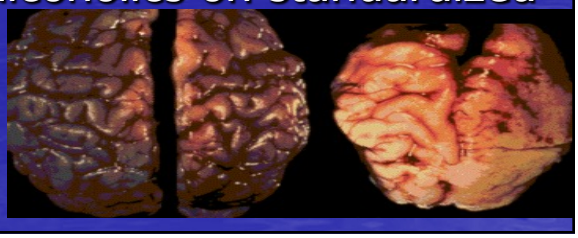


Source: Littleton J. *Alcohol Health Res World.* 1998;22:13-24.

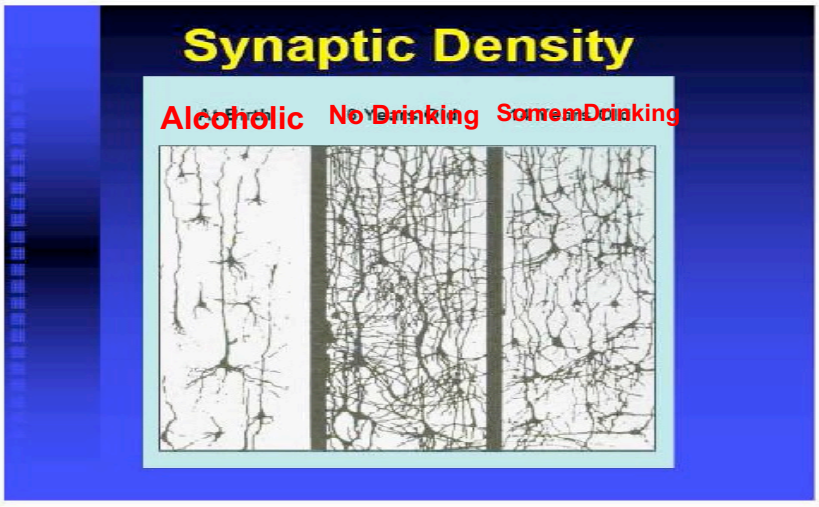
Brain recovery

- Brain dysfunction exists for the first 6-18 months of sobriety
- Most dramatic recovery from alcoholism is in the first three years
- Additional 3-5 years for alcoholics

to look like non-alcoholics on standardized psych testing



Alcohol damages dendrites and white matter, reducing message traffic between neurons and transmission speed.



Long Term Effect of Alcohol

Cognition and Alcohol

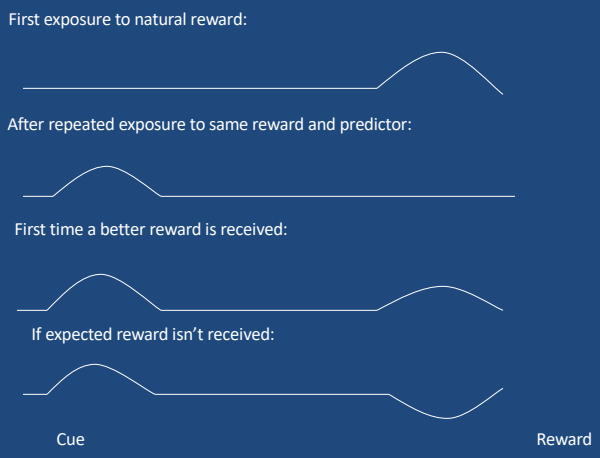
Drinking on a regular basis -- cognitive deficits such as:

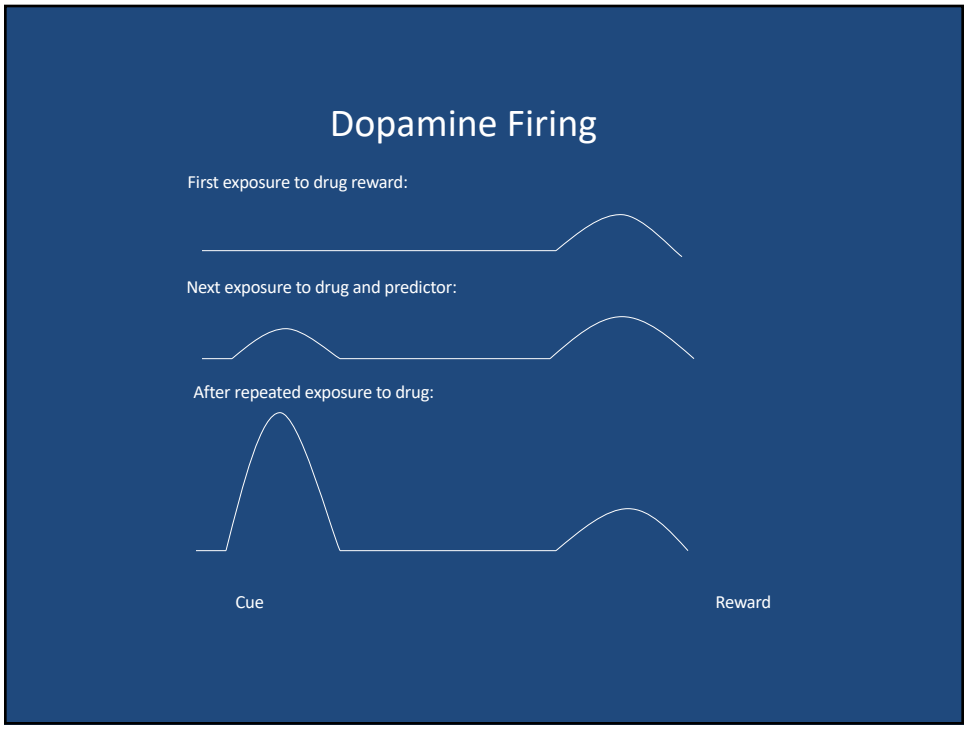
- ↓performance on tests of visual and spatial perception
- ↓visual and spatial learning ability
- ↓ ability to make fine motor movements
- ↓ adaptive abilities
- ↓ short-term memory
- ↓ non-verbal abstract learning
- ↓ abstract thinking ability
- ↓ conceptual thinking ability

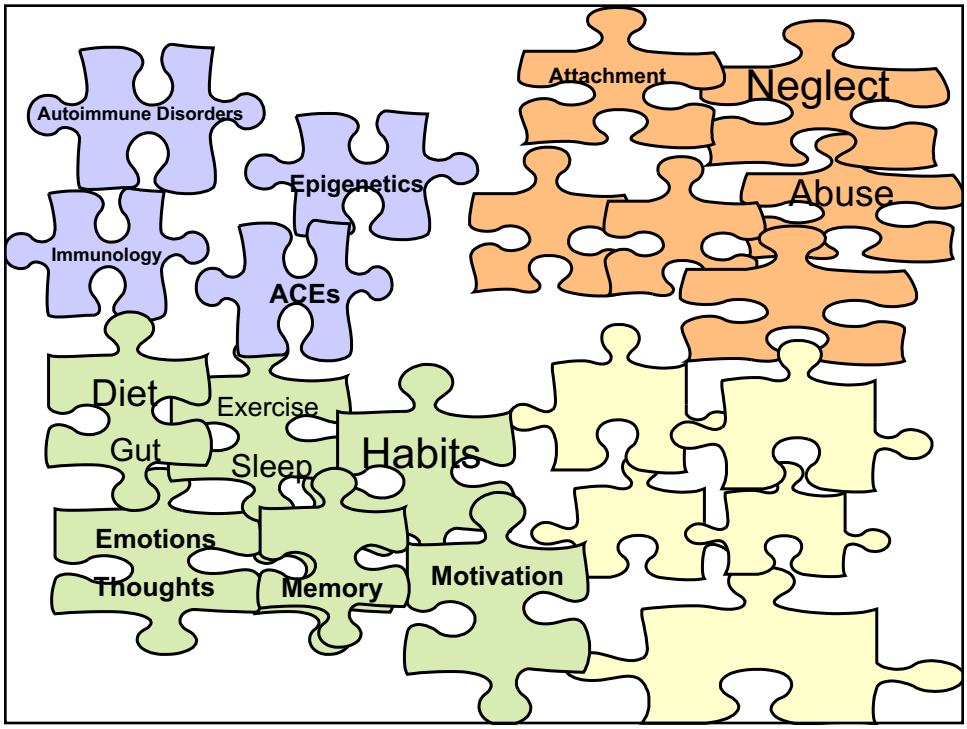
Alcohol, Mood and Sleep

- Alcohol contributes to the following problems as much as several days to weeks after drinking:
  - ↑stress and anxiety
    - ↓ GABA—panic attacks common
  - ↑depression
    - ↓ serotonin and DA
  - Alcohol-related insomnia (mid sleep cycle awakening).
    - ↓ deep sleep (Stage 4)
    - ↓ REM sleep.

Dopamine Firing




Dopamine Firing
First exposure to drug reward:
Next exposure to drug and predictor:
After repeated exposure to drug:
Cue
Reward


Autoimmune Disorders
Epigenetics
Immunology
ACEs
Attachment
Neglect
Abuse
Diet
Exercise
Gut
Sleep
Habits
Emotions
Thoughts
Memory
Motivation

Wanting vs. Liking

- Wanting—dopamine
- Liking—opioids
  - Sometimes you get wanting without liking
- Dopamine firing like a Geiger counter approaching a radiation source
- D1 receptors direct to the BG –mindless habit
- D2 receptors indirect—grow with a wide variety of positive experiences

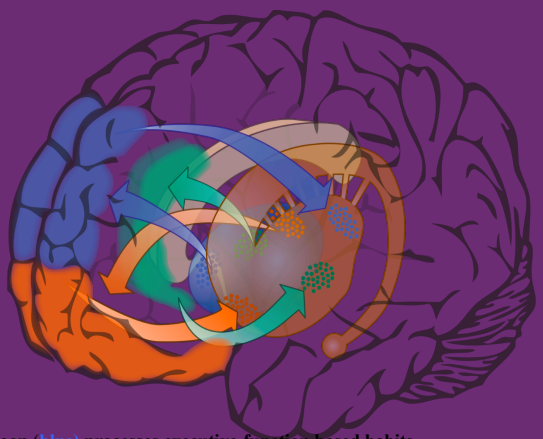
The "White Knuckle" Paradox

- "Just say no" produces working memory load, increasing the activity in the anterior cingulate cortex to monitor and assess errors in learned behaviors.
- Addiction can cause trouble activating the anterior cingulate cortex.
  - This is why many recovery programs incorporate contingency planning and relapse prevention so that problem solving ahead of time can minimize working memory load.

The Middle Path

- Normally, when dopamine binds to D2 dopamine receptors, the receptors change shape and cannot send another signal until they go through a recycling process.
  - The receptor is taken inside the neuron and chemically treated so that it can return to a functional state. This recycling process is messy, with the loss of some receptors in the process. If loss of receptors outpaces the rate at which the neuron makes new ones, D2 dopamine receptor levels will decline.
  - Moderate- size rewards stimulate moderate dopamine release, and a relatively small portion of the receptors go through this recycling process, leaving a large population of D2 dopamine receptors available to put on the indirect pathway brakes.
  - In contrast, drug use surges dopamine release to the extreme; with overwhelming dopamine release the D2 dopamine receptor population becomes depleted. The person becomes less able to put the brakes on habits. In recovery those receptors come back over a period of weeks and month

The Habit Circuits

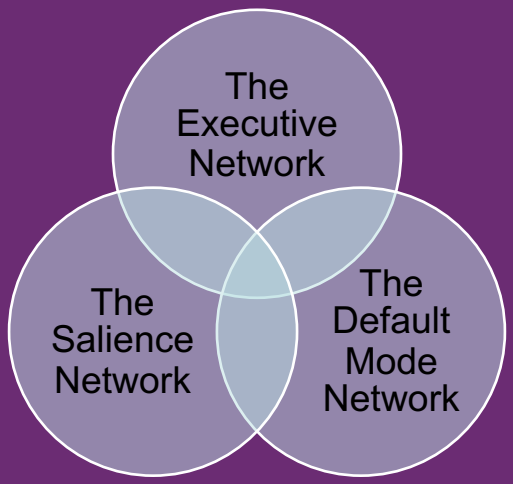


The upper loop (blue) processes executive-function based habits.

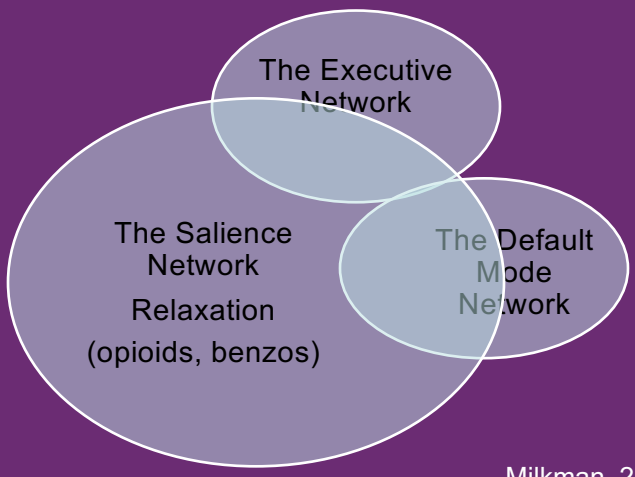
The middle loop (green) processes attention-based habits.

The lower loop (orange) processes social-emotional and reward-based habits

Balancing the Mental Networks

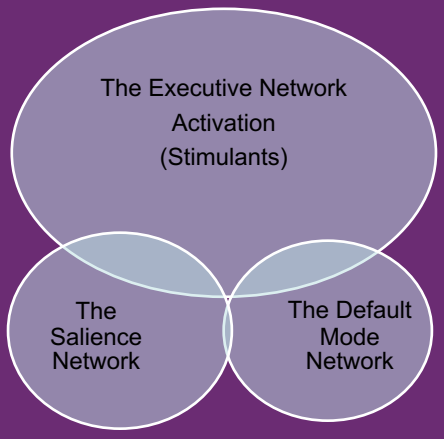


Styles of Coping Pharmacological Defenses



Milkman, 2019

Styles of Coping
Pharmacological Defenses



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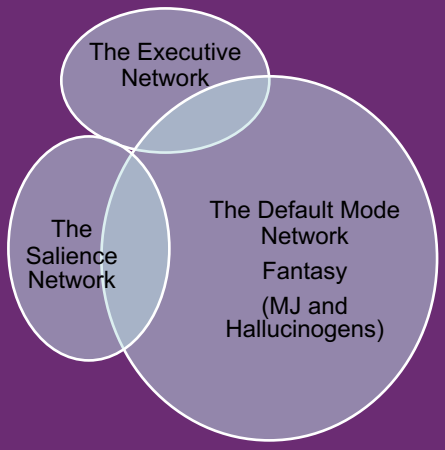
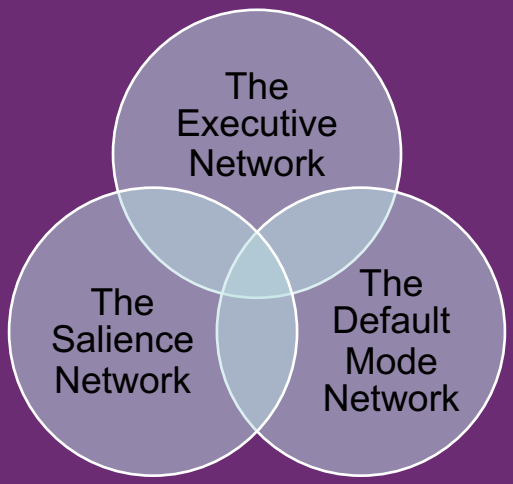
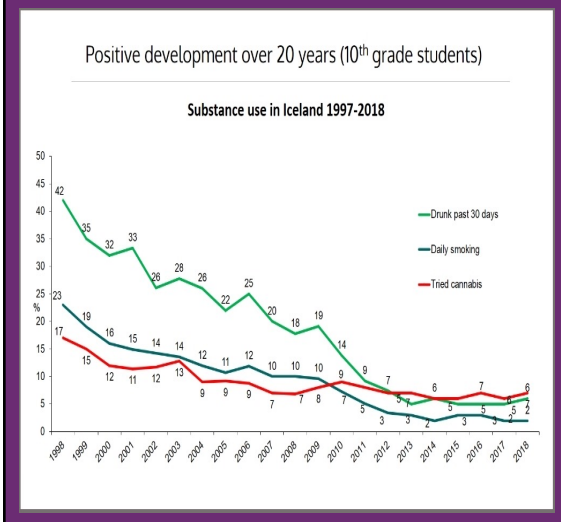


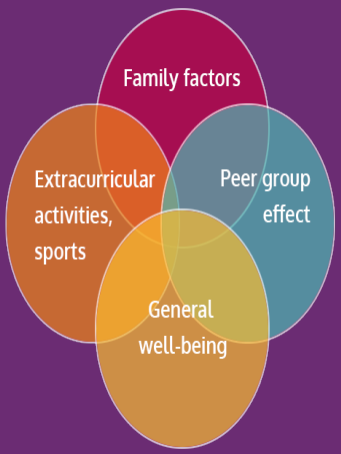
Milkman, 2019

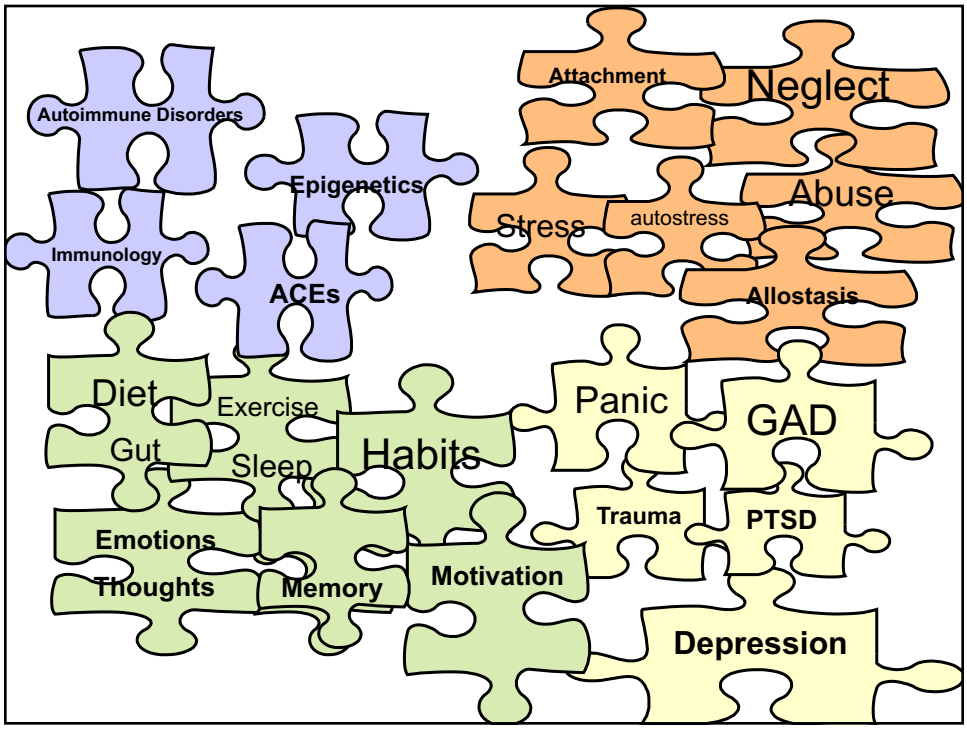
Balancing the Mental Networks



The Iceland Project






Autoimmune Disorders
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autostress
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PTSD
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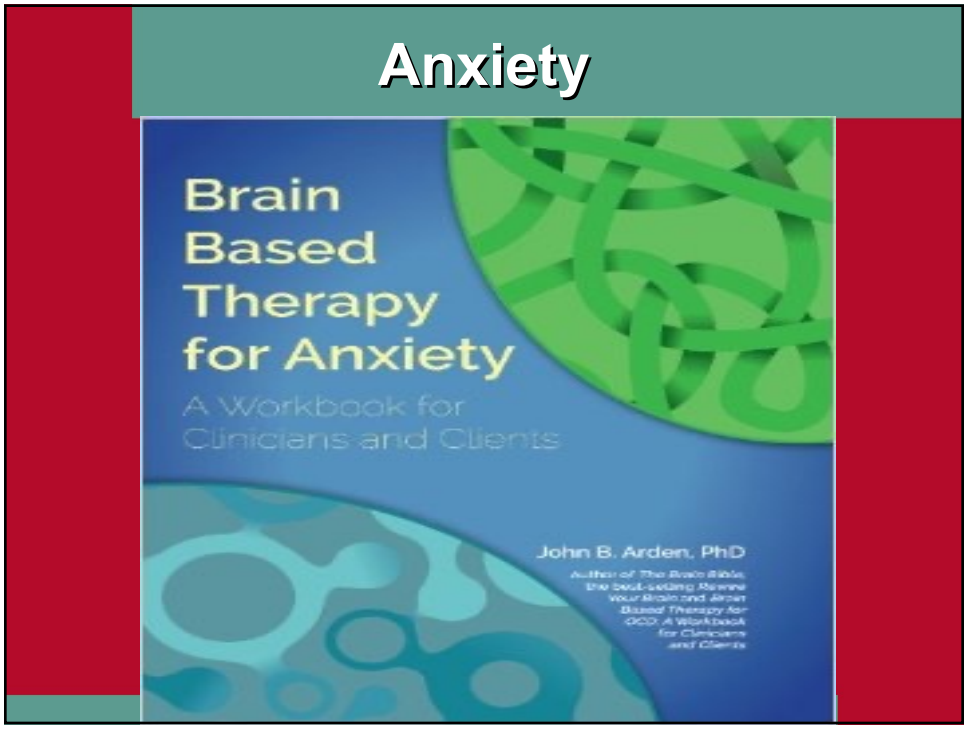
Depression


Anxiety
Brain Based Therapy for Anxiety
A Workbook for Clinicians and Clients
John B. Arden, PhD

Medical and Drug Related Factors that Mimic Anxiety

- Neurological: complex partial seizures, head injuries
- Pulmonary: Asthma, hyperventilation, COPD, lung cancer
- Various meds, drugs, and alcohol in withdrawal
- Endocrinological: Hyperthyroidism etc.
- Cardio: MVP, high blood pressure,
- Toxins such s hydrocarbons, mercury, and carbon dioxide
- Deficiencies in magnesium, Vitamin B-12, potassium, and calcium

Stress—Bottom Up or Top Down?

- William James—bottom up--"I am running from the lion –I must be scared"
- Walter Cannon—top down—emotions are determined by what you decide. Arms up!
- Schacter and Singer (1962) 2 Factor Model
  - Injection of epinephrine—arousal
- Paul Ekman—support for James
  - Moving facial muscles changes emotions

Those that think stress is harmful are more stressed

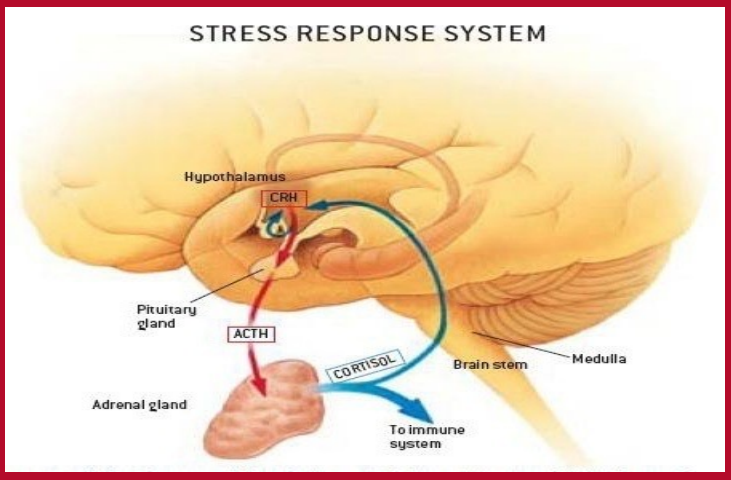
Allostasis

- Allostatic adjustments are adaptive over the short term with moderate and fluctuating levels of cortisol to help orchestrate adjustments by:
  - enhancing or inhibiting gene transcription
  - regulation of BDNF
  - up regulates amygdala activity
  - targets prefrontal systems involved in stress and the emotion (Sullivan & Gratton, 2002).
  - maintaining stability through a change (McEwen, 1998).
- *Allostatic load* --When demands exceed the balance of energy and regulatory gains from rest and recuperation. (McEwen and Wingfield, 2003).

Client Education

- Just as your car needs shock absorbers for bumpy roads, so too can you develop the durability to adapt to daily challenges.

Sympathetic ANS and Neuroendocrine Systems

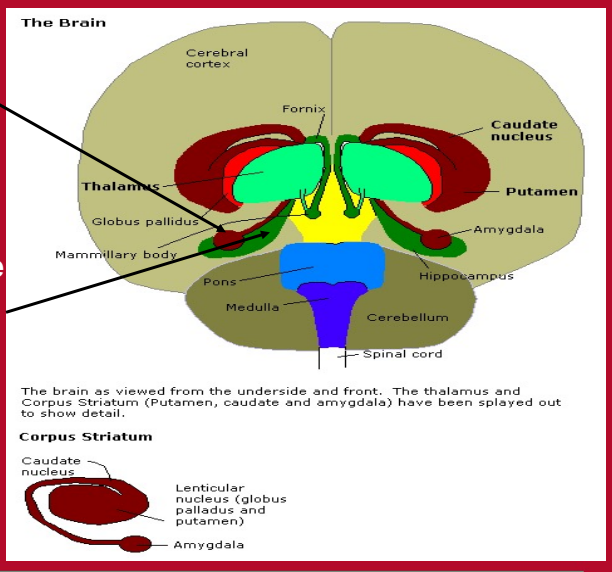


Locus Coeruleus (LC) source of NE which has extensive projections throughout the brain and can trigger the HPA axis (Aston-Jones, et al., 1994).

The Seahorse and the Almond

Amygdala *turns up* the HPA axis and sympathetic NS

Hippocampus *turns down* the HPA but may get saturated with too much cortisol and the thermostat can break



Cytokines

- Proteins released by immune cells that act on target cells to regulate immunity
  - Proinflammatory (IL-1, IL-6, TNFά) *coordinates* inflammatory responses
  - Anti-inflammatory (IL-10) *controls* proinflammatory responses.

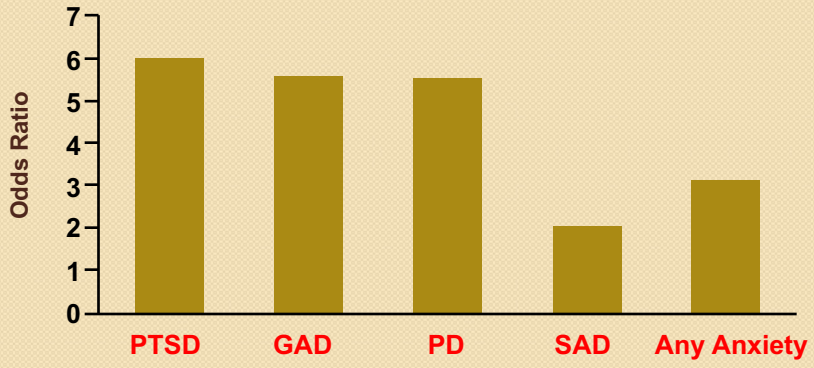
Hypocortisol vs. Hypercortisol Activity

- Chronic stress (especially uncontrollable) alters the cortisol system
- Early on there can be *higher* cortisol
  - Can lead to agitated depression
  - Kills white blood cells
  - Metabolic syndrome
- More distant traumas may result in an inadequate cortisol response
  - Autoimmune disease
  - Inflammation
  - depression

Dysregulation of the HPA axis

- Adrenaline and NE increases PICs
- PICs increase HPA axis
- Excessive CRH and low ATCH results in:
  - Low cortisol= high PICs
  - High PICs increase depression
    - Suicide victims—higher IL-6, TNFά and lower IL-2

Risk of Suicide Attempts Among Patients with Anxiety Disorders

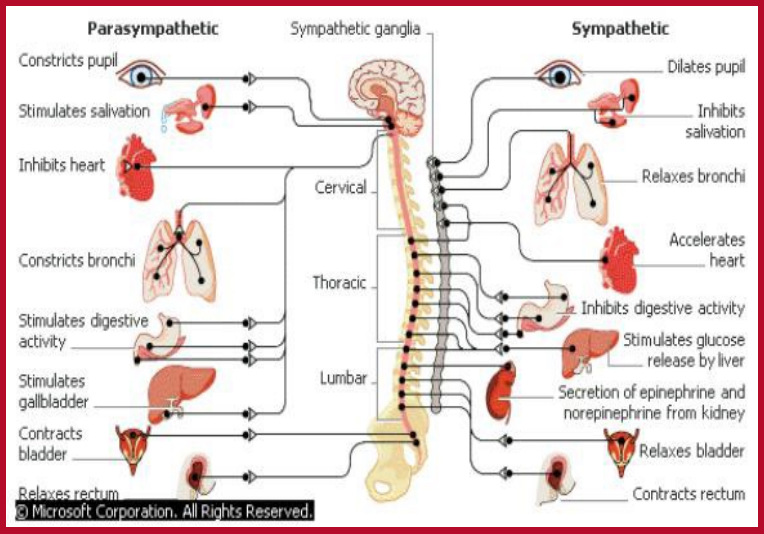


Kessler et al. Arch Gen Psychiatry. 1999;56:617

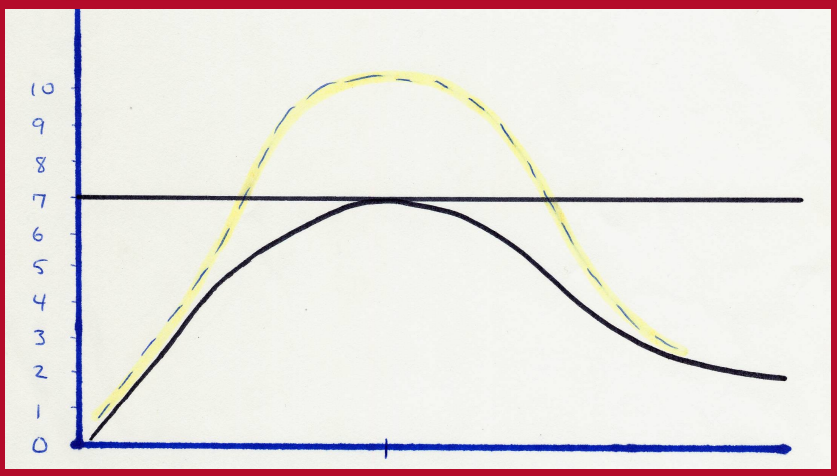
Physiology of GAD

- Less parasympathetic more sympathetic-- reduced vagal tone
- Bed nucleus of the stria terminalis (BNST)
  - –Free-floating anxiety
- Amygdala—an intolerance for ambiguity
  - – Anxious individuals select more threatening interpretations of ambiguous stimuli (e.g., Mathews & Mackintosh, 2000)

Balancing the ANS



Abnormal Respiration



Symptoms: Shortness of breath, smothering

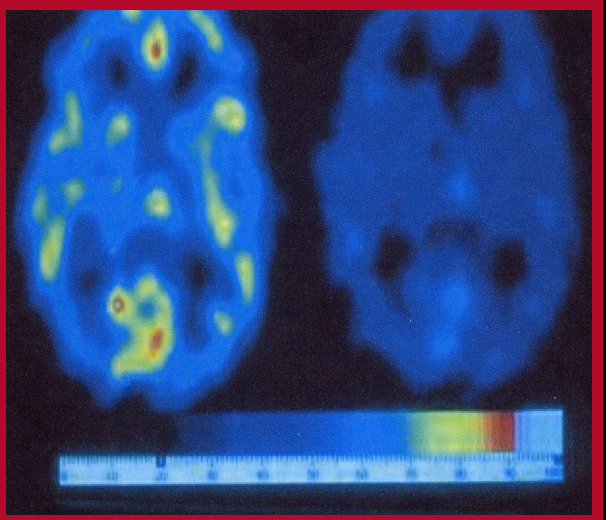
Hyperventilation 1 ½ minutes
Vaso-constriction: too little CO2

↑ Oxygen

↓↓ CO2

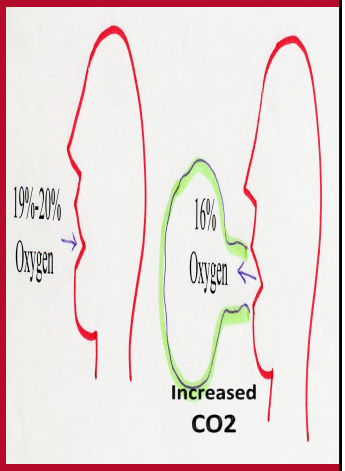
respiratory alkalosis

causes vasoconstriction in the brain



Breathing and Over-Breathing

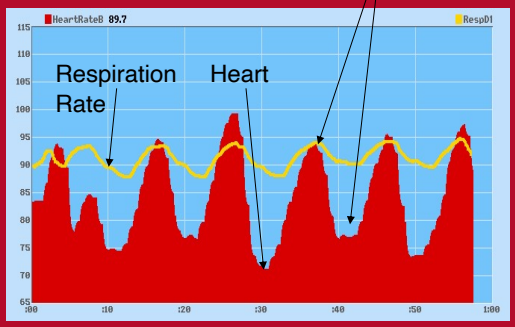
- Most people breathe 9 to 16 breaths per minute. Panic attacks - 27 breaths
- Over-breathing pulls in too much oxygen forces down the carbon dioxide level in the blood stream.
- Carbon dioxide helps maintain the critical acid base (pH) level in blood. Lower pH level causes nerve cells become more excitable and people associate the feelings with a panic attack.



Variability is healthy

Notice how heart rate increases with inhale. Heart rate decreases with exhale. This pattern shows high vagal tone (high PSNS activity) and a high amount of heart rate variability.

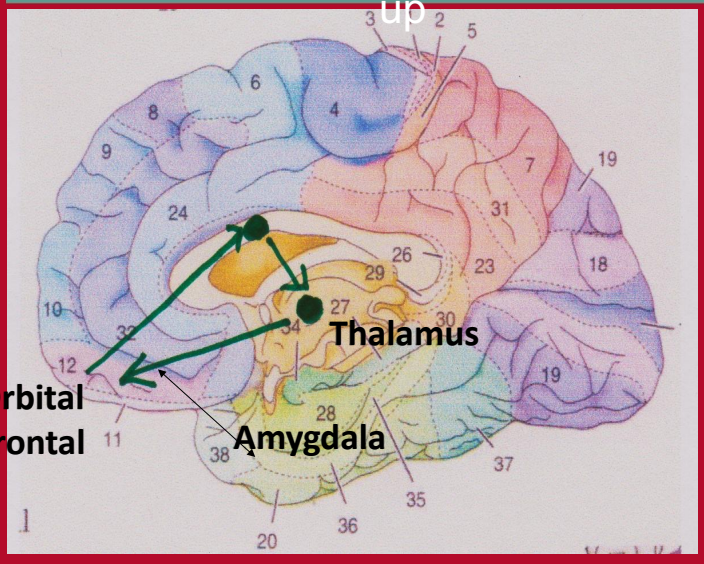
Peak/valley differences = vagal tone *when respiration is in normal range*



Activating the PNS

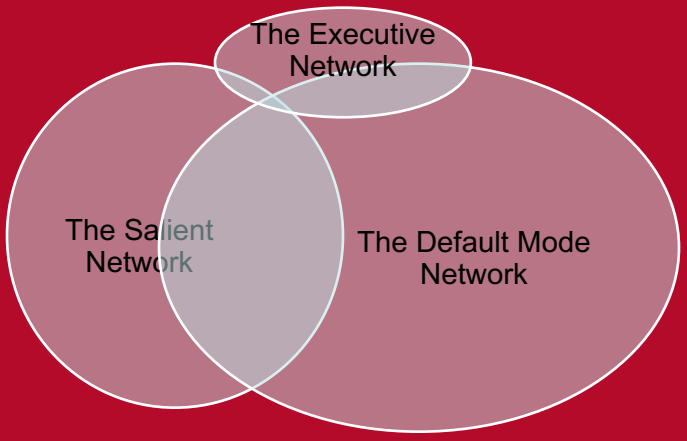
- Diaphragmatic Breathing
- Stretching
- Yoga
- Meditation
- Cuddling
- Orgasm
- Pulling the Kegel

Worry Loop attempts dampen autonomic arousal only to crank it back up

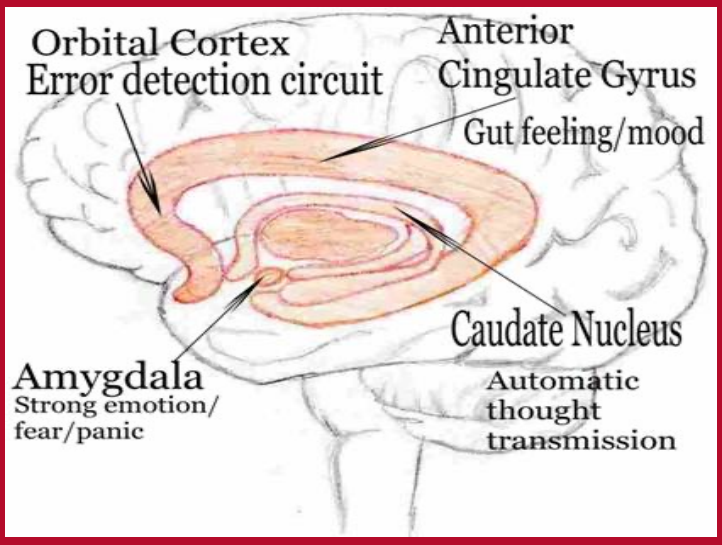


Worry as Cognitive Avoidance

- **Excessive DMN ruminations with little Executive Network**



Interrupting the Worry Loop



Challenging Feared Outcomes and Gaining Perspective

- **Worse possibility?—exaggerate it**
  - **Re-Attribution (it's just my body)**
- **Worse realistic possibility?**
  - **So what if….**
- **Physiological Symptoms (e.g. this is not dangerous)**
- **Temporal perspective**
  - **When was the last time I died from this?**

CBT vs. Metacognitive Models

(ACT, DBT, MBCBT, etc.)

CBT	MC Models
Rationale=control	Rationale=relinquish control
Cognitive restructuring	Thought Diffusion
Breathing retraining	Observe & accept
Interoceptive exposure to lessen fear & avoidance	Interoceptive exposure with acceptance of internal cues
Situational exposure to lessen fear fear and avoidance	Situational exposure to achieve life values and goals

Client Education

- The next time a well-meaning person tries to reassure you that there is certainty in life, say:
- "Thanks, but I'm learning how to appreciate uncertainty and the shades of grey."

REAL not GAD

"R" is for relaxation, including deep breathing, stretching, self hypnosis, mediation, and prayer to activate your parasympathetic nervous system and increase vagal tone.

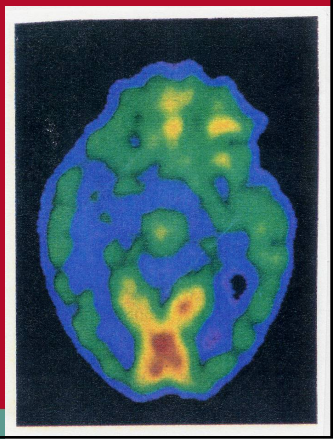
"E" is for exposure such as in scheduling an hour of worry time, allowing focused exposure to all your worries, and giving your higher brain a chance to work on developing the capability of dealing with the ambiguities inherent to life.

"A" is for acceptance. Since there is no ultimate certainty with much of life, acceptance of uncertainties allows worries to fade into the texture of normal living.

"L" is for labeling. When you have an anxious thought you can label it as just "an anxious thought," thereby detaching from the feeling of anxiety.

Neurodynamics of Anxiety

- Two routes to the amygdala, the fast and slow
- Right frontal bias in general for anxiety disorders
- Under-activation of the left frontal lobes and in Broca's area explains why some people feel "speechless" when they're scared (Rauch et al., 1997).



Slow Track—Allostasis

- *Automatic thoughts*—fast track impulse—interrupt with curiosity and time
- *Assumptions*—from pessimism to incremental optimism
  - "I'm working on it and can tolerate distress"
- *Core beliefs*—existential self descriptor
  - "I'm a survivor."

- Global/Passive (R-PFC) vs. Detail/Action (L-PFC)

Shifting Perspective to Speed Up the Slow Track

- Labeling thoughts—"That is an anxiety provoking thought" vs. "This makes me anxious!"—R-vlPFC
- Externalizing—"What would another person in this situation say and how is s/he right?"
- Temporal Distance—"How will I sensibly view this situation in six months?"
- Humor—"What is funny about this?"
- Wisdom—"How can I grow from this?"

Avoidance: the Polarizer

- **Over-Sensitizing the Amygdala**
  - **Forms of Avoidance**
    - **»Escape behaviors**
    - **»Avoidant behaviors**
    - **»Procrastinating**
    - **»Safety behaviors**

Avoidance

- **Interpersonal trauma vs. natural disasters, etc…**
  "mistrust schemas"
- **Do not reach out to others**
  for comfort (withdrawal)

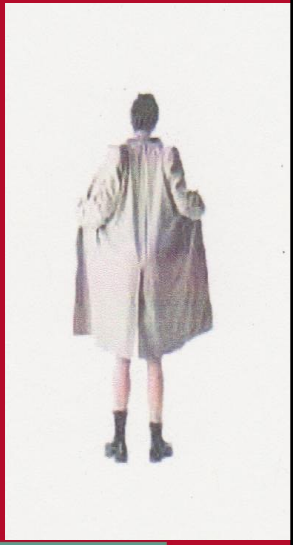
Why avoidance is hard to resist

- **It works to reduce fear over the short term**
- **The more you avoid the harder it is to resist repeating --they become habits**
- **There is a superficial logic to avoidance, --- "Why wouldn't I avoid something that makes me anxious?"**
- **You get some secondary gain from it like extra care because people around you feel sympathy**

Deceptively Simple but so Complex Exposure Techniques

Beta- endorphin is co-released along with ACTH but is momentarily blocked by ACTH at the common receptor sites.

The therapeutic effects from exposure in part result from beta-endorphin anxiolytic effects 20 minutes after the exposure



Critical Aspects of Exposure

1. To maximize violation of expectancies
2. To multiple feared conditioned stimuli individually and in concert
3. Occasionally reinforcing a CS with an UCS
4. Removal of safety signals or safety behaviors
5. Stimulus variability
6. Retrieval skills in other contexts that are transferable for real life situations
7. Multiple contexts

Exercise and Anxiety

- **Since fight/flight is meant for action exercise provides the method to feelings – take action.**
- **Exercise:**
  - **Reduces muscle tension**
  - **Builds brain resources (neuroplasticity and neurogenesis)**
  - **Increases GABA and serotonin**
  - **Interoceptive exposure**
  - **Improves resilience – self-mastery**

REAL not GAD

"R" is for relaxation, including deep breathing, stretching, self hypnosis, mediation, and prayer to activate your parasympathetic nervous system and increase vagal tone.

"E" is for exposure such as in scheduling an hour of worry time, allowing focused exposure to all your worries, and giving your higher brain a chance to work on developing the capability of dealing with the ambiguities inherent to life.

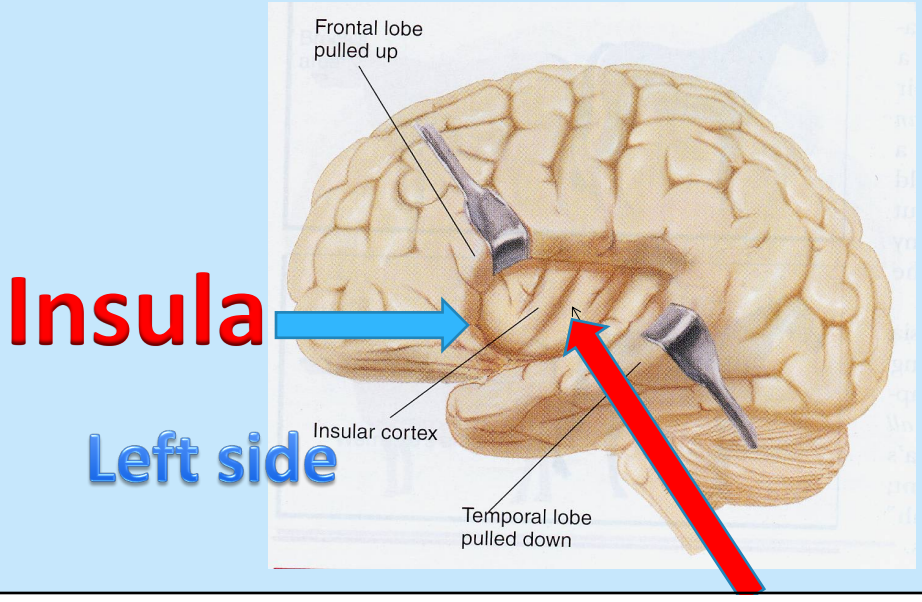
"A" is for acceptance. Since there is no ultimate certainty with much of life, acceptance of uncertainties allows worries to fade into the texture of normal living.

"L" is for labeling. When you have an anxious thought you can label it as just "an anxious thought," thereby detaching from the feeling of anxiety.

Client Education

- Sensations from your own body should not be the cause for alarm.
- Don't let your body be the boy who cried wolf.

Interoceptive Feedback



Client Education

- Do you have shortness of breath, rapid heartbeat, sweating, headaches, or nausea?
- Each one of these are normal body sensations. It's when you overreact to them you may tumble into a panic attack.
- Befriend your own body sensations.

Interoceptive Exposure +

- **Swallowing quickly--- to cause a lump in the throat**
- **Tensing the body--- leading to chest constriction**
- **Standing up quickly from lying on the floor---to cause dizziness.**
- **Staring at one spot---to increase the feeling of being trapped**

Interoceptive Exposure +

- **There are a variety of interoceptive exercises including:**
  - **–Running in place--- to increase heart rate and hyperventilation**
  - **–Holding your breath--- to simulate sensations of suffocation**
  - **–Spinning--- leading to dizziness**
  - **–Hyperventilation or breathing through a straw---leading to light-headedness**

BBT and Panic Disorder

- Desensitizing the Amygdala—Avoiding avoidance
- Interceptive exposure exercises—Embracing body sensations
- Speeding up the slow track—Getting the L-PFC and L-Anterior Insula cortex involved

BEAT Panic

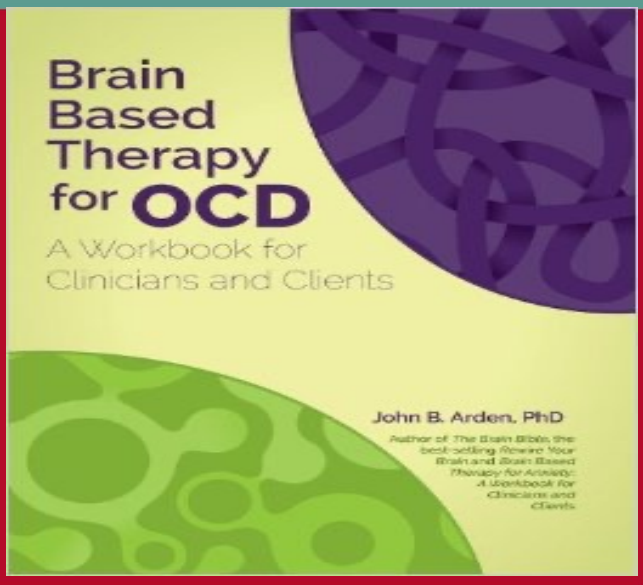
"B" is for body. When you feel your heart race or breathe too fast just ride it out. Say, "I can befriend my own body!

"E" is for exposure. Through interceptive exposure exercises you can regain tolerance to body sensations. Say, "this is not a heart attack but just my own body sensations that I've felt many times before."

"A" is for the amygdala. With its fast and slow tracks. "I can learn to slow down my fast track and speed up my slow track."

"T" is for thinking. To speed up your slow track, remind yourself that what you think is happening has a dramatic effect on what you feel is happening.

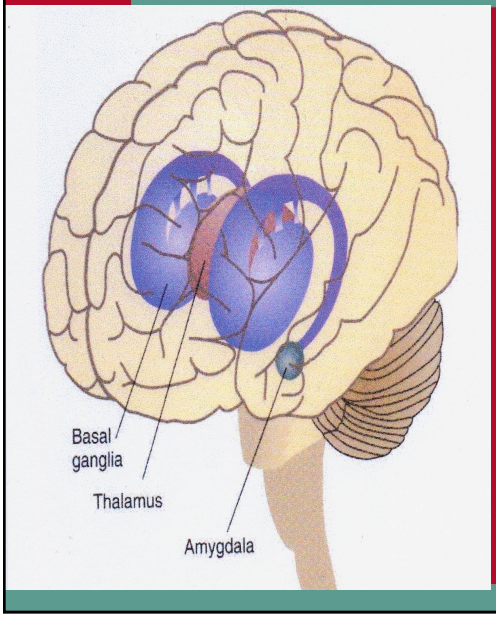
OCD



Structures with Roles in OCD

- Striatum-- gate is left open for habit
  - caudate part serves as a gate for thoughts and emotions
  - putamen part serves as the gate movement
- Anterior Cingulate Cortex– error detection
- Malfunctions in the action of Glutamate
- Orbital frontal cortex-- gets flooded with information and generates error messages:
  - "Better do something!" Then you engage in compulsive behaviors to "make it right."

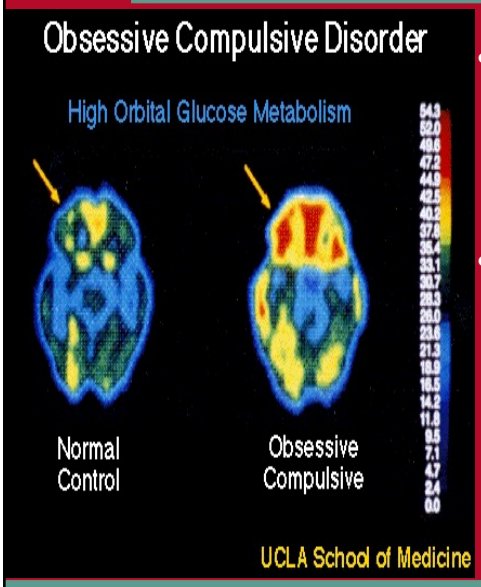
The Habit Brain and OCD



Cues: e.g. an emotional state, stress, fatigue, addictive cue

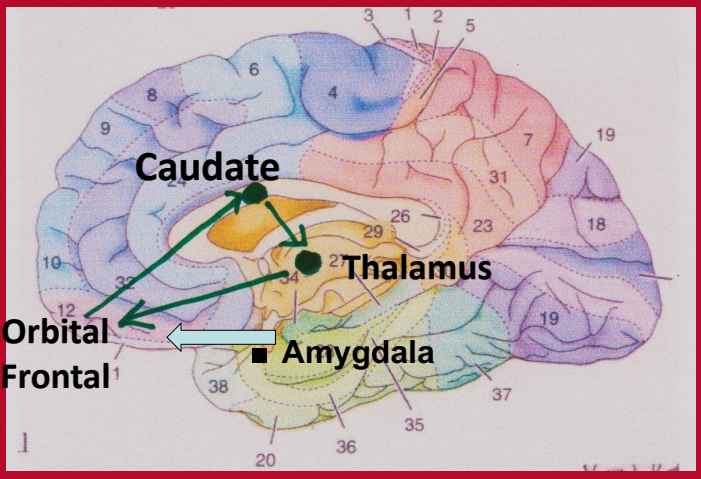
Ignites a Behavioral routine: previously associated with reward or relief (e.g. counting, food, sorting, bite finger nails, hair pulling, tics…)

Flooded OFC in OCD



- OFC flooded with nuisance info and tries to make sense of it
- Given its inhibitory role pts try to use it to "stop that thinking!" But that results in a paradox—"try not to think about pink elephants"

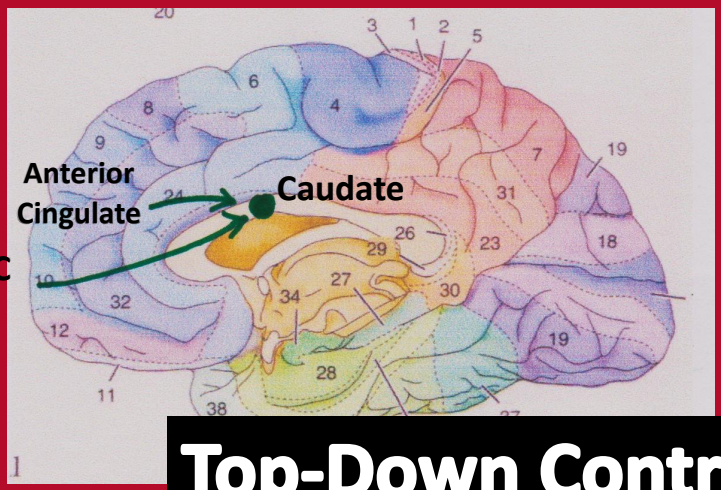
OCD: failure of top down control



Pulling Out of the OCD Circuit

- Prefrontal Cortex (DLPFC and OFC)
  - DLPFC—Breaks out of auto pilot and decides "time to do something new"
  - With help the OFC can now learn to inhibit the amygdala and the fear network
- Anterior Cingulate Cortex—error correction
- Hippocampus-- provides context and what is worthy of fear
  - Remembers that you engaged in a compulsive behavior that never seems to solve the problem.

Strengthened Pathways and Improved Gating



Top-Down Control

ORDER

- **O—Observe--the OCD thoughts and behaviors.**
  - **–DLPFC activation.**
  - **–Attention key first step for learning something new.**
  - **–Break out of autopilot**

Client Education

- The first step in breaking the OCD habit is to observe what you are thinking and about to do, as if you are watching someone else. This will shift you out of autopilot and interrupt your OCD habit.
- For example, when you ride a bicycle as soon as you observe how you are peddling or keeping your balance, you start to wobble as if to cast doubt upon it.

ORDER

- **R—Remind--By reminding that obsessing itself is the problem, not what is being obsessed about:**
  - **call it a symptom of the brain's OCD habit and nothing more to be concerned about.**
  - **"This is just OCD.**

Client Education

- Remind yourself that obsessive thoughts and compulsive behaviors are simply your OCD habit. This helps to shift from the feeling that you need to do something to the knowledge that you don't.

ORDER

- **D—Doing--By doing something different than the usual OCD compulsive behaviors establishes a new practical habit. The new behavior draws attention and interest to expand upon:**
  - **–The new habit builds a circuits of practical and enjoyable behaviors through neuroplasticity.**

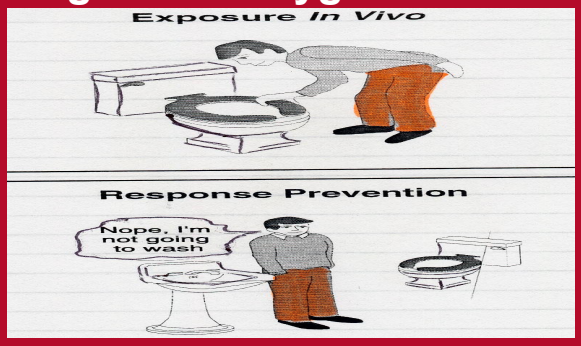
Client Education

- Every time you feel the need to do your old OCD habit do the new habit instead. Make the new on practical and enjoyable.
- By doing the new habit it branches out into other positive activities related to it.

ORDER

E—Exposure--to the situation or place that had been intolerable. Exposure allows habituation.

–Taming of the amygdala



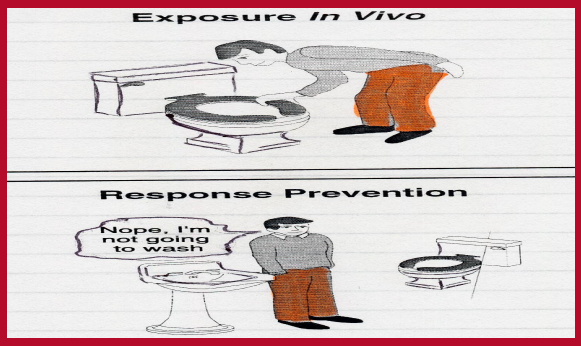
Client Education

- When you do not engage in your old compulsive behavior, while you are exposing yourself to the situation. The discomfort will eventually pass.

ORDER

R—Response Prevention--Refraining from compulsive behaviors that contribute only to momentarily "feeling better."

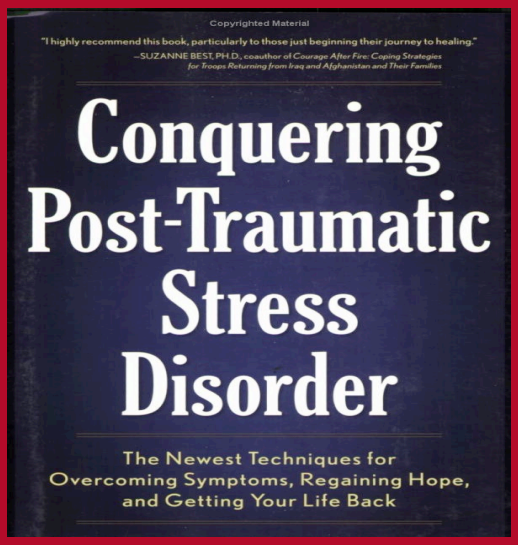
This step strengthens the inhibitory circuits



Client Education

- When you prevent yourself from engaging in your compulsive ritual note that nothing bad seems to happen other than feeling uncomfortable.
- This strengthens the top down brain networks that shut off OCD.

Post Traumatic Stress Disorder



Chronic, severe, inescapable

- War Zones
- Rape
- Child abuse
- Elder abuse
- Domestic violence
- POWs and refugees

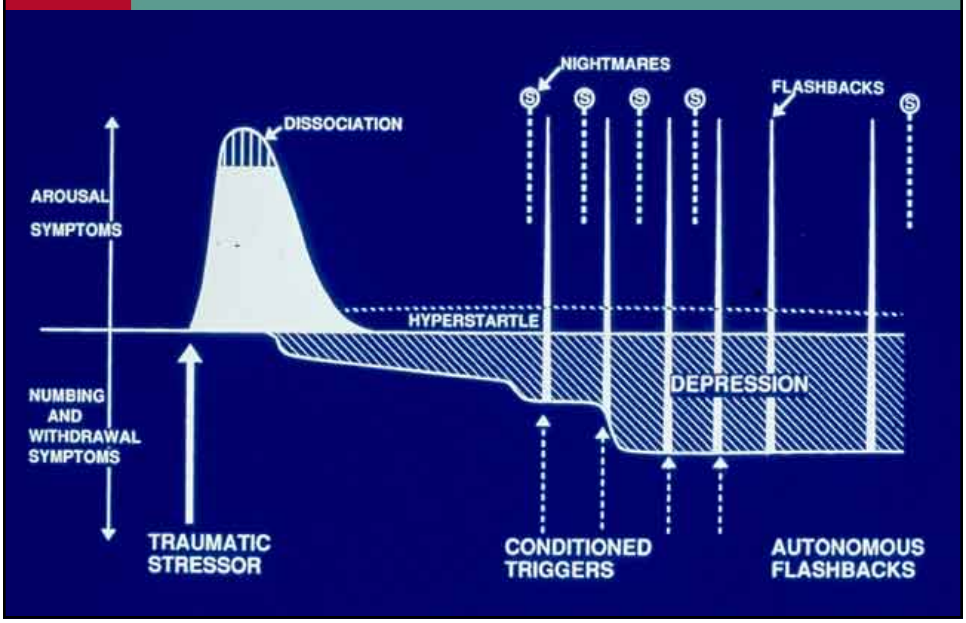
WHO estimates the prevalence of PTSD

- In Ukraine at approximately 25%.
- **In Gaza:** 63.40%
- Upward of 40% of refugees, and as many as 90% of refugee children

Risk Factors for PTSD

- Greater distress before/after the trauma
- Poverty and low socioeconomic status
- Previous or current psychological disorder and poor affect regulation
- Family discord and/or insecure attachment
- Cognitive disengagement at the time of the trauma and dissociation involving depersonalization and de-realization
  - Especially with early and repeated trauma

Time Sequence



Phylogenetic Responses to Stress

- 1) Trigger the social engagement system—the myelinated vagus
- 2) Fight or flight—SNS and HPA axis arousal
- 3) Immobilization—freeze, collapse, and feigned death:
  - 2 stages
    - Freezing in terror
    - Paralyzed—shut down—total submission, trancelike, dissociation

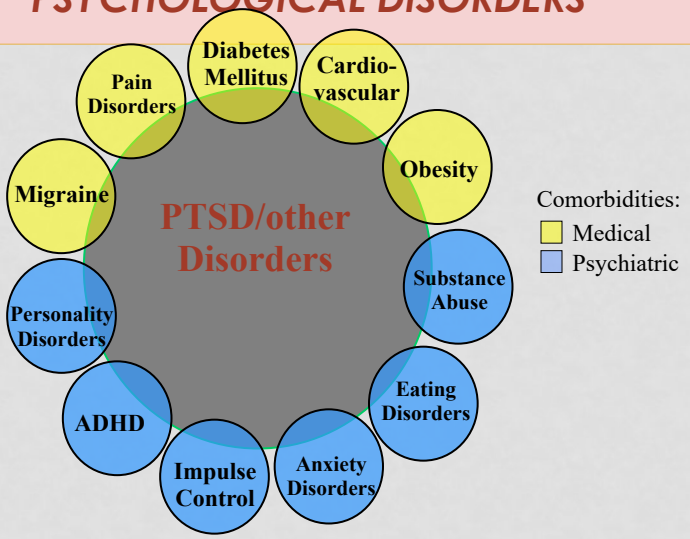
PTSD Neurodynamic Aspects

- ↑ amygdala—general false positives for threat
- ↓ mPFC especially the ACC (reduced neurointegration and cortical volumes) (De Bellis, et. al., 2000) (inadequate top down inhibition of the amygdala)
- ↓ hippocampus (cortisol, excitotoxity, blocking of neurogenesis)

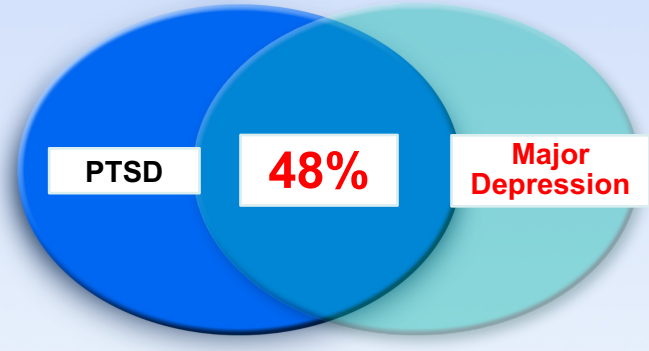
Most Common Acute Post-Traumatic Stress Response

- **Depression**
- **Anxiety Disorders**
- **Substance use / abuse**
- **Acute Stress (ASD) only later PTSD**
- **Adjustment disorders**
- **Persistent complex bereavement**

THE RULE NOT THE EXCEPTION
THE MULTIDIMENSIONALITY OF NEURO-PSYCHOLOGICAL DISORDERS



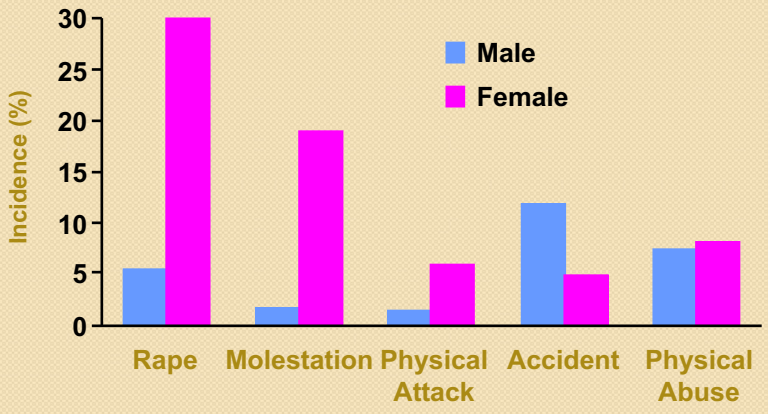
Common Occurrence of PTSD and Depression



A Big Problem:
Reluctance to tell or seek out help

- **Sexual assaults**
- **Bullying** (kids and adults)
- **Work-place violence**
- **Domestic violence**

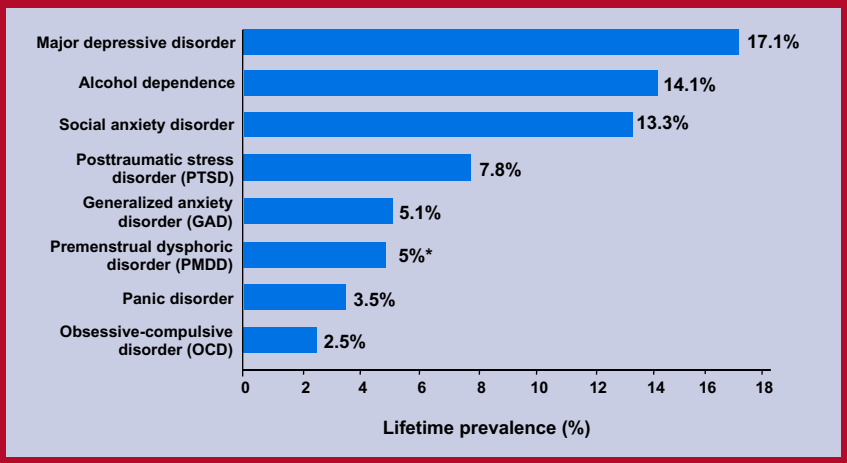
Non-Combat-Related Trauma Associated with PTSD



Kessler et al. Arch Gen Psychiatry. 1995;52:1048

Courtesy of: David V. Sheehan, M.D., M.B.A.

Lifetime Prevalence of Common Psychological Disorders



Predicting PTSD

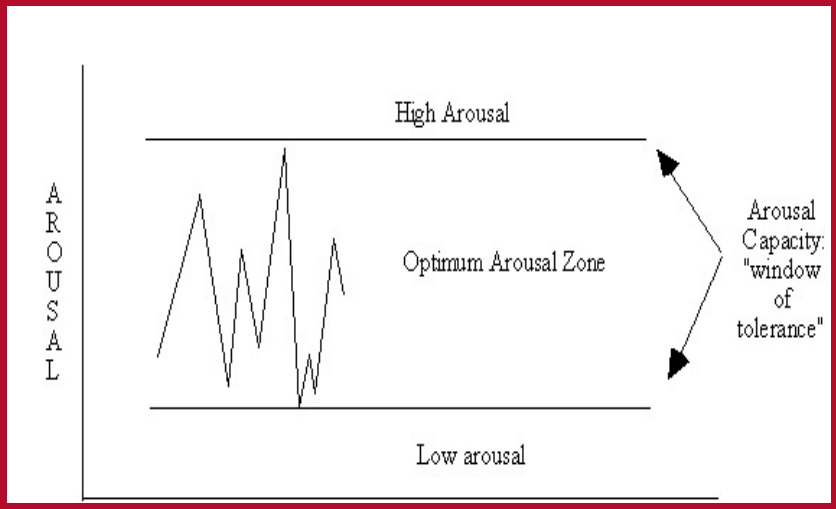
Dissociation or amnesia at the time of traumatic event

Panic attack: first 24 hours

70% greater risk

The Severity of the Traumatic Event is not predictive of outcome

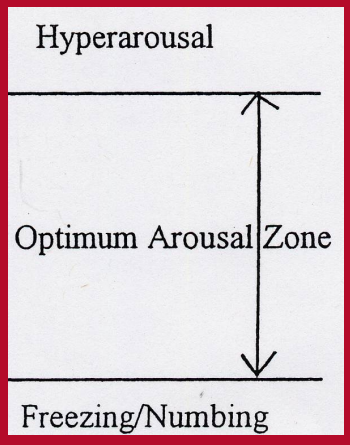
Window of Tolerance



Working the "Therapeutic Window"

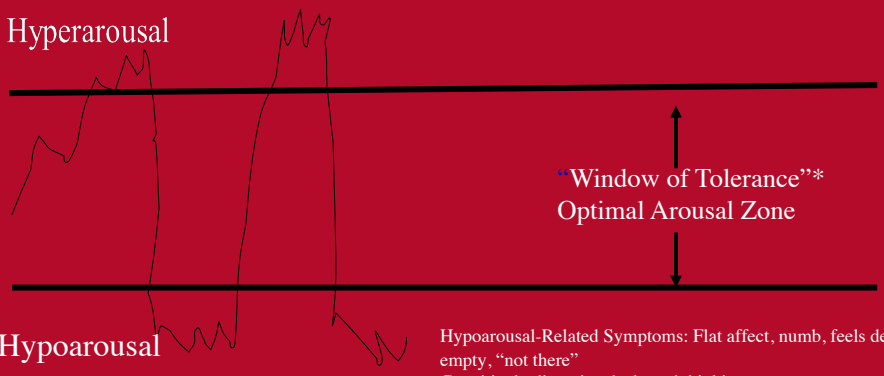
Over-Shoot

Under-Shoot



Trauma Responses are Autonomically Driven

Hyperarousal-Related Symptoms:
High activation resulting in impulsivity, risk-taking, poor judgment
Chronic hypervigilance, post-traumatic paranoia, chronic dread
Intrusive emotions and images, flashbacks, nightmares, racing thoughts
Obsessive thoughts and behavior, cognitive schemas focused on worthlessness and dread



Hypoarousal-Related Symptoms: Flat affect, numb, feels dead or empty, "not there"
Cognitively dissociated, slowed thinking process
Cognitive schemas focused on hopelessness

Hippocampal atrophy

Client Education

- Though your memory may be temporarily impaired, you can revitalize these areas of your brain by aerobic exercise followed by learning and goal oriented behaviors.

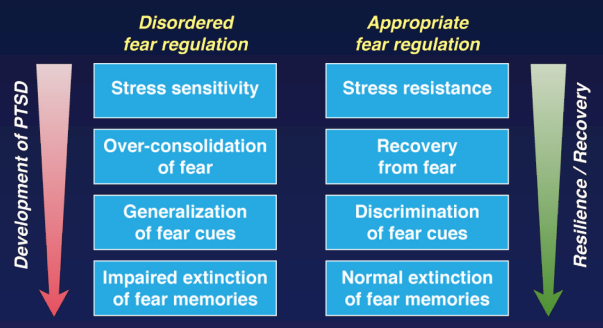
Possible Neurochemical Vulnerability of PTSD

- ↑ NE post trauma may predict PTSD (Yehuda, et. al., 1998)
- ↑ cortisol in the evening not in the morning
- ↑ proinflammatory cytokines post trauma
  - The secretion of IL-6 inflammatory cytokines can be triggered by B-adrenergic receptors with ↑ NE
  - Inflammation can occur post trauma via CRH/substance P-histamine axis with ↑ cortisol and IL-6 (Elenkov, et. al., 2005)

Client Education

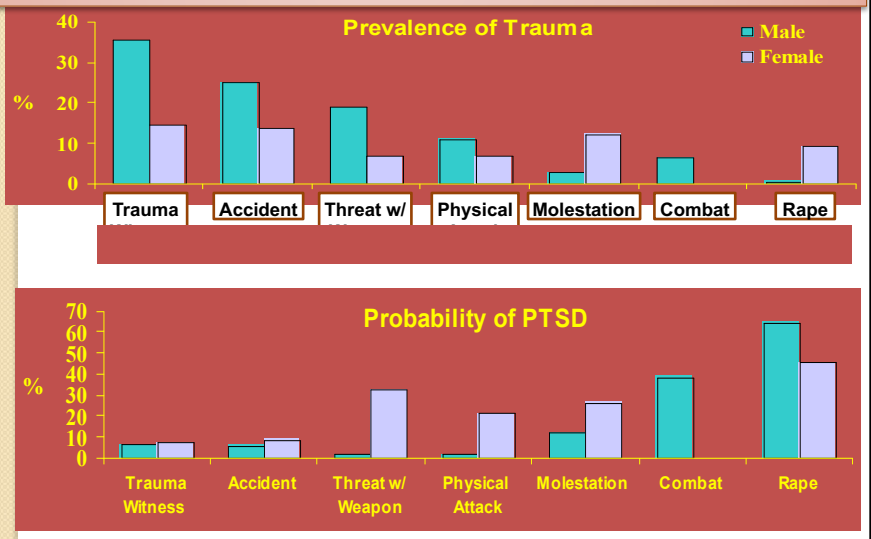
- It's common to feel like being alone after a traumatic event. But, isolating now will make you worse and feel even more alone.
- Parts of your brain activate when you are with people which helps you buffer anxiety and lift depression.

Disordered Fear Regulation in PTSD



From: Mahan AL, Ressler KJ. Trends Neurosci. 2012, 35:24-35.

Prevalence of Trauma and Probability of PTSD



Kessler. *J Clin Psychiatry*. 2000;61(suppl 5):4.
Kessler et al. *Arch Gen Psychiatry*. 1995;52:1048.

Avoidance

The major factor in perpetuating PTSD and contributing to a more chronic course

Avoiding specific trauma triggers; Reminders:

- People
- Situations
- Conversations
- Media
- Medical Treatment

Suicidality and PTSD

- *PTSD patients are 6 times more likely to attempt suicide than the general population*
- *PTSD has higher risk of increased number of suicide attempts than all other anxiety disorders*

Amygdala-Level Processing

Rapid, Crude, Generalized
Many false alarms
Non-Responsive to new "Data"
Outside awareness & Automatic
Beneath the radar of consciousness

Watch for Implicit Memory of Trauma

- Notice that….
- Wow! What just happened
- Did you feel the change in….
- Noting somatic communication
  - "The body knows the score"
- Gentle exposure to changing somatic
  - sensory motor experience

Research on PTSD Treatments

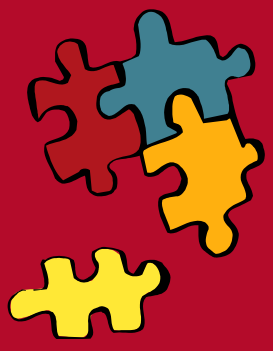
- **Institute of Medicine (IOM) 2007 Review**
  - **Thorough review of psychotherapy research for PTSD (requested by the VA)**
- **Treatments not found to have clear empirical support:**
  - **EMDR, group therapy, hypnotherapy, eclectic, CBT alone….**
- **Exceptions: review found strong efficacy of exposure:**
  - **Prolonged Exposure (PE)**
  - **Cognitive Processing Therapy (CPT)**

Exposure

- Imaginal exposure (trauma memory)
  - Exposes client to memory of the trauma in structured, controlled way
  - Trauma exposure helps client in two ways:
    - Helps reduce anxiety associated with trauma memory (via extinction of conditioned fear)
    - Helps client organize memory into coherent narrative (calms overactive amygdala)
  - Generally need minimum of 12 sessions (CBT, PE, CPT)
    - CBT approach starts with psychoeducation, anxiety management, and coping skills
    - Minimum 4-6 imaginal exposure sessions (temp. increase of anxiety and re-experiencing symptoms)
    - Cognitive processing of trauma memory & associated meaning (beliefs)
- Situational exposure (CBT & PE)
  - targets avoidance of trauma-related situations (and agoraphobic avoidance)
- Interoceptive exposure
  - Targets "fear of fear" or somatic phobia (treatment for panic disorder)

Impaired Information Processing in Post-Traumatic Stress Disorder

Dissociation at time of trauma (encoding)
Fragmented, "jigsaw" memories
images, emotions, bodily sensations, cognitions……
dis-integrated



Watch for Implicit Memory of Trauma

- Muscle tension
- Motor impulses
- Heart rate
- Facial expression
- Trembling
- Breathing rate
- Mood changes

Dual Processing Theory

- **Limitations of the "fear network" theory – doesn't account for implicit memory:**
  - **Verbally accessible memories (VAMs) on the conscious memory level. VAMs can be accessed in therapy through deliberate recall.**
  - **Situationally accessible memories (SAMs) non-conscious. SAMs are only accessible through exposure cues that activate the non-conscious network** (Brewin, Dalgleish, and Joseph, 1996).

The Explicit system

- Verbally accessible memory (VAM) system—the narrative—autobiographic
  - Can be deliberately retrieved (Brewin, 2005)
  - Cortex and hippocampus
  - Past, present, and future
  - Available to verbally communicate
  - Restricted by attention and arousal
- Traumatized people use the VAM system to evaluate the trauma
  - They ask themselves "could it have been prevented?"
  - "What are the consequences….the meaning?"

The Explicit system

- VAM system memories are accompanied by "secondary emotions" (not experienced at the time of the trauma)
  - Directed at the past—i.e. regret or anger about the risks taken
  - Often involves guilt or shame over perceived failure or not preventing the event
  - Thoughts about the future—i.e. sadness at the loss of cherished plans or hopeless at the thought of not finding fulfillment

The Implicit System

- Lower level perceptual processing—too briefly apprehended to be bounded together in consciousness memory required for VAMs
  - Sights
  - Sounds
  - Physiological sensations including changes in heart rates, temp, or pain

The Implicit System

- Primary emotions—fear, horror, helplessness
- Accounts for flashbacks that can be triggered involuntary by cues related to the trauma (sight/sounds etc.)
- Not structured by verbally coded memories—therefore more extensive
- The more drawn out the trauma, the greater the tendency to experience a range of sensations and emotion
- Difficult to access in therapy

Client Education

- Every time you go through this exposure exercise it will get easier.
- The higher parts of your brain, will rewire to put the brakes on the alarm button in the lower part of your brain.

Converting traumatic memories into meaning

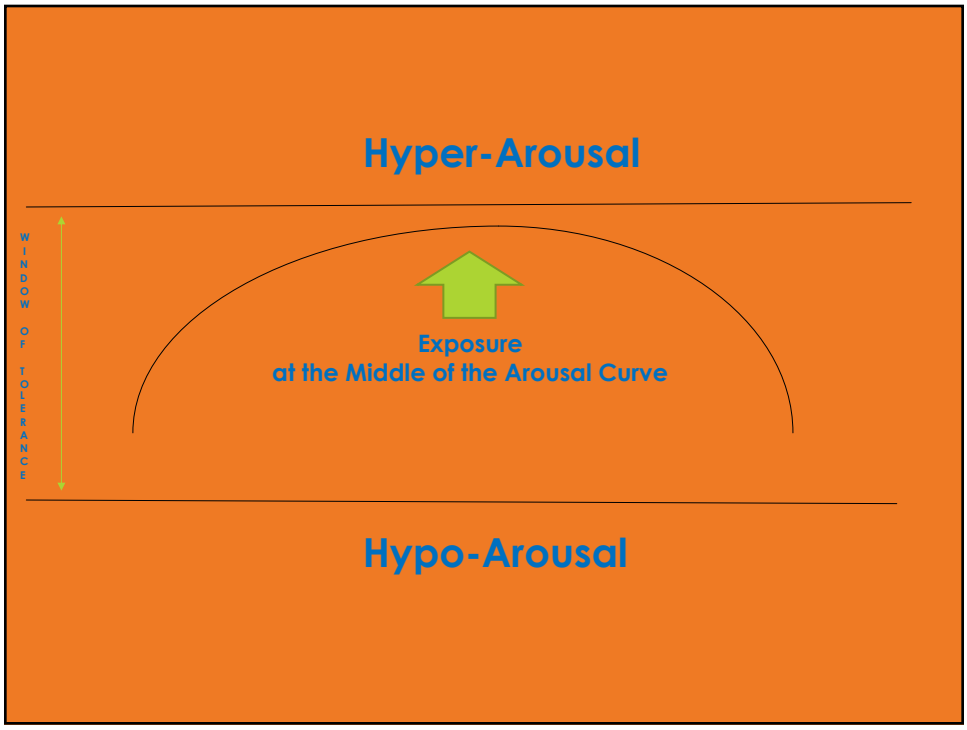
- Traumatic memories are fragmented and disorganized into “hotspots” which can spur flashbacks
- Hotspots occur where there is maximal functioning separation between SAMs and VAMs (i.e. less integration) (Brewin, 2005)
- They need to be integrated and converted into a coherent and an organized form to reduce the risk intrusions into flashbacks (Ehlers & Clark, 2000; Conway & Playdell-Pearch, 2000)

Client Education

- Step-by-step. I am going to help you expose yourself to the cues that trigger the flashbacks so that you can bring them under control.

Explicit and Implicit Integration

- The process needs to be repeated for:
  - Neuroplasticity—the inverted "U"
  - To neutralize the traumatizing quality of the SAM system
  - So that VAMs can compete with SAMs and integrate them
    - The new VAM system puts the SAM system in perspective



Client Education

- By getting your memory systems in sync, what had triggered flashbacks will fade away.
- Those flashbacks will lose their ever presence and be placed where they belong, in the past as you develop a meaningful future.

Continuum of Detachment

- **Traumatized people can experience:**
  - **Mild detachment or absorption: involving a breakdown in the ability to notice outside events and extending to an altered sense of self.**
  - **Moderate detachment: involving feelings of depersonalization and derealization. The person sees himself as if from afar as an observer.**
  - **Extreme detachment: involving a state of unresponsiveness. The person can act catatonic and have no sense of self or time.** (Allen, 2001)

Affective Regulation of Condition Emotional Response (CERS)

- The skill of perceiving, labeling, and accepting emotion
- Identifying and modifying thoughts that exacerbate emotions
- Practical action—act in concert with values
- Insight into why/how the emotions are coming up
- Titrate the exposure within the window of tolerance in the middle of the inverse "U"
  - Highest affect in the middle of the session then calm at the intensity curve at the end

Exposure

- An activity that provokes or triggers memories of the traumatic event:
  - Repeated or extended (prolonged) to objectively harmless but feared stimulus
  - For at least 20 minutes allows enough time to habituate and enough time to recoup with sufficient support
  - Also allows for the release of BE release
  - Start low—go slow

Exposure

Goal—for traumatic memories to lose their power

- a disparity between what a client is feeling (i.e. fear) and the objective reality that there is nothing to fear in the current environment
- Counterconditioning—the presence of positive phenomena that are antithetical to physical or psychological danger. "Cells that fire out of link lose their link." LTD

Client Education

- Delay tension reduction behaviors
  - "Urge surfing"-ride it out, they are only temporary
  - Hold off long enough to defuse the power
  - The upsetting feeling will eventually become tolerable
  - Don't try to change the feeling but change your relationship to it.

Activation

- Conditioned Emotional Responses (CERs e.g. fear, sadness, or horror)
- CERs are critical to trauma processing to extinguish emotional-cognitive associations to a given trauma memory must be:
  - Activated
  - Not reinforced
  - Counter-conditioned

Dissociative Disorders

- Depersonalization/Derealization disorders + persistent or reoccurring experiences of unreality from mind, self, body, and/or surroundings
- Dissociative amnesia – psychogenic inability to recall autobiographical info. Specifier—dissociative
- Dissociative identity disorder (DID)—2 or more personalities with reoccurring memory "gaps" (episodes of amnesia can include possession)

Dissociative Dynamics

- Because the development of a coherent and durable sense of self thrives on safety and positive attachment:
  - When interpersonal environment is dangerous hypervigilance and attention is drawn outward away from the development of a coherent self-system
  - Attention inward could be punished
  - Internal representations could be fragmented

"Identity Training" from Dissociation

- Therapy entails helping the client build a coherent and positive model of the self by facilitating self-exploration and self-reference
  - Helping the client identify, label, accept feelings, and needs
  - Development of a coherent internal life (DMN) and self-determination (EN)

"Identity training" from Dissociation

- Because relational schemas (internal working model—attachment styles) are framed before explicit memory, their implicit nature are "triggered" by situations & feelings states that need reconditioning—activation—reconsolidation
  - Emergent "relational feedback" do not contain the contextual representation of the past (i.e. abuse)
  - "corrective emotional experience" (psychodynamic)

PTSD Treatment

- Increased size and activity of DLPFC
- Increased size and activity of the hippocampus
- Decreased activity of the amygdala
- SNS activity within the window of tolerence
- Decreased PICs
- Recalibrated HPA

Culture, DMN, and PTSD

- **People with high neural variability between the DMN, SN, and EN tend to enjoy wellbeing.**
- **A Collectivist orientation in DMN tend toward social connectiveness**
- **However, with PTSD diminished activity in the vmPFC (part of the DMN)**
- **The vmPFC is critical for affect regulation**
- **Self-identity undermined by emotional dysregulation**
- **Healthy DMN is bolstered by social connections**

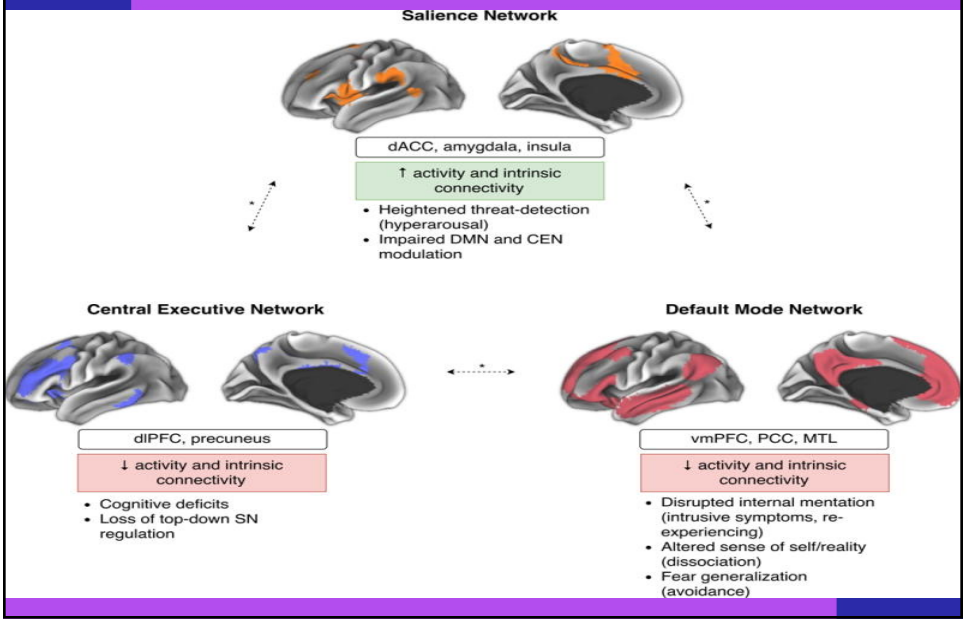
The DMN Narrative

- Connects with autobiographical memory, reflecting on the past and future, producing cohesive self-organization.
- Provides meaning—ongoing narrative, commentary of experience
- Reflects on what others are thinking—TOM
- From me to we—to fit in
- What we think about relates to predicting how best to change or stay the same

Culture and the DMN

- People with high neural variability between the DMN, SN, and EN tend to enjoy wellbeing
  - A person with collectivist orientation is quite socially oriented in their DMN
    - With PTSD diminished activity in the vmPFC
    - The vmPFC is critical for affect regulation
  - Self-identity undermined by emotional dysregulation

States of mind in conflict



Orienting Response and Somatic Stimulation

- First identified by Pavlov in 1927
  - *Shto takoe?* (Что такое? or *What is it?)*
  - Reorienting of attention -- triggered automatically when a sudden movement grabs attention or intentionally when you chose to look at an object
  - The reorienting of attention requires you to release your focus on one location so that it can shift to a new location
- Somatic stimulation of the orienting response (i.e. via EMDR, EFT, acupressure etc.) involve involves:
  - The orienting response (Sokolov, 1990)
  - facilitate cortical integration of memories

Orienting Response

"I have long thought that, if there is any analogy between psychic and physical processes, the orienting system of the brain must lie subcortically on the brainstem," (Jung, 1958).

- **Superior colliculus--**sensorimotor structure that is specialized for detecting, localizing, and orienting toward environmental events **–the "where"**
- **Periaqueductal gray (PAG)--** integrated behavioral responses to internal (e.g., pain) or external (e.g., threat) stressors—the "what"
- **Locus coeruleus**--modulating pain and stress, releasing norepinephrine—the "shock"

Orienting Response

- **Amygdala—relevance, threat detector**
- **ATP—circulation of blood and energy**
- **Norepinephrine, dopamine, acetylcholine**
- **Hippocampus—context**
- **PFC—conscious attention**

Orienting Prediction Error

- Surprise activates the dACC and amygdala which increases vigilance
- When stimulus is surprising and novel there is a causal link between prediction errors, dopamine neurons, and learning.
- The superior colliculus, positioned next to the thalamus, and connection to the amygdala
- Shifts in attention activates the PFC, hippocampus, and dopamine networks

Priming the DMN

- **New narratives practiced in sessions between sessions**
- **Therapy anticipates the challenges—the different contexts that new narratives must be practiced**
- **Narratives maximized social connectiveness and post-traumatic growth**

Orienting and Recoding

- A stimulus that prompts a person to notice what happens next primes PFC activity.
- Coding in novelty, an unexpected somatic sensation, integrates PFC, anterior cingular cortex, hippocampus, and basal ganglia circuits by moderate bursts of dopamine,
  - orienting serves as a sort of a kickstart to the connectivity between the executive and the salience networks

Shifts in attention and asymmetry

- Why activate the RH when it is already overactive? How about tapping the right hand and/or foot?
- The right limb tapping method still includes:
  - reorientation response
  - attentional shift
  - grounding
- This method is portable—the client can practice on his own (neuroplasticity)

Client Education

- I'm going to ask you to direct your attention to the specific movement while at the same time you describe the traumatic event.
- This will help you reset your brain so that it will no longer be stuck in the past and you can move ahead to a positive future.

Trauma Reactions

- **Alerting the superior colliculi, PAG, and locus coeruleus**
- **BG, hypothalamus, amygdala**
- **With hippocampus and PFC impairment fear gets generalized. Without context any situation elicits fear**
- **Dysfunction in contextual processing leads to maladaptive interpretations and rigid perceptions.**

Activate to recalibrate

- Recalibrate visceral and memory networks
- Using somatic awareness to normalize interoceptive reactions
- Simultaneously build in new and adaptive narrative with post-traumatic growth

Post-Traumatic Growth

- "That which does not kill us makes us stronger"
  - –Nietzsche
- Key narrative is to see oneself as a survivor not a victim
- Transformational coping-- beyond resilience (not returning to the old self)
  - – self-organization—a new self

Post-Traumatic Growth

- Greater connection with others
- Inclusiveness
- Feeling felt and understood
- Increased altruism. (giving is receiving)

Post-Traumatic Growth

- Greater meaning in life
- Beyond the whole is greater than the sum of it parts—its different
- Wisdom of inclusive and interdependence
- Operationalizing wisdom

Resiliency

- Changing the narrative
- Seeing life through the eyes of others
- Learning from mistakes
- Acceptance
- Purpose

Personal growth following trauma

- Enhanced relationships and increased empathy
- New opportunities and paths
- A newfound sense of resilience in facing challenges.
- A shift in spiritual beliefs or a deeper spirituality.

Personal growth following trauma

- *An increased appreciation for life.*
- Cognitive, making sense of the event, reevaluating life priorities, and developing a new narrative about their experience.
- Resilience, individuals use new coping strategies.

Growth may not be immediate; it often takes time and reflection.

Resiliency

- Ability to withstand adversity and bounce back from difficult life events
- The 5Cs:
  - Commitment,
  - Control,
  - Challenge,
  - Connected,
  - Confidence

BBT and PTSD

- Phase 1: Psychological first aid—stabilizing ASD and preventing PTSD
- Phase 2: Integration of implicit and explicit memory systems:
  - Explicit memories (VAMs) –The conscious memory level, which can be accessed in therapy through deliberate recall.
  - Implicit memories (SAMs) –The nonconscious, which are only accessible through cues that activate the network.
  - Aided by somatic reorienting method
- Phase 3: Posttraumatic growth—developing meaning and direction (Constructivism)

SAFE from PTSD

"S" is for stabilizing. To establish a healthy foundation for recovery.

"A" is for acceptance of what happened.

"F" is for future. To visualize a hopeful future--posttraumatic growth.

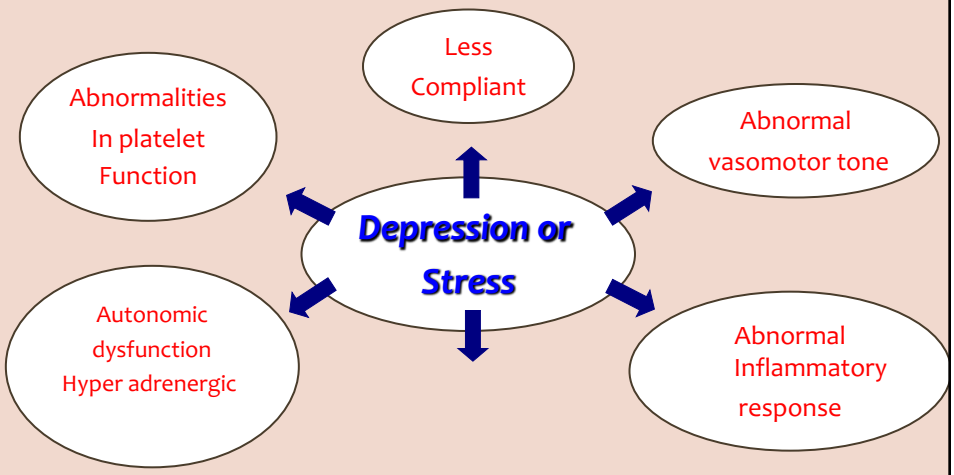
"E" is for exposure. To confront the feelings and sensations that trigger flashbacks.

Depression

Illness and Depression

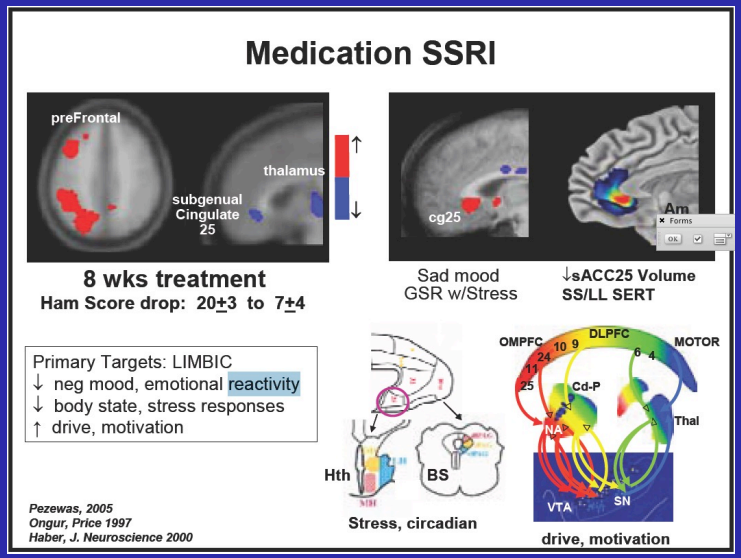
- Anemia
- Mono
- Asthma
- Diabetes
- Hepatitis
- Congestive Heart Failure
- Hypothyroidism
- MS
- Obesity
- inflammation
- Medications, drugs, and alcohol

Biologically plausible mechanisms linking depression with CHD



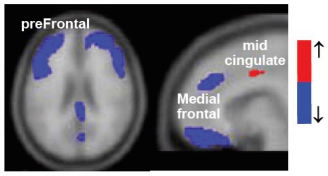
Beyond the Blues: Understanding the Link Between Coronary Artery Disease and Depression, Medscape Published: 12/13/2002

Bottom Up

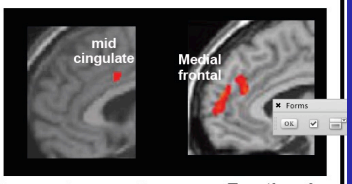


Top Down

Cognitive Behavior Therapy



16 wks treatment
Ham Score drop: 22±3 to 6±4



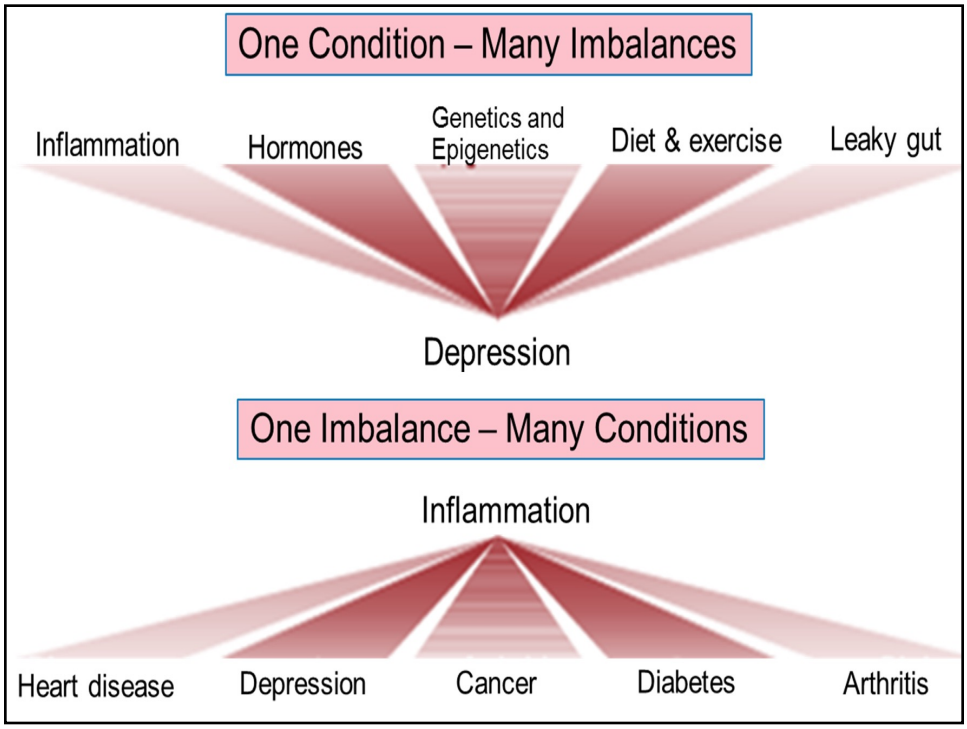
Reappraise emotion
Body-state awareness

Emotional
Self-relevance

Primary Targets of CBT: CORTEX
↑ awareness of body state reaction
↑ cognitive re-appraisal of stimulus/response
↓ self referencing, personal salience

TOP-DOWN

Goldapple et al. Arch Gen Psych 61:34-41, 2004



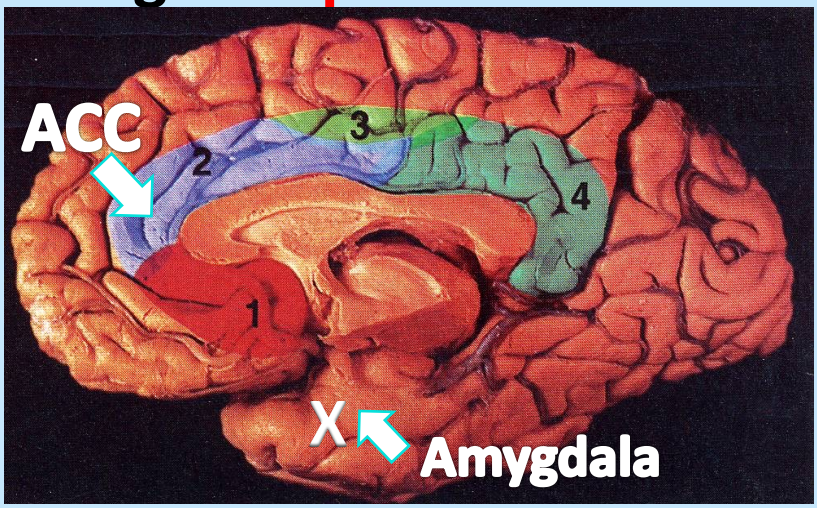
Pro-inflammatory Cytokines

- Stress can increase PICs levels
- High PICs can lower the concentration of serotonin and DA
  - –Cognitive dysfunction, anxiety, fearfulness, depression, thoughts about suicide
- "Sickness behavior"---fatigue, social withdrawal, and immobility--depression (Hickie and Lloyd 1995).

Inflammation and low serotonin

- PICs increase the enzyme IDO, which depletes tryptophan
  - – Thus, IDO indirectly lowers serotonin.
  - – IDO also catabolizes tryptophan into kynurenine and its neuroexcitotoxic metabolite, quinolinic acid.
  - – IDO and quinolinic acid have been associated with increased suicidality.
- Inflammation- induced quinolinic acid can spur excitotoxicity through direct activation of NMDA receptors.
- Loss of neurons and glia cells in mood- relevant brain areas such as the subgenual ACC has emerged as one of the hallmarks of depression.
- Compromised integrity of the amygdala- ACC circuitry,
  - – reduced ACC, amygdala, and hippocampal volumes, are associated with greater risk for depression

Anterior Cingulate…Amygdala Damage: Depression & anxiety



Symptoms of Sickness Behavior

- Anhedonia
- Feelings of helplessness
- Depressed mood
- Cognitive deficits
- Loss of social interest
- Fatigue
- Low libido
- Poor appetite
- Somnolence
- Pain sensitivity
- Anxiety
- Anhedonia

Client Education

- Feeling ill makes you act ill and if you do, the feelings of depression will increase.

Bidirectional Systems of Depression

- **Mood changes (dysphoria, hopelessness, suicidality, anhedonia, anxiety)**
- **Circadian dysregulations (low drive, energy, appetite, sleep, libido)**
- **Motor deficits (slow movement, restlessness, agitation)**
- **Cognitive impairments (poor attention, working memory, executive functions, ruminations)**

Gender Differences and Depression

- **2:1 women > men--** Only Post pubescence
- **Male symptoms –anger, irritability, recklessness**
- **Female symptoms—sadness**
- **4:1—men from suicide**

"Women seek help, men die"

Stress Induced Depression

- **↓ DA, NE, and 5-HT as much as 90 minutes post stress** (Irwin, 2000)
- **↓ DA is associated with psychomotor retardation**
- **Psychomotor retardation is associated with ↓ blood flow to the PFC**
- **L-PFC can inhibit negative affect ↓ amygdala activation** (Davidson & Sutton, 1995)

Re-balancing Hemispheric Asymmetry

- Instead of putting details into context, depressed patients are overwhelmed by a global negative perspective.
- Creating a constructive and goal oriented narrative generates positive, optimistic emotions which are all products of robust left hemispheric functioning
- Behavioral activation (left PFC) is one of the principal EBPs for depression

Effort-Driven Reward Circuit (Lambert, 2008)

- Nucleus accumbens-striatal PFC network
  - ↓ accumbens—loss of pleasure
  - ↓ striatum—sluggishness and slow motor responses
  - ↓ PFC—poor concentration

Client Education

- When depressed, if you do what you feel like doing, which is not much, you will become more depressed.
- Inactivity will fuel your depression.

Effort-Driven Reward Circuit (Lambert, 2008)

- **PFC activates when you plan an activity**
- **Striatum activates as you do it**
- **Accumbens activates when you feel the pleasure of doing it**
- **All the above increases the sense of self control**

Effort-Driven Reward Circuit (Lambert, 2008)

- Kindling this circuit by activities (Behavioral Activation)
  - ↑ DA and 5-HT
  - ↑ positive feelings
  - Reap rewards of problem solving

Impaired Hippocampus and Over-generalizing

- The denate gyrus facilitates "orthogonalization" of information, ensuring that new patterns do not interfere with old
- The CA3 region has many connections with other regions
- Impairment in the denate and CA3 results in black-and-white generalizations (Viamentes & Beitman, 2006)

Exercise and Depression

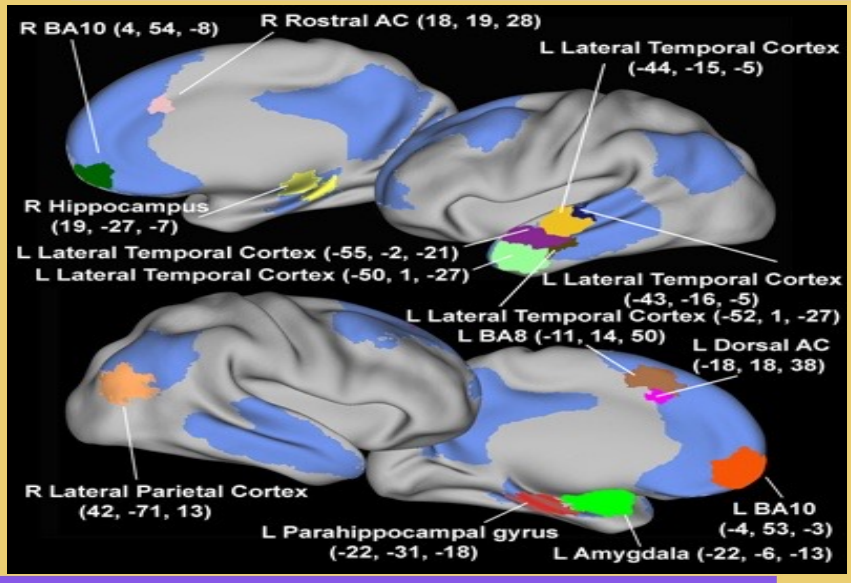
- **Alameda County study of 8,023 tracked for 26 years**
  - **Those that didn't exercise were 1.5 times more likely to be depressed**
- **Finnish study of 3.403**
  - **those that exercised 2 to 3 times per week were less depressed, angry, stressed and cynical**
- **Dutch study of 19,288 twins and their families –**
  - **those that exercised were less anxious, depressed, neurotic and more socially outgoing**
- **Columbia University study of 8,098**
  - **–inverse relationship between exercise and depression** (reviewed in Ratey, 2008)

Exercise and Depression

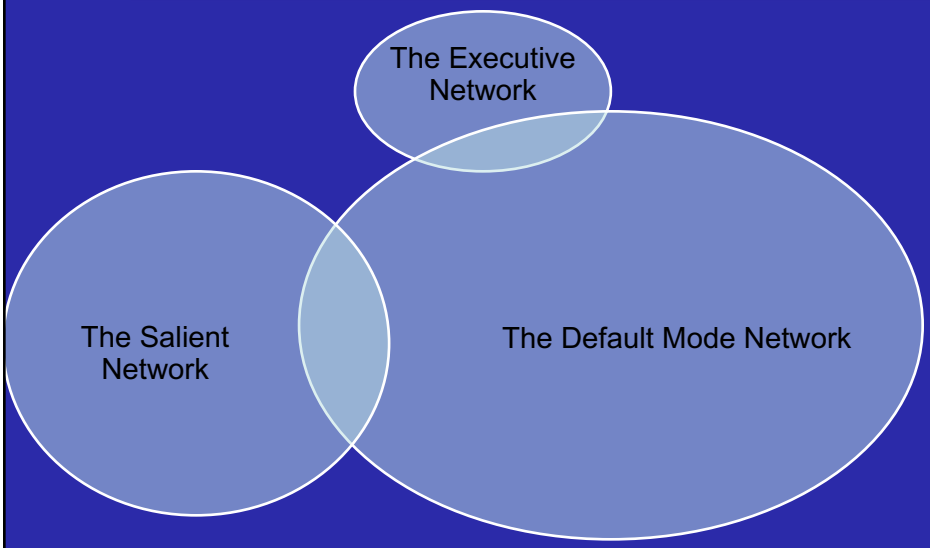
- Ohio State study---45 minutes of walking per day/ 5 days per week (heart rate at 60% to 70% of their maximum) lowered BDI mean scores from 14.81 to 3.27 compared to no change for controls (depressed non-walkers)
- Univ. of Wisconsin – exercise (jogging) as effective as psychotherapy for moderate depression
  - After one year 90% of exercise group were no longer depressed. 50% of psychotherapy group
- Duke Univ. – found that exercise was as effective as Zoloft
  - At 6 month follow-up exercise was 50% more effective in preventing relapse
  - Combining exercise and Zoloft added no benefit re: relapse

  (Babyak, et. al. 2000)
- NIMH panel concluded that long-term exercise reduces moderate depression.

DMN (in blue). All of the other colors are overactive in people with depression.



Dysregulated Mental Networks



DMN and Depression

- The DMN increases when DLPFC (EN) is not engaged:
  - Stressed, bored, no novelty, or tired
  - Obsessive ruminations over negative experiences

  Ruminations fade with:
  - Goal directed behaviors
  - Exercise
  - Social activities
  - mindfulness

Client Education

- When you find yourself drifting into ruminations bring yourself back to the present moment.
- Pulling out of the rumination stew and into the now will help you climb out of the black hole of depression.

Mindfulness and Depression

Targets depression by neutralizing:

- **Monotony: via attention to novelty and cultivation of curiosity**
- **Ruminations: via wide spectrum thought and detachment**
- **Thinking errors: via affective labeling**
- **Fixations on imperfections: via acceptance**

Client Education

- When you have a depressing thought, call it just that, a depressing thought.
- This will help you put distance between the thought and the feeling.

Meta-awareness: General Concepts

- **Decentering – thoughts and feelings are events—not realities**
  - Meta-Cognitive Awareness: Change your relationship to the thought.
- **Intentionality – breaking out of automatic thoughts and behaviors**
- **Reducing Avoidance -- facing difficulties**
- **Anti-ruminative – here and now focus not the past or future**

Therapy: Mind-Brain-Gene Feedback Loops

Up regulate

- **The Social Brain Networks**
  - Individual psychotherapy
  - Groups
  - Expanding social supports
- **Activity Reward Circuit**
  - **Behavioral activation**
- **Hippocampus**
  - Exercise
  - Rebuilding a positive explicit memory system
- **Prefrontal Cortex**
  - Mindfulness
  - Goal planning and follow-through
  - Meta-awareness

Therapy: Working the Mind-Brain-Gene Feedback Loops

Down regulate

- **Right hemi withdrawal tendency by:**
  - Social engagement
  - Active behavior
  - Challenging negative generalizations
  - **Humor**
  - Labeling moods
- **The amygdala and the HPA axis by:**
  - Exposure
  - Exercise
  - Goal directed behavior
- **The ACC by:**
  - Challenging self-criticism

Therapy: Working the Mind-Brain-Gene Feedback Loops

Interventions that bolster under-active areas of the brain

- **Metabolism**
  - **Exercise**
  - **Sleep hygiene**
  - **Diet, including Omega 3**
- **Hippocampus**
  - **Counter mood-congruent bias with inquiry**
- **Rebalance left PFC**
  - **Details**
  - **Active**
  - **Goal directed behavior**
- **Activity Reward Circuit**
- **Mindfulness**
  - **Quieting ruminations and monotony**

Client Education

- Because many factors can contribute to your depression you'll need to do all the things we talk about doing simultaneously to climb out of depression.

TEAM for Depression

T is for thinking to defuse negativistic thinking associated with depression.

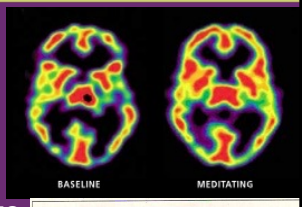
E is for effort, to activate the approach circuits of the L-PFC and the effort driven reward circuit.

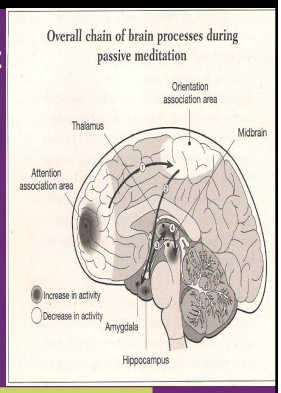
A is for accepting that the world is not perfect and the things that happen are not always good.

M is for mindfulness to focus on the present moment and novelty of each experience, gratitude, and forgiveness (Meta-awareness)

Mindfulness and the Brain

- Long-term meditators show increased thickness of the medial prefrontal cortex and also enlargement of the right insula (Lazar, et al, 2005).
- The process of verbal labeling of affective states reduces anxiety and negative affect (Leiberman, et al, 2004)
- The middle prefrontal cortex has been associated with self observation and mindfulness meditation (Cahn and Polich, 2006).
- A shift to the left PFC which puts a positive spin on the experience (Davidson, et al., 2003).

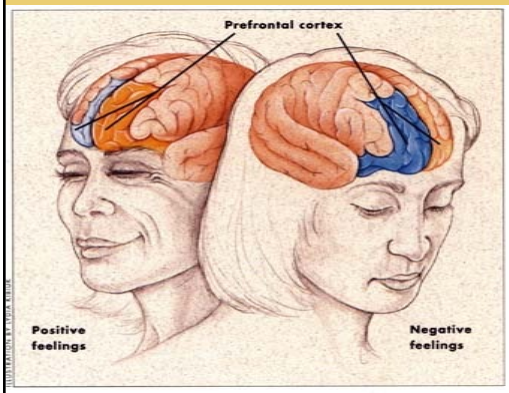


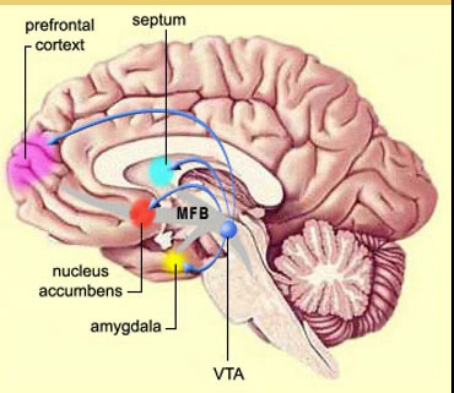


Mindfulness: Brain Changes

(Sara Lazar: Harvard, Davidson and Kabat-Zinn, 2003)

- Shifting attention activates prefrontal circuits
- Increase left PFC activation (better affect regulation)





Mindfulness for Various Groups

- Borderline via Dialectic Behavior Therapy-DBT (Linehan, 1993)
- OCD (Baxter, et al., 1992)
- Depression (Teasdale, Sigal)
- General medical problems such as chronic pain (Kabit-Zinn, 1990).

Mindfulness and Open Focus

- Increases in Gama waves with meditation
- Neurofeedback
  - –Global coherence
  - –Open focus—widened

7 Principles Common to prayer, meditation, relaxation exercises, and hypnosis.

- 1) Breathing Rhythmically—deep, deliberate, and focused breathing allows you to slow your heart beat.
- 2) Focused attention—to the present moment can transform each experience into a rich and calm experience by turning on your brain's brain.

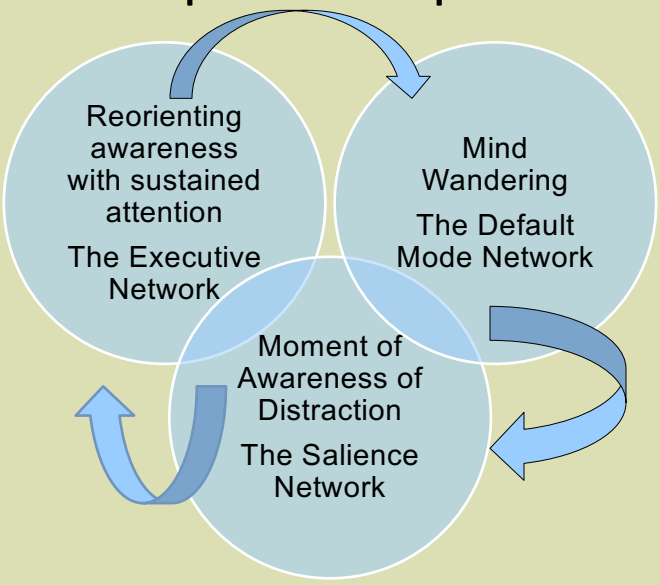
7 Principles of Relaxation

- 3) An accepting and a nonjudgmental attitude shift away from rigid expectations that helps you appreciate reality as it is, rather than what you fear it could be.
- 4) Observation—This allows you to detach from bad feelings by not denying their existence.

7 Principles of Relaxation

- 5) Labeling what you experience can calm your amygdala.
- 6) A quiet environment—This will give you an opportunity to learn how quiet your mind without distractions.
- 7) A relaxed posture—This can reduce tension include sitting in a relaxed posture or stretching (e.g. hybrid yoga)

Contemplative Experiences



Balancing the Mental Operating Networks

- The forest and trees together—not one or the other
  - A symphony—all pieces in synch
- Not passivity—instead of mindless action -- move with purpose with time
  - Mindful action—Zen is not like chopping wood. Zen *is* chopping wood.

Sustaining Positive Habits

- **Pleasure…often fleeting**
- **Positive habits --associated with sustained levels of well being**
  - **But during stressful times: having fun, self-nurturing and humor are the first to go**
- **Ongoing work toward a valued goal**
- **Daily contact with nature**
-

Transcendent Awareness

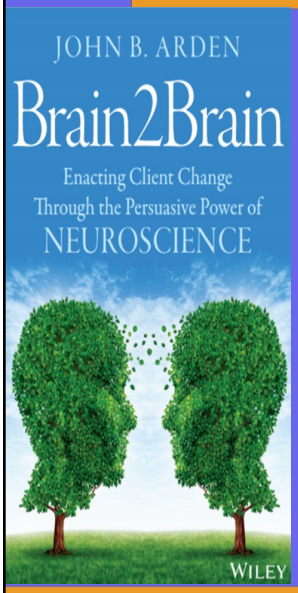
- Contemplative Attention
- Mindfulness
- Acceptance
- Forgiveness
- Gratitude
- Compassion

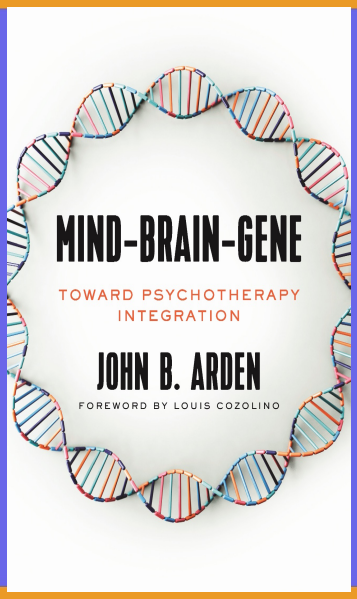
»The 9th!

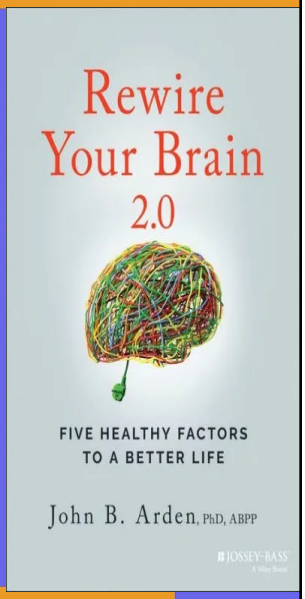
Victor Frankl's Wisdom

- "What man actually needs is not a tensionless state but rather the striving and struggling for some goal worthy of him."
- "No one can become fully aware of the very essence of another human being unless he loves him"
- "In some way, suffering ceases to be suffering at the moment it finds a meaning, such as the meaning of a sacrifice."

References







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Abbreviation Glossary

- AAI—Adult Attachment Inventory
- ACTH—Adrenocorticotropin Hormone
- ACC—Anterior Cingulate Cortex
- BDNF—Brain Derived Neurotrophic Factor
- CRH—Corticotropin Releasing Hormone
- DA—dopamine
- DLPFC—Dorsolateral Prefrontal Cortex
- DMN—Default Mode Network
- ISS—Infant Strange Situation
- OFC—Orbital Frontal Cortex
- NE—Norepinphrine
- NMDA—n-methyl-D-asparate receptors
- 5-HT—Serotonin