

MIND-BRAIN-GENE TOWARD PSYCHOTHERAPY INTEGRATION

ON DEMAND | AVAILABLE UNTIL MARCH 1, 2020

WORKSHOP AGENDA

- Explain the relationship between health and mental health
- Discuss the interaction between the immune system, genes, brain dynamics, and mental health
- Describe the pandemic facing the US with obesity and autoimmune disorders
- Clarify about how early adverse experiences can effect long-term health
- Explain how genes can be expressed or suppressed
- Assess how the stress systems can be turned on and are difficult to turn off
- Analyze how the immune system is intricately connected to brain systems
- Rate how chronic and acute stress can dysregulate the immune system
- Critique how autoimmune disorders contribute to depression, anxiety, and cognitive problem


LEARNING OBJECTIVES

- Contrast: The overly compartmental field of psychotherapy of the 20th Century to the integrative vision of psychotherapy in the 21st Century
- Distinguish: Between various health conditions and psychological disorders and their overlap
- Explain: Explain how poor health contributes to poor mental health as well as visa versa
- Analyze: How an overactive immune system contributes to depression and anxiety
- Evaluate: How adverse childhood experiences contributes to long-term chronic health and mental health conditions and what to do about it.
- Plan: Where to encourage lifestyle changes that improve health and mental health
- Measure: The effect of poor sleep, diet, and lack of exercise contributions to changes in mental health
- Choose: What psychotherapeutic intervention to use for various psychological conditions
- Assess: The effects of various psychotherapeutic interventions
- Select: Brain-based and evidence-based approaches with the most practical outcomes
- Formulate: A treatment plan most appropriate for the individual based on her/his ethnicity, socio-economic position, and LGBTQ identification.

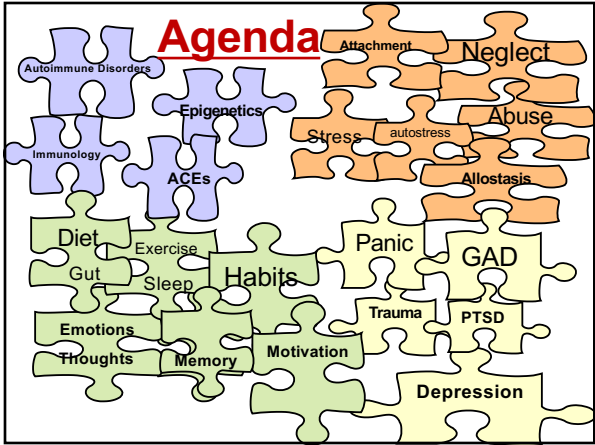


John Arden, Ph.D. is the author of 14 books, including Brain2Brain, The Brain Bible, Rewire Your Brain, and Brain-Based Therapy With Adults and Brain-Based Therapy with Children and Adolescents (with Lloyd Linford). Dr. Arden serves as Director of Training in Mental Health for Kaiser Permanente in the Northern California region. He oversees the training programs in 24 medical centers where over 100 postdoctoral residents and interns are trained each year. Dr. Arden also provides individual, group and family therapy and chemical dependency counselling through Kaiser Permanente. He presents workshops on brain-based therapy internationally and in the United States. Dr. Arden has written books on anxiety (The Brain-Based Anxiety Workbook), OCD (The Brain-Based OCD Workbook) and PTSD (Conquering Post-Traumatic Stress Disorder, with Dr. Victoria Beckner).

Mind-Brain-Gene:
The Integration of Psychotherapy



John B. Arden, PhD, ABPP



The Science was Changing

“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

The Science has Changed

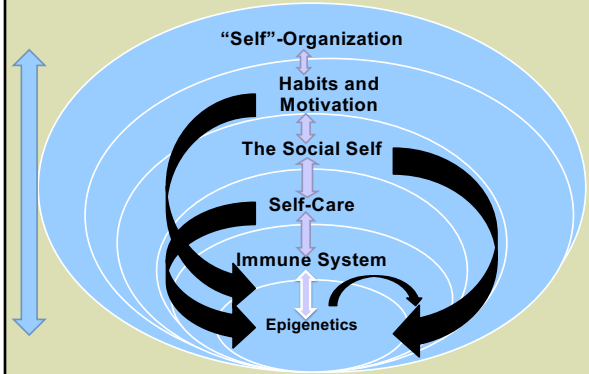
“Mental functions direct electrochemical traffic at the cellular level” Roger Sperry

“Psychotherapy works by producing changes in gene expression that alter the strength of synaptic connections...” Eric Kandel

Mind-Brain-Gene Feedback Loops

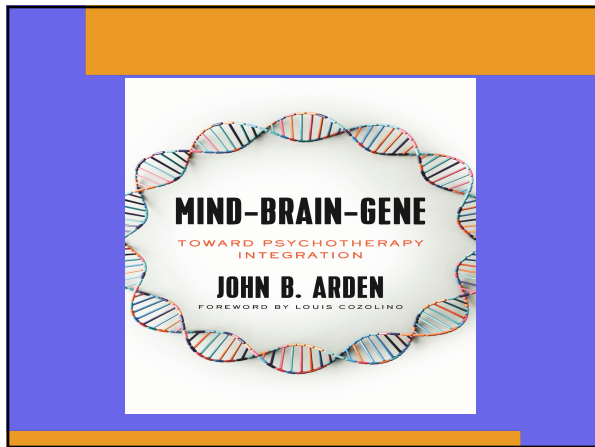


Mind-Brain-Gene Feedback Loops



Mind-Brain-Gene Feedback Loops





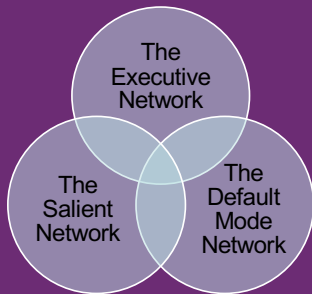
Mind-Brain-Gene Feedback Loops



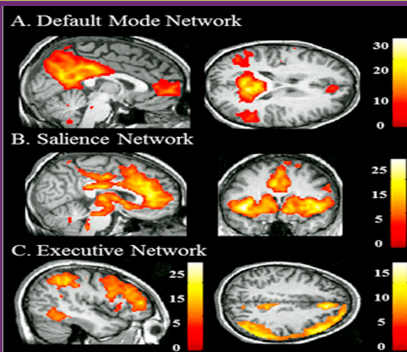
The Mind's Operating Systems:

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

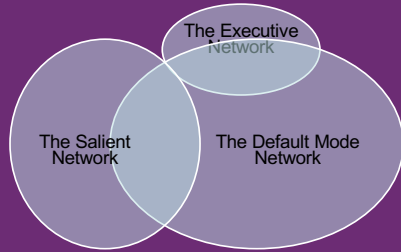
The Mental Networks



The Mental Networks



Imbalanced Mental Networks

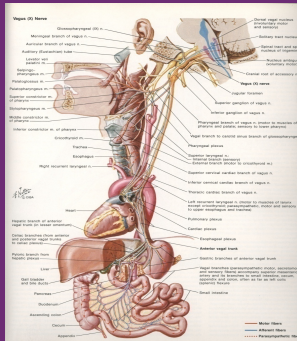


Salience Network:

- 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.

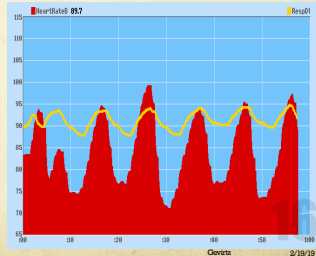


Variability is good

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.

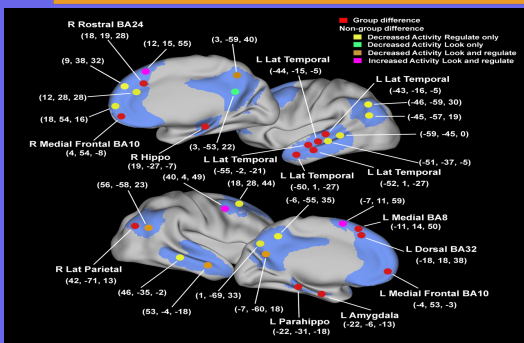
Peak/valley differences
= vagal tone *when resp is in normal range*



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

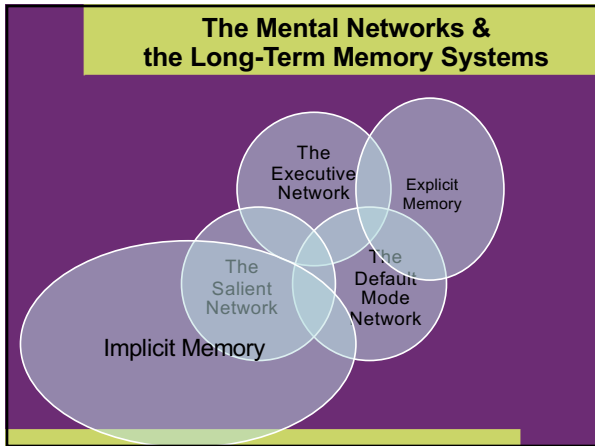
- Increases when DLPFC is not engaged:
 - Stressed, bored, no novelty, or tired
- Social and self-referential –needed for sense of self
- Malfunctions in the DMN:
 - Schizophrenia—impaired self reflection—not sure where thoughts come from
 - Depression—negative ruminations

Central Executive Network:

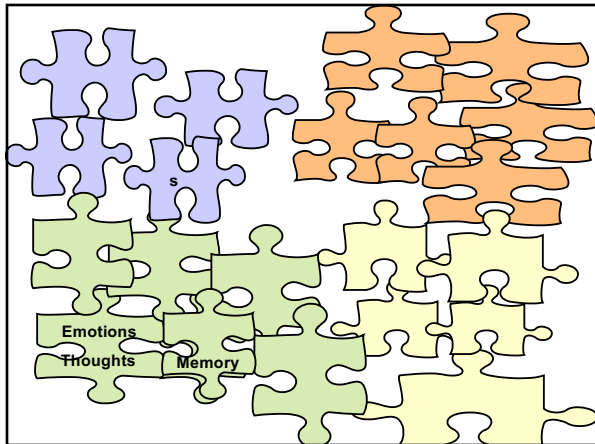
- moment to moment monitoring of experience (meta-cognition)
- responsible for selection, planning, and decision-making toward goals;
- working memory that helps select, orient, and maintain an object in the mind;
- bilateral dorsolateral prefrontal cortex

The PFC and The Executive Network

- The Dorsolateral PFC (DLPFC)
 - Last to develop and first to go
 - Working memory (20-30 seconds)
 - 7 + or - 2
 - Planning and follow-through
- Different from the OFC
 - Affect regulation
 - Attachment – social brain networks




- ### Incidence of Placebo Response
- 10% to 70%
sometimes 100%
 - Average 35% across studies and diseases
 - Works best for subjective outcomes like pain
 - Half as effective as morphine
 - Effective with depression

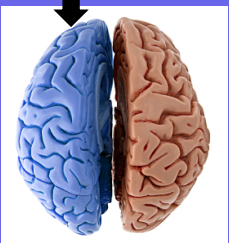


Affect Asymmetry
Set points

Left Hemisphere	Right Hemisphere
Positive emotions	Negative emotions
Approach behaviors	Withdrawal and Avoidance
Feeling engaged	Feeling overwhelmed



Left PFC:

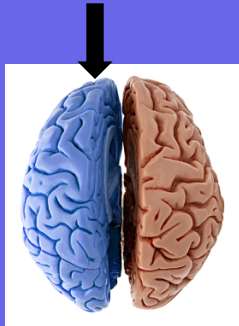
Suppressing Sadness	
Activating Positive Emotions	

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, incremental manner.

Left PFC:

**Activation
&
Approach
Behaviors**
(curiosity; assertion)



Right PFC:

**Activating
Behavioral
Inhibition**

**Associated
With negative
Emotions**



Neuroplasticity

Increases in:

- Receptor density
- Receptor efficiency
- Growth new dendrites (dendritogenesis)
- Neurogenesis
- Number of receptors
 - Changes in shape and structure
- Glial cells

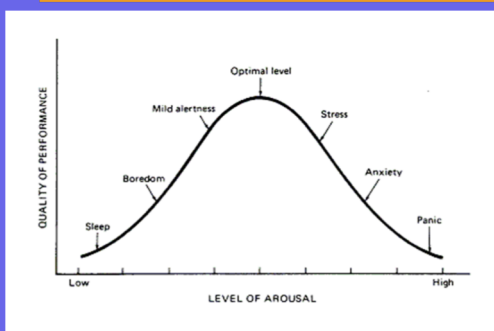
Client Education

- 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 Cabbies
- Violinists
- Musicians in general
- Jugglers
- Braille readers
- Bilingual people

Yerkes Dodson arousal curve



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!

Psychotherapy and the Brain

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

- **Reduced amygdalar activity in:**
 - **phobics** (Strabus, et al., 2003)
 - **panickers** (Pruker et al., 2006)
 - **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

- **Focus**—activating the PFC
- **Effort**—for neuroplasticity
- **Effortlessness**—learned
- **Determination**—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)

Neurotrophic Factors: Brain Fertilizers

- Insulin-like growth factor (IGF), is associated with brain growth and maturation and can be epigenetically facilitated by prosocial circuits in the brain
- Well nurtured involves the transcription factor called nerve growth factor (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 function, so that dopaminergic circuits reshape in the prefrontal cortex, impairing decision making and inhibiting maladaptive habits and working memory.

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.

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
- Elevated inflammation, especially in gut
- Increased incidence of pain conditions including fibromyalgia & irritable bowel syndrome
- Epigenetic changes to genes involved in inflammation

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 (Thomas, 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)

Cell Aging: Telomeres Length

- “Psychobiomarker”: Linked to social status, perceived stress, depression, 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.

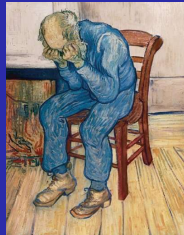
• Psychobiomarker: Linked to social status, perceived stress, depression, predictive of mortality (Epel, 2009, Current Directions)

The Cost of Loneliness

- In the long-run as detrimental as smoking to longevity (Cacioppo & 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 accumbens
 - Less of a sense of pleasure

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)



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)

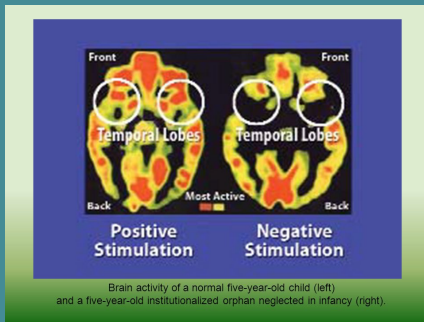
Deprived Social Brain Networks

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

Sustained impairment if over one year

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

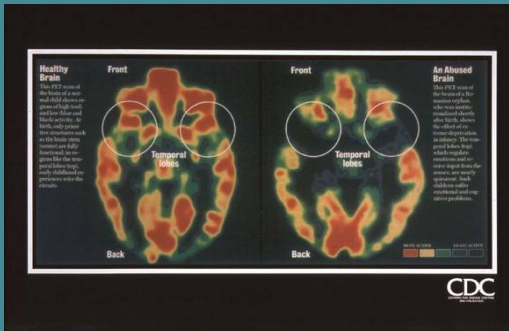
“Normal” vs Romanian Brains



Child Abuse and Neuropathology

- Diminished left hemisphere and left hippocampal volume (Brammer 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, Ruth, & Cockcroft, 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.
- Epigenetic changes to the developing child's stress response system
- 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

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)

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 (Papoušek & Bigas, 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.

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)

Correspondence between Child & Adult Attachment Categories

Child (ISS)

• *Adult (AAI)*

- secure
 - avoidant
 - ambivalent
 - disorganized
- - free/autonomous
 - - dismissing
 - - preoccupied
 - - unresolved

The Neurochemistry of Attachment

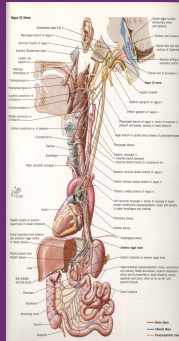
- Early attachment experiences regulate the opioid and GABA systems so that the developing child can generate feelings of comfort and buffer stress. (Curley, 2011).
 - Feeling soothed with less pain occurs through opioid release into the anterior cingulate cortex.
 - Increased GABA receptors resulting in less anxiety
- Maternal nurturance stimulates the expansion of BDNF.
- BDNF and NMDA expression and 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).

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.



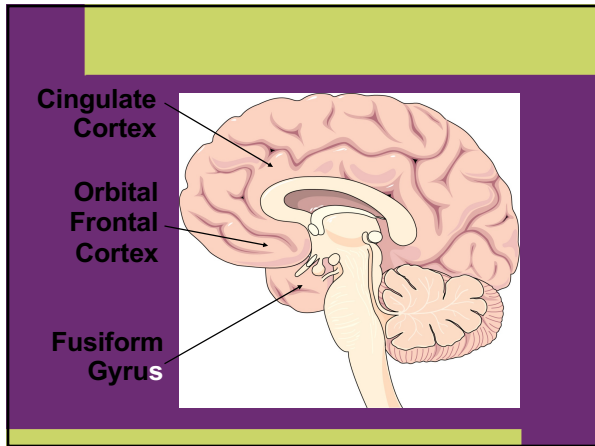
Vagal Brake^(Porges)

- *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 (Tabibzadeh, 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

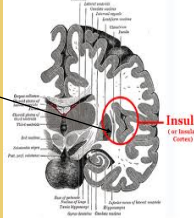
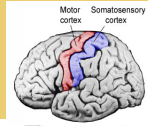
- Conduit between subcortical areas and cortex
- Draws on information from body areas, and input from amygdala and hippocampus
- Works with medial PFC to interpret and regulate emotional experiences
- Links mirror neuron systems with body states “Insula Hypothesis of empathy” (Carr, et al, 2003)

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 people struggling with forming relationships



Mirror Neurons

- Originally found in monkeys (Rizzolatti & Arbib, 1996)
- 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

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 (Kitts, 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 patient'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, et al, 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

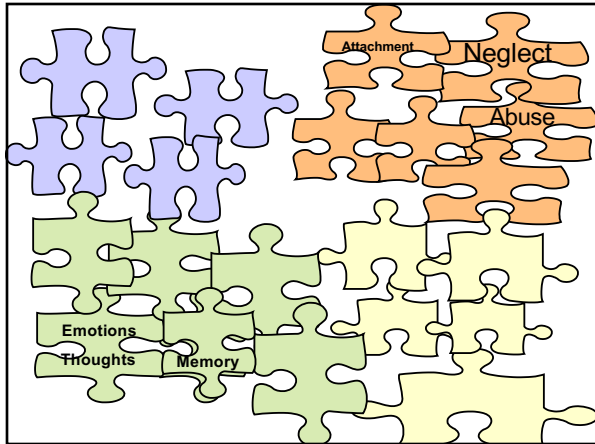
- The saying ‘laughter is good medicine’ is true.
- The more you practice laughing, the more likely you will feel good and feel like laughing.

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)

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



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

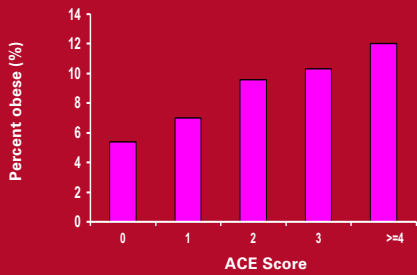
ACE Score
Prevalence

0	48%
1	25%
2	13%
3	7%
4	7%

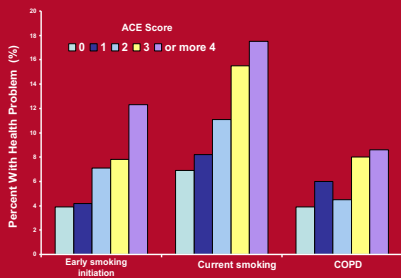


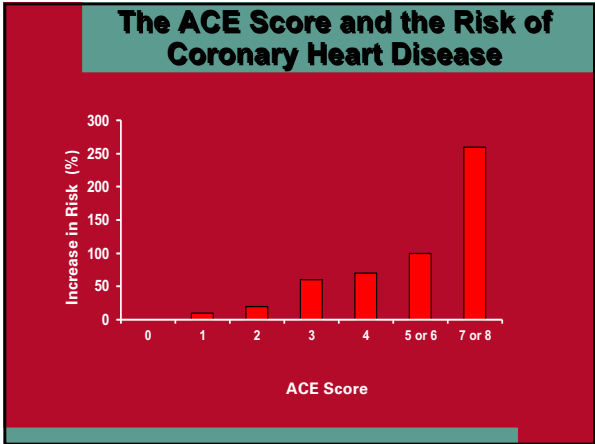
- More than *half* have at least one ACE
- Slightly more than one quarter have experienced 2 – 4 ACE categories

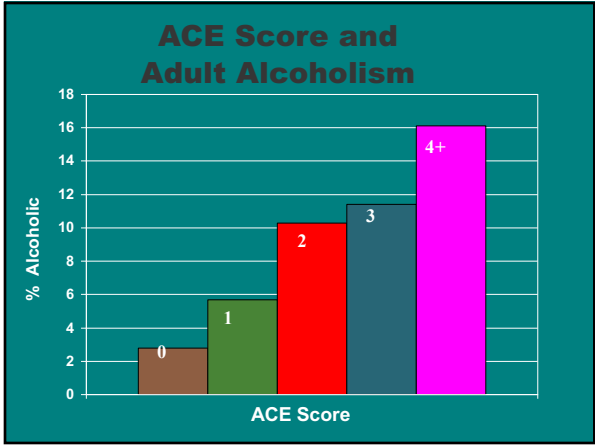
The ACE Score and the Prevalence of Severe Obesity (BMI>35)

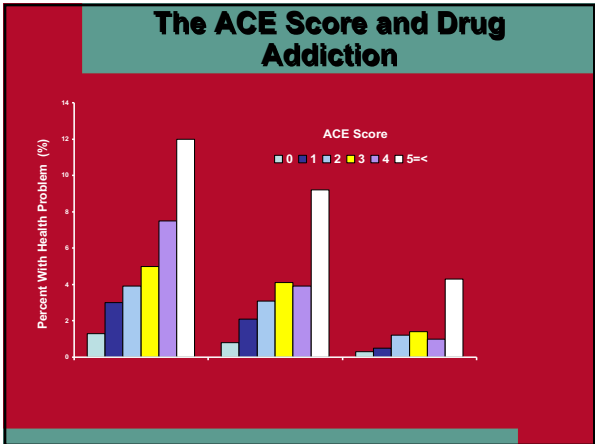


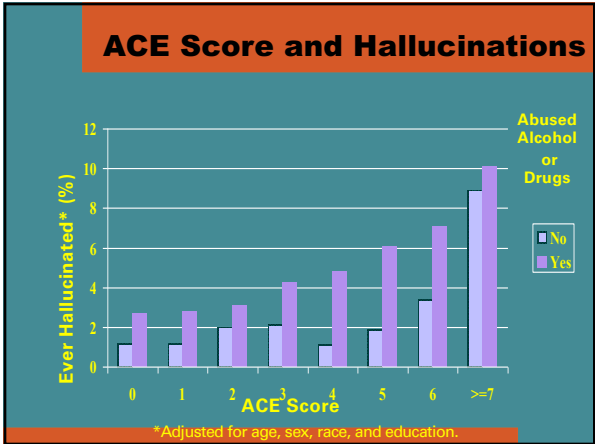
ACE's Smoking and Lung Disease

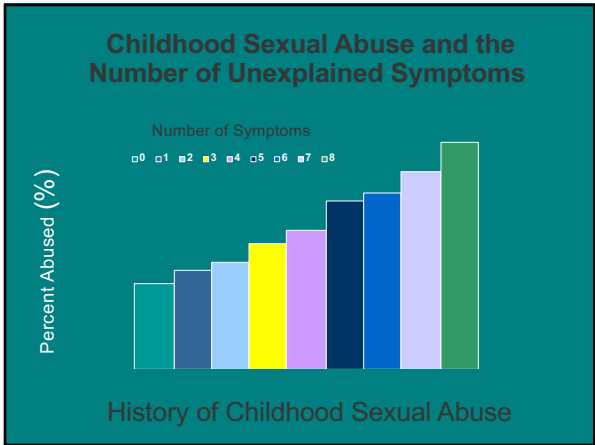


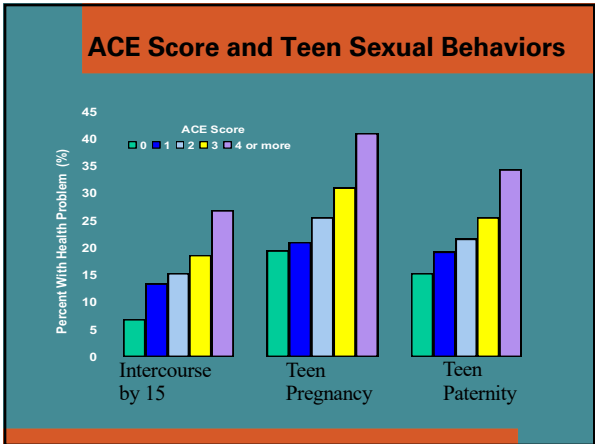




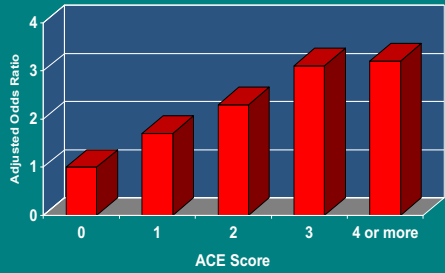




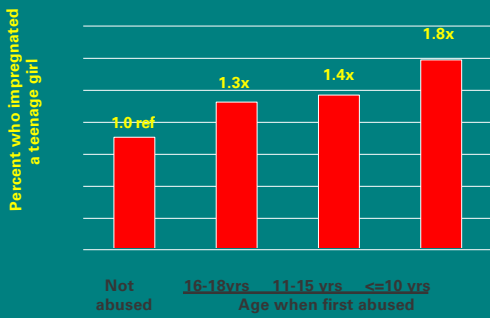




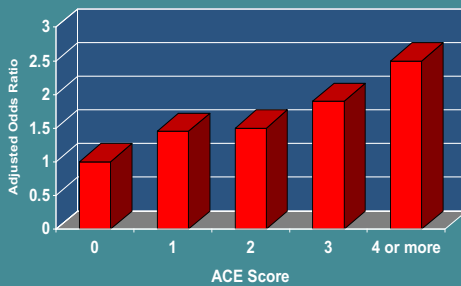
ACE Scores and Likelihood of > 50 Sexual Partners

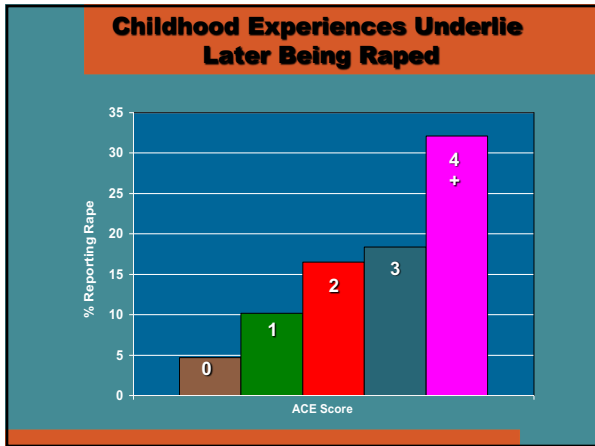


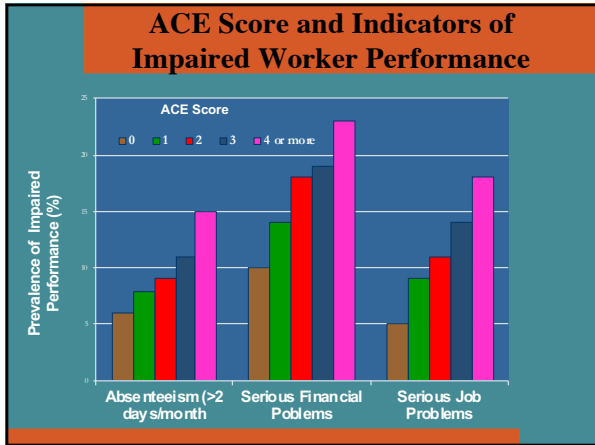
Sexual Abuse of Male Children and Their Likelihood of Impregnating a Teenage Girl

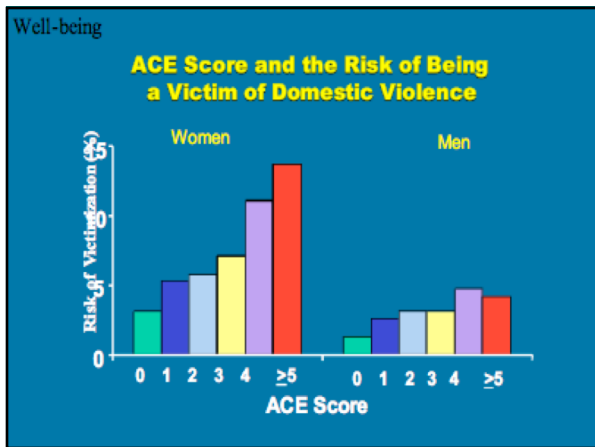


ACE Scores and History of STDs



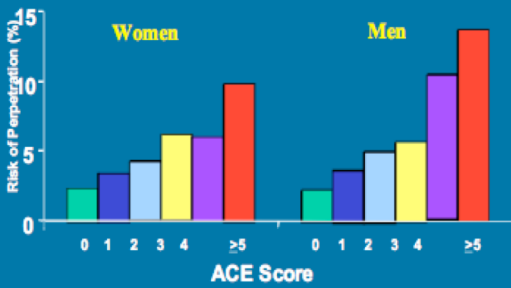




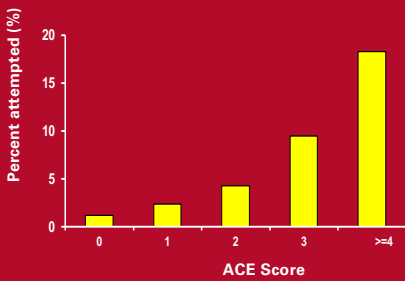


Well-being

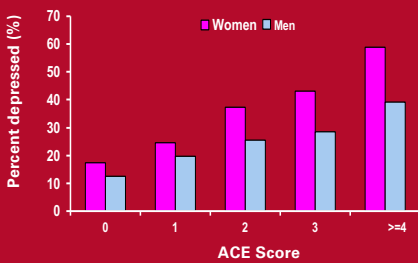
ACE Score and the Risk of Perpetrating Domestic Violence



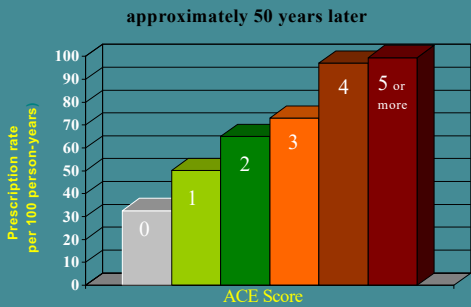
The ACE Score and the Prevalence of Attempted Suicide



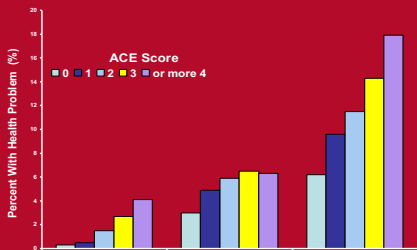
The ACE Score and a History of Lifetime Depression



ACE Score and Rates of Antidepressant Prescriptions

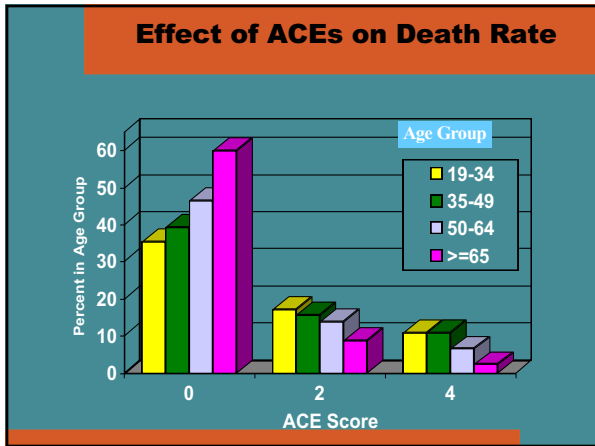


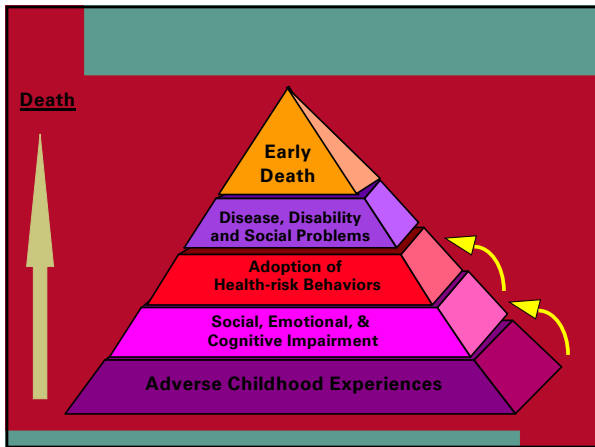
ACE Score and HIV Risks

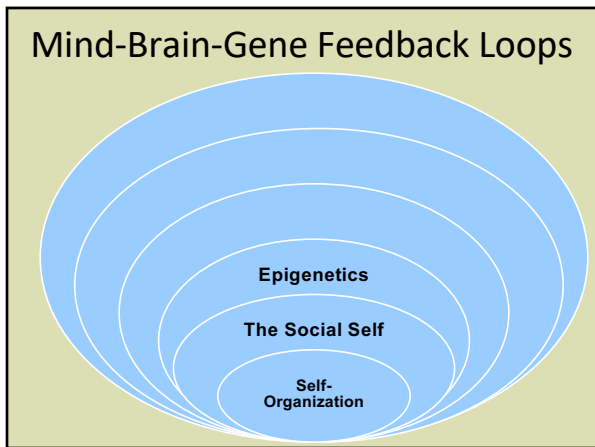


Social Systemic Problems

- Mental illness and substance abuse problems are more common among homeless people
- ACEs connection to substance abuse and mental illness
- Even non-homeless people with either substance abuse problems or mental illness are less likely to hold a job
- More than half of sample with ACE Score of 4 or higher

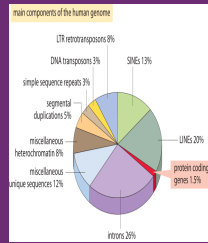






Epigenetics

- 24,000 genes (that code for protein)
- Worm and human
- 2% (the rest—"junk genes")
- As the complexity of the species increases so does the amount of "junk genes"



Epigenetics 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 off the stress response system more easily

Epigenetics in Gene Expression

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

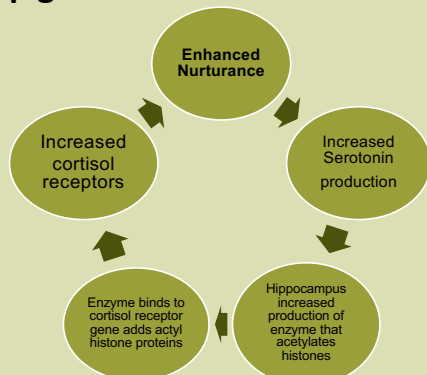
Epigenetics and Decreased Stress

- 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



**SEVERE NEGLECT:
Persistent Neurobiological Changes**

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

Epigenetics and Increased Stress

- Increased methylation levels of cortisol receptor gene:
 - In suicide victims with a family history of abuse and/or neglect
 - Also in preemies:
 - Can't easily turn off the stress response
- Decreased methylation of the arginine vasopressin gene
 - If stressed early in life:
 - Resulting in increased vasopressin and stimulating the stress response

Epigenetics and Increased Stress

- Maternal separation;
 - leads to decreased DNA methylation of the arginine vasopressin and CRH genes.
 - This results in the increased production of arginine vasopressin and CRH, which stimulates the HPA axis— the stress response system.
 - because of the methylation of the cortisol receptor gene, it is difficult to turn off the stress response.

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** disproportionately from supportive environments.

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

- 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 involves an enzyme that breaks down dopamine, norepinephrine, and epinephrine.

Cell Aging: Telomeres Length

- “Psychobiomarker”: Linked to social status, perceived stress, depression, predictive of mortality (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)

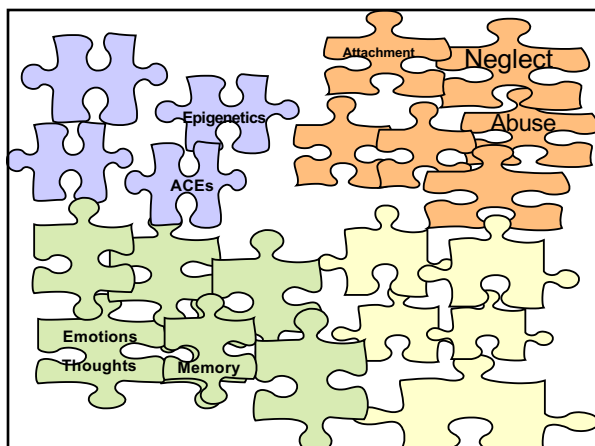


Factors that Shorten Telomeres

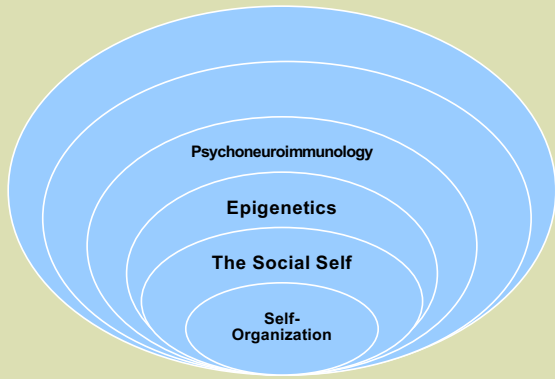
- Aging
- Cardiovascular disease
- Smoking
- Obesity (more than smoking)
- Diabetes
- Social isolation
- Poor diet
- No exercise
- Poor sleep



- Planting SEEDS protects telomeres!

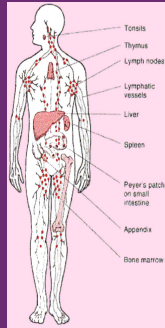


Mind-Brain-Gene Feedback Loops

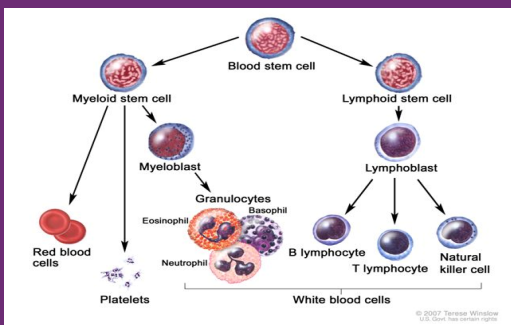


Components of the Immune System

- 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.



Components of the Immune System



The Immune System Can Affect Your Emotions:

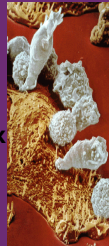
- PICs contributes to depression as underlying inflammatory conditions
- Stressors may contribute to depression or depression exacerbation via PICs
- Depression in medical conditions involves PICs
- Link between depression and vulnerability to medical diseases (CVD, autoimmune)

Short Term Stress Can Suppress Immune System

Examination 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

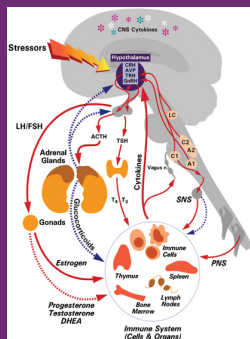
The Brain Controls the Stress Pathways

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.

It also controls the body's stress response systems: the hypothalamic pituitary adrenal axis and the autonomic nervous system.



Inflammatory pathways in the brain adversely affect memory and mood.

- PICs cause cognitive deficits that involve disturbances in 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.

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, TNF α , 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**



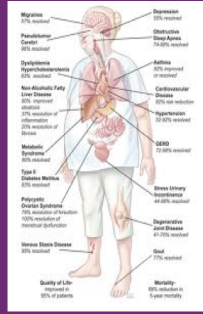
Stress

Activation of corticotropin releasing factor (CRF):

- **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**

Cardo-Metabolic Syndrome

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



What drives inflammation in cardio-metabolic syndrome?

- Obesity- fat releases pro-inflammatory mediators, and contains pro-inflammatory immune cells
- Gut barrier dysfunction
- Dysbiosis
- Inflammatory diet (high intake of saturated fats, refined sugar, processed foods, additives, lack of anti-oxidants)
- AGEs/RAGE
- Pro-inflammatory cytokines

Metabolic Syndrome

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

Diabetes and Psychological Disorders

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

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?
- A nasty positive-feedback loop

Pre-diabetes

- Occurs when blood glucose levels higher than normal but not yet high enough for dx of diabetes
- Dept of Health estimates 1 in 4 adults (57 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

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
- -probiotics- diets low in probiotics are associated with type-II diabetes

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

Depression Has a Relationship to Inflammation

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- --Depression is associated with inflammation in the brain
- So- does depression *cause* the increase in these cytokines or do these cytokines *cause* depression?
- **A nasty positive-feedback loop**

Proinflammatory Cytokines and Depression

- Depressed patients have increased levels of proinflammatory cytokines (PICs)
- Inflammatory diseases are often associated with depression
- Injections of PIC can increase depressive symptoms (dysphoria, anhedonia, fatigue, apathy, helplessness, which regresses)
- PICs cause a depression-like **Sickness Behavior**

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).

How does inflammation affect the brain: Sickness behavior

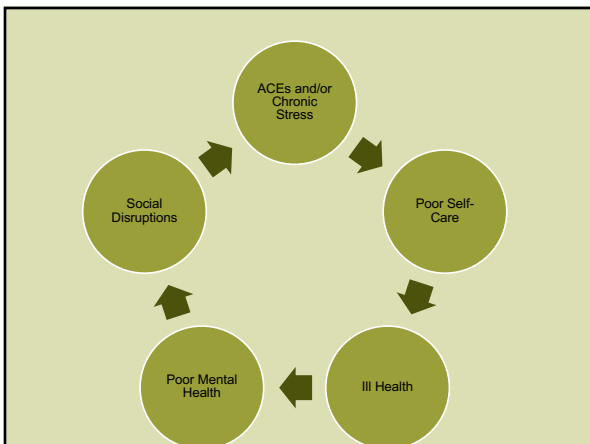
- *a symptom cluster also seen in chronic stress
- Depressed and/or anxious mood
- * increased sensitivity to pain
- *loss of interest in food
- * social withdrawal
- * disordered sleep
- *fatigue, “cognitive fuzziness”

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*
- Short term real-life stressors like exams can also increase production of these cytokines
- Chronic stressors (caregiving for a child with cancer) can also have this effect-prolonged

How does stress affect inflammation?

- Chronic stress- leads to increased inflammation (via cortisol resistance-immune cells –eg. 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**

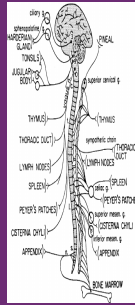


Inflammation and Dementia

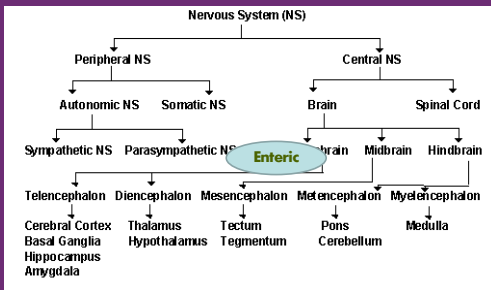
- Dementing conditions may be exacerbated by chronic inflammation.
- Obesity and diabetes as risk factors
- Small strokes may be caused by inflammation.
- Inflammation may play a role in deterioration of brain cells, formation of plaques. Some of the protein in plaques are products of inflammation.
- Inflammatory mediators can cross into the brain and influence learning and memory.
- Frequent use of non-steroidal anti-inflammatory drugs may prevent or delay Alzheimer's Disease.
 - In a study conducted at Johns Hopkins, those who took such medications for two years had a decreased chance of developing Alzheimer's Disease (60% less chance).
- 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
- Both pro-inflammatory and anti-inflammatory effects
- C-fibers modulate pain and inflammation
- Parasympathetic nerves reduce inflammation (especially vagus)

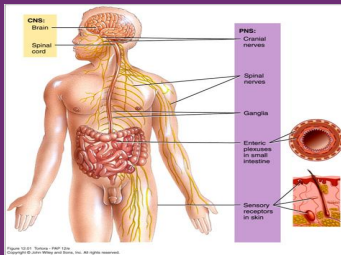


The Gut Brain?



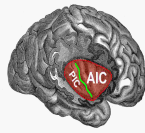
Enteric Nervous System

- **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**
- **Plays role in emotions & body homeostasis**
- **Regulates the immune system**
- **Conscious desires – food, drugs**



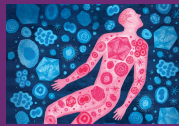
Microbiome



- **The GOOD:** helps digest certain foods the stomach/small intestine doesn't, can combat invading microorganisms. Our own microbes generally do not cause disease unless they grow abnormally; they exist in harmony with us. No bacteria causes *exaggerated* HPA response to psychological stress, which normalizes when certain bacteria colonize again.
- **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

- Produce nutrients, e.g. short chain fatty acids and vitamins
- 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 thiamine (B₁), folic acid (B₉), pyridoxine (B₆), and vitamin K
- Produce digestive enzymes to absorption calcium, magnesium, and iron.

Gut Bacteria

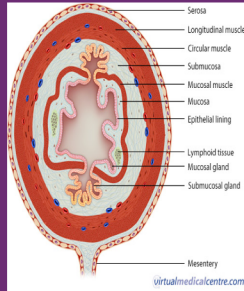
- 90% of bacteria in the colon F/B ratio:
- Firmicutes
 - Fat loving—increases fat absorption
 - Efficient at extracting calories from carbs
 - Turns on genes that increase the risk for obesity, diabetes, and CVD
- Bacteroidetes
 - More dominant in lean people

Stress/Depression and the Gut Microbiome

- Stress can induce increased permeability of the gut allowing bacteria to cross the epithelial barrier (thin tissue that lines the internal/external surfaces of the body) 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
- In IBS, the increased permeability can respond to probiotic therapy (live microorganisms (bacteria) that may provide health benefit when consumed.

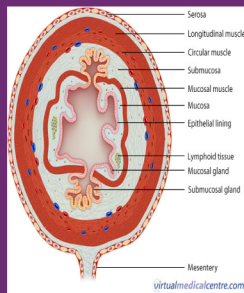
Leaky gutTM: the consequences of stress and inflammation and link between diet and health

- AKA "increased intestinal permeability"
- Increased intestinal permeability is associated with many disorders (diabetes, metabolic syndrome, allergies, neurological etc.)
- Single layer of cells between us and outside
- Absorbs nutrients- increased permeability allows more absorption of nutrients, but also toxins and lets fluid out e.g. during inflammation and infection (diarrhea)
- Many factors regulate this: immune cells and molecules, microbes, stress



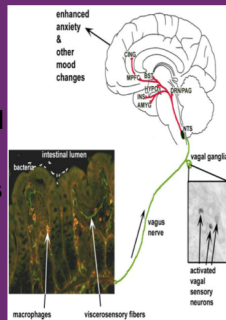
Leaky gutTM: the consequences of stress and inflammation and link between diet and health

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



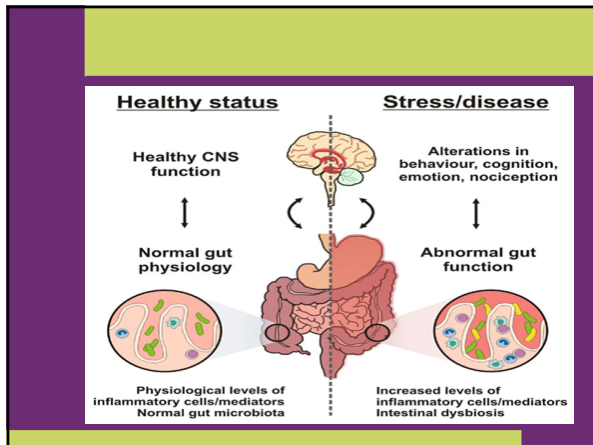
Inflammation, microbes and anxiety

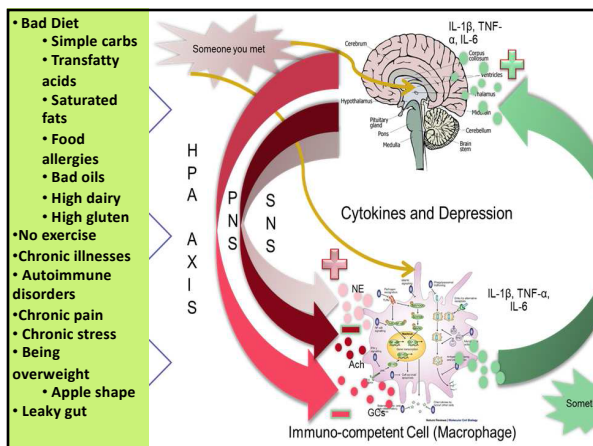
- Anxiety is common in illness, and inflammatory signals from the body contribute, e.g. TNF, vagal activation
- A signal that something is not right
- Special role of dysbiosis (imbalance in microbes)

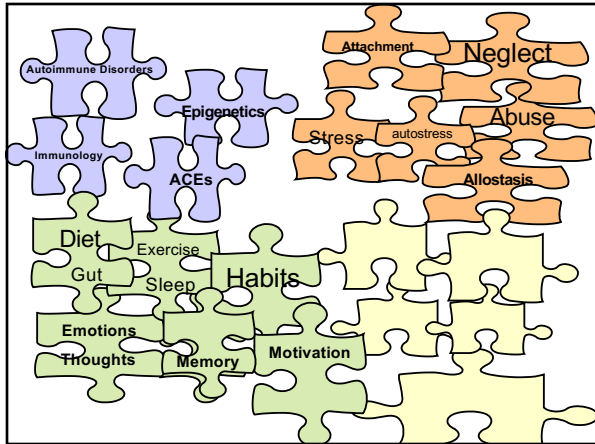


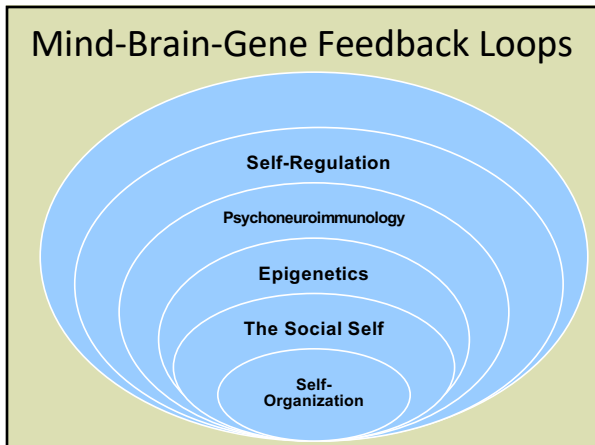
Dysbiosis and Microbial Diversity: the Importance of Balance

- 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**









Self-Regulation Factors

- Social
- Exercise
- Education
- Diet
- Sleep

SEEDS

**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

Beta-Endorphin and the High

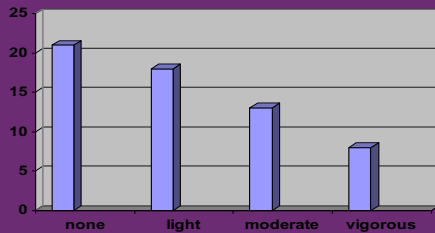
Exercise, a form of voluntary stress, activates the
hypothalamic-pituitary-adrenal axis
Beta-endorphin is released from anterior
pituitary
Subjective feelings of euphoria are mediated by
rising levels of beta-endorphin
Beta-endorphin increases in prefrontal and
limbic regions of the brain after 2 hours of
endurance running and levels correlate with
euphoria ratings

Exercise Increases Neurotransmitters

NE increases abruptly at exercise
• NE turnover is increased in the frontal cortex and is
helpful in alleviated 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

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

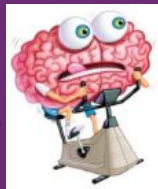
–↑ neurotransmitters

» 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)	Neuroplasticity (Adlard, et al, 2005)
Insulin-like Growth Factor (IGF-1)	Enhanced Neural (Carro, et al 200)
Nerve Growth Factor	Enhanced Neuroplasticity (Neepar, et al, 1996)
Vascular Endothelial Growth factor (VEGF)	Enhanced Neurogenesis (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

Professors BC. The disease of physical inactivity - and the role of myokines in muscle-fat cross-talk. The Journal of Physiology. 2009;511(2):559-568. doi:10.1111/jphysiol.2009.17815.

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 other part of the day (Gauvin, et al., 2000)

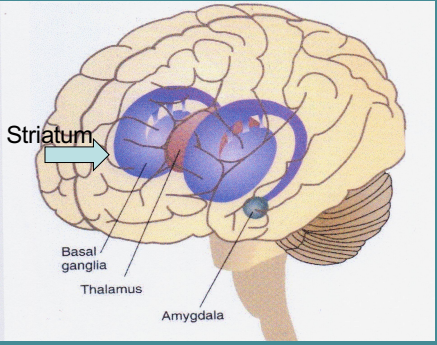
Exercise Summary

- Evolutionary imperative
- Not exercising is worst than “Smokadiabesity”
- Exercise boosts mood
- Exercise boost cognition
- Miracle grow—neurogenesis

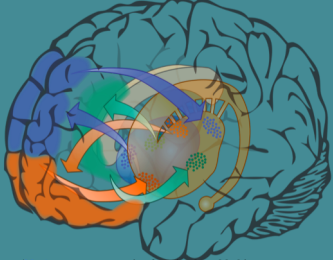
Two LT Memory Systems

Implicit	Explicit
Non-declarative	Declarative
<ul style="list-style-type: none"> • Procedural • Emotional • Generalized • Classical conditioning 	<ul style="list-style-type: none"> • Episodic • Autobiographical • Semantic • Context Specific
Amygdala and BG-driven	Hippocampus-driven

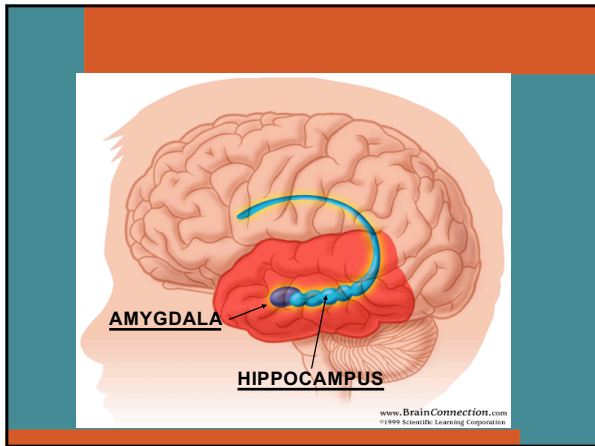
The Habit Circuits



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



<u>AMYGDALA</u> <i>Implicit Memory System</i>	<u>HIPPOCAMPUS</u> <i>Explicit Memory System</i>
<ul style="list-style-type: none"> •Fear Conditioning •Emotional Valance •Generalized •Cortisol Heightened •Sensitivity • (Hypervigilance) •Matures Early •“Little Albert” •“LSMFT” 	<ul style="list-style-type: none"> • Many Cortisol Receptors • Context Specific • Heightened Cortisol leads to atrophy • Matures Later <ul style="list-style-type: none"> • Vs. Infantile Amnesia • “H.M.”

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: (dentate 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
- Limitations:
 - Worries and GAD
 - Fears and Phobias
- Benefits:
 - Tames the Amygdala
 - With exposure, New Thinking (cortex)
- “Top down”

Flashbulb Memories

- A particular type, not class
- 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 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

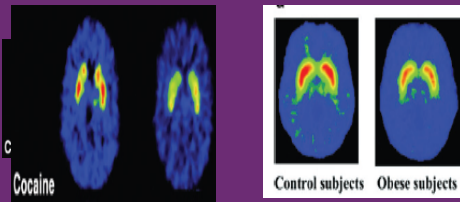
- Fructose blunts the effects of leptin which normally tells
 - Fructose produces uric acid
- Increased cardiovascular disease
- Increasing risk of metabolic syndrome
- **Shrinks the left hippocampus**
- Increased blood pressure
- LDL cholesterol
- Increased stroke
- Diabetes

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 Food Addicts

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



Metabolic Syndrome

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

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

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
 - -probiotics- diets low in probiotics are associated with type-II diabetes

WHO—World Population

7,505,257,673

- 4.7% with diabetes in 1980
- 8.5% with diabetes in 2014
- 10% forecast 2035
- Australia
 - 5.1% of the population (2016)

Diabetes

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

Diabetes

- Increased leptin and insulin resistance
 - Leptin insensitivity
- Increased blood pressure
- Increased cardiovascular disease
- Increased depression
- Neurocognitive impairment

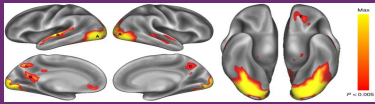
Diabetes and Neuropathology

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

Diabetes and Psychological Disorders

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

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

Break a Fast

Skipping Breakfast contributes to:

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

- ↑ Mood swings
- ↑ depression
- ↑ stress reactivity
- ↑ anxiety

Deficiencies of B Vitamins

Low B-1	Low B-2	Low B-6	Low B-12	Folic Acid
<ul style="list-style-type: none"> *Decreased Alertness *fatigue *Emotional Instability *Decreased reaction time 	<ul style="list-style-type: none"> *Trembling *Sluggish *Tension *Depression *Eye problems *Stress 	<ul style="list-style-type: none"> *Nervousness *Irritable *Depression *Muscle weakness *Headaches *Muscle Tingling 	<ul style="list-style-type: none"> *Mental slowness *Confusion *Psychosis *Stammering *Limb weakness 	<ul style="list-style-type: none"> *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.

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 your 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.
- It increases LPS by as much as 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)

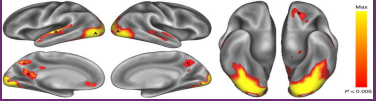
trans-fatty acids can:

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 effect on the brain
 - i.e. proinflammatory cytokines

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

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

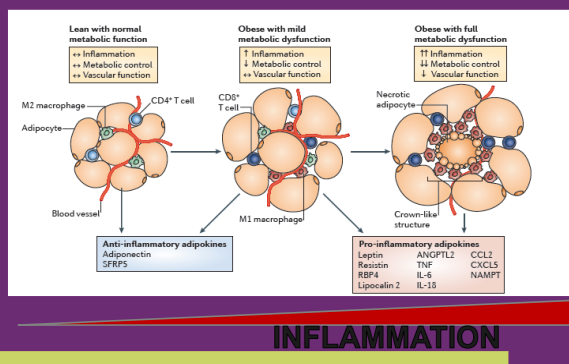
Diabetes and Psychological Disorders

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

Pro-inflammatory Cytokines

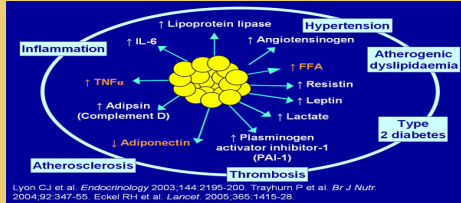
- Stress can increase PICs levels
- High PICs can lower the concentration of serotonin and DA
 - Cognitive dysfunction, anxiety, fearfulness, depression, thoughts about suicide
- “Sickness behavior”---fatigue, social withdrawal, and immobility--depression (Hickie and Lloyd 1995).

Obesity-Associated Adipose Tissue Inflammation



Obesity, Inflammation, and Diabetes

- Fat cells secrete IL-6
- IL-6 can induce insulin resistance
Higher IL-6 may predict diabetes type 2



Belly fat

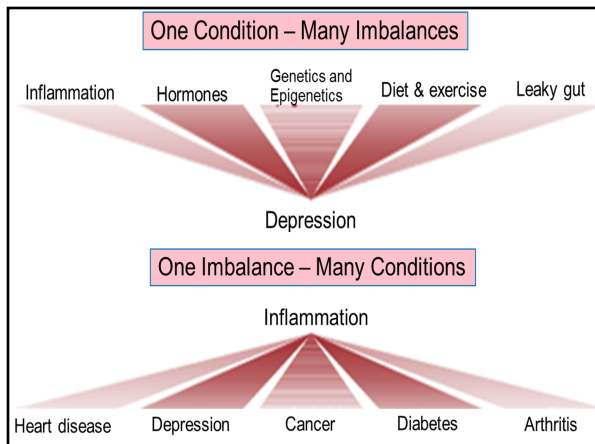
Belly fat generates inflammation by releasing proinflammatory cytokines

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



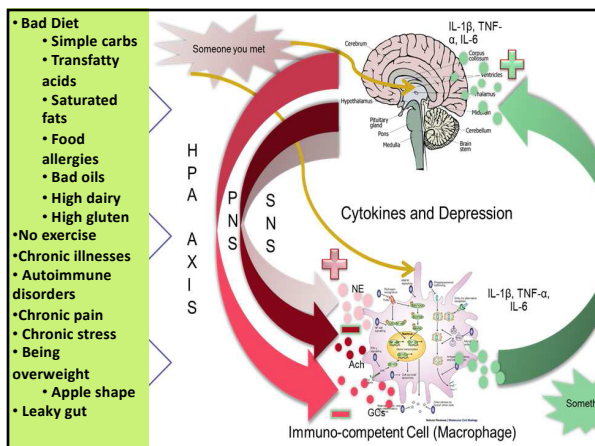
Client Education

- 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.



Metabolic Syndrome

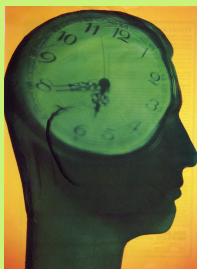
- **Increasing risk factors for:**
 - Heart disease
 - Diabetes
 - Obesity
 - Low HDL, high LDL
 - High blood pressure
- **All lead to depression**



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)

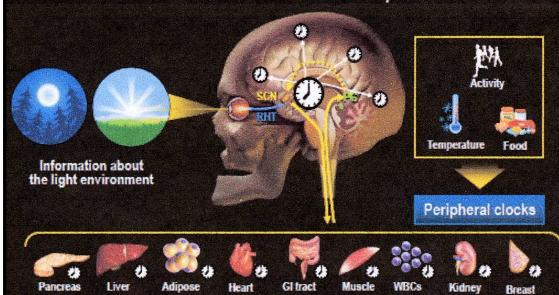
Circadian Rhythm



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

Synchronizing Circadian Rhythms

Entrainment of the SCN and Peripheral Clocks



GI, gastrointestinal; PG, pineal gland; RHT, retinohypothalamic tract; SCN, suprachiasmatic nucleus; WBC, white blood cell.
Buckell M, Rodden L.C. *S Afr J Sci*. 2009;105(11-12):415-420; Dibner C, et al. *Annu Rev Physiol*. 2010;72:517-549; Young M, et al. *Sleep Med*. 2007;8(6):656-667.

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 (Talsh, 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 May be 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

70 older adults, average age 76; those who said they got the least sleep, 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

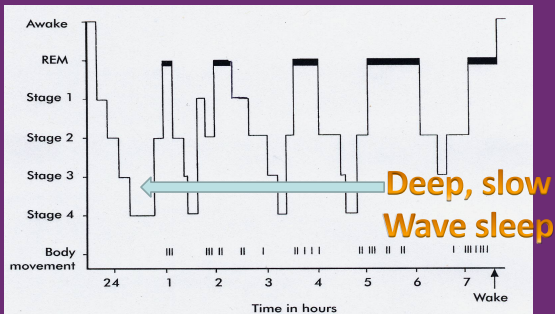
Sleep Hygiene

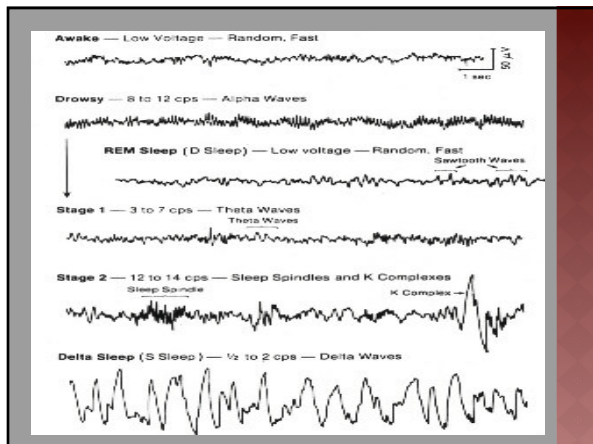
- Don't do anything in your bed other than sleep (except for sex). Do not watch television, balance your checkbook, discuss finances with your spouse, or argue in bed. Make your bed carry only one association—sleep.
- If you can't sleep and find yourself tossing and turning, get up and go to another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

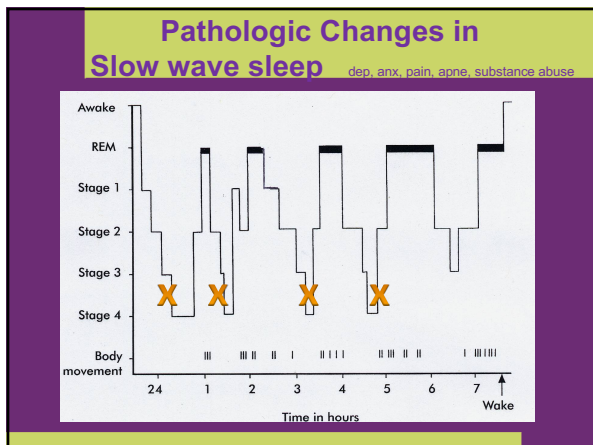
Sleep and Metabolism

- **Sleep loss causes:**
 - decrease in leptin
 - increase in ghrelin
 - increase in hunger and weight
 - decreased glucose tolerance
 - increase in food intake (without related increase in energy)

Normal Sleep Architecture







- ### Slow wave sleep deprivation
- > **Fatigue**
 - > increases in cortisol
 - > **inflammation**
 - > **Troubles concentrating**
 - > **Impaired emotion regulation**
- Increase in negative memories**
- Increase in depression**

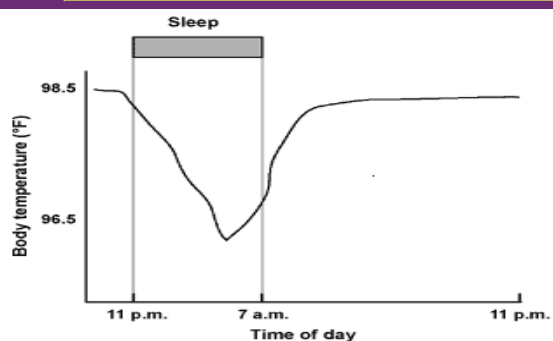
Sleep deprivation

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

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

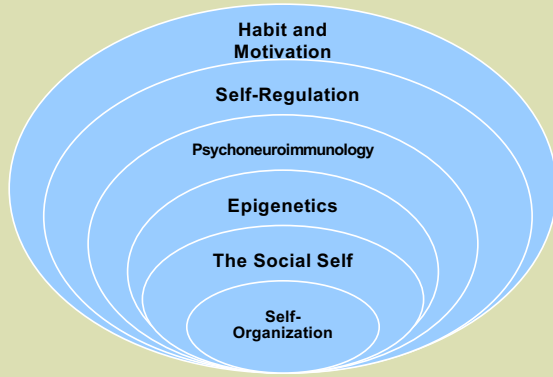
Body Temp and Sleep



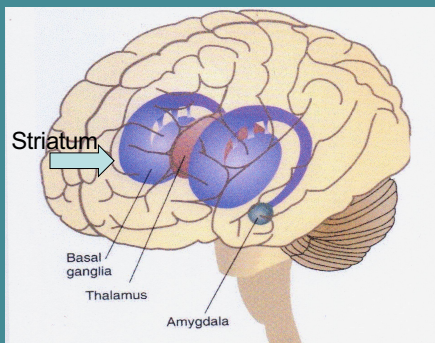
Sleep Summary

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

Mind-Brain-Gene Feedback Loops



The Habit Circuits

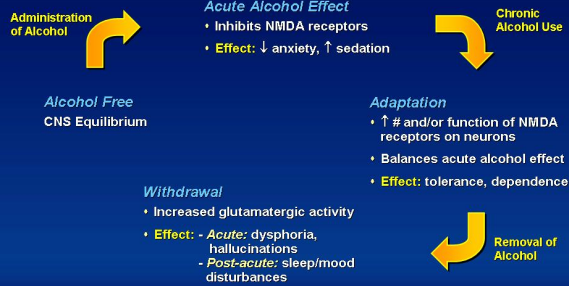


Drugs Associated with Neurotransmitters

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

Effects of Alcohol on Neural Circuits

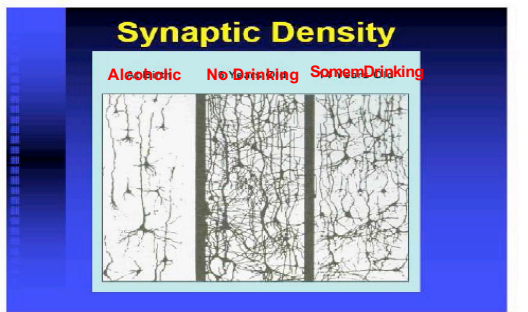
Glutamate System



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 testing

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



Cognition and Alcohol

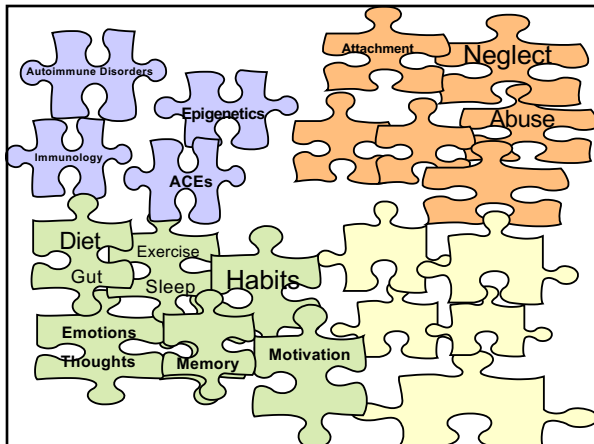
Drinking on a regular basis -- cognitive deficits such as:

- ↓ 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.



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

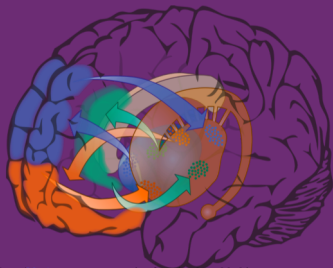
The Middle Path

- 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

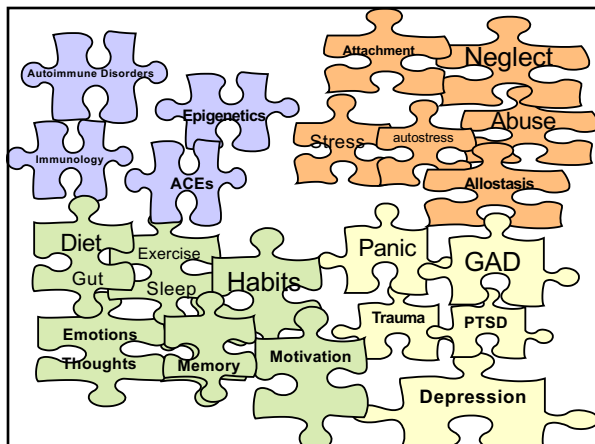
The Paradox

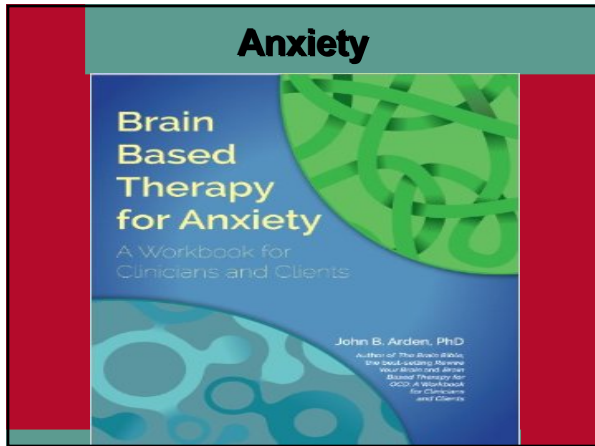
- Multitasking, produces working memory load, increasing the activity in the anterior cingulate cortex to monitor and assess errors in learned behaviors.
- Addiction can cause trouble activating the anterior cingulate cortex.
 - This is why many recovery programs incorporate contingency planning and relapse prevention so that problem solving ahead of time can minimize working memory load.

The 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





Medical and Drug Related Factors that Mimic Anxiety

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

Stress—Bottom Up or Top Down?

- William James—bottom up--"My hands are shaking –I must be nervous"
- Walter Cannon—top down—emotions are determined by what you decide.
 - 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

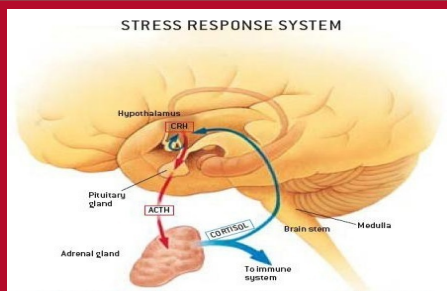
Allostasis

- **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

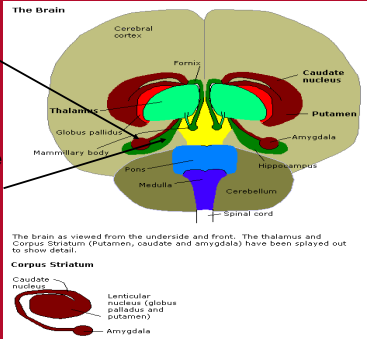


Locus Coeruleus (LC) source of NE which has extensive projections throughout the brain and can trigger the HPA axis (Aston-Jones, et al., 1994).

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, TNF α) *coordinates* inflammatory responses
 - Anti-inflammatory (IL-10) *controls* proinflammatory responses.

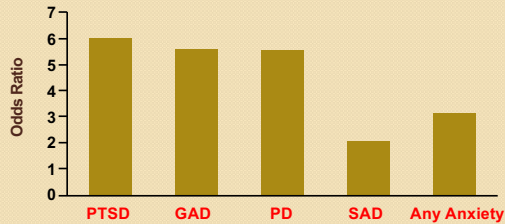
Hypocortisol vs. Hypercortisol Activity

- 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, TNF α and lower IL-2

Risk of Suicide Attempts Among Patients with Anxiety Disorders

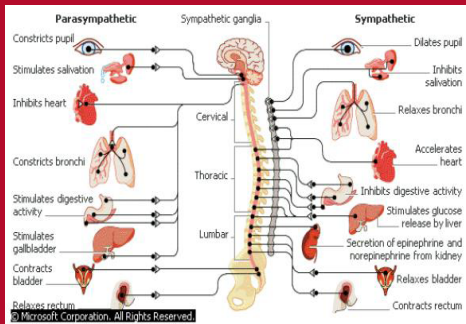


Kessler et al. Arch Gen Psychiatry. 1999;56:617

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)

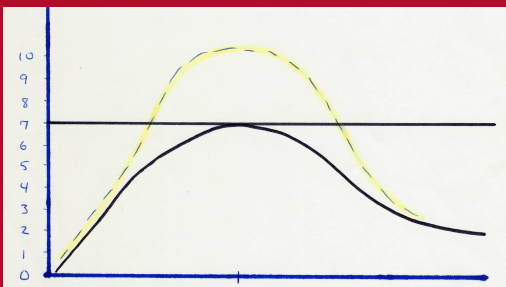
Balancing the ANS



Activating the PNS

- Diaphragmatic Breathing: Stretch
- Yoga
- Meditation
- Cuddling
- Orgasm
- Pulling the Kegel

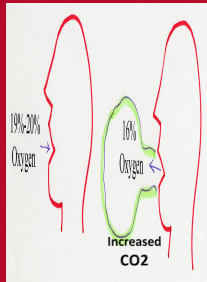
Abnormal Respiration



Symptoms: Shortness of breath, smothering

Breathing and Over-Breathing

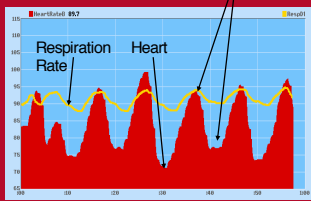
- Most people breathe 9 to 16 breaths per minute. Panic attacks - 27 breaths
- Over-breathing pulls in too much oxygen forces down the carbon dioxide level in the blood stream.
- Carbon dioxide helps maintain the critical acid base (pH) level in blood. Lower pH level causes nerve cells become more excitable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

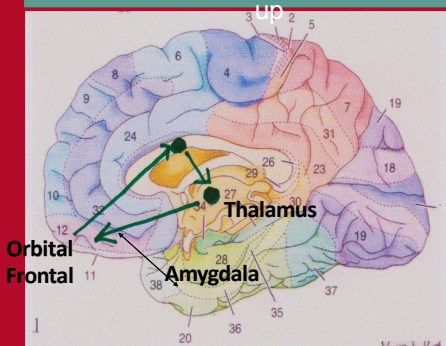
Peak/valley differences = vagal tone *when respiration is in normal range*



Challenging Feared Outcomes and Gaining Perspective

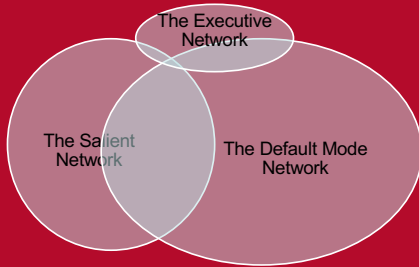
- Worse possibility? (exaggerate it)
 - Re-Attribution (it's just my body)
- Worse realistic possibility?
 - So what if....
- > Physiological Symptoms (e.g. this is not dangerous)
- Temporal perspective
 - I've never died from this yet

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



Worry as Cognitive Avoidance

- Excessive DMN ruminations with little Executive Network



**Challenging Feared Outcomes
and Gaining Perspective**

- **Worse possibility? (exaggerate it)**
 - Re-Attribution (it's just my body)
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 - So what if....
- **> Physiological Symptoms**
(e.g. this is not dangerous)

- **Temporal perspective**
 - I've never died from this yet

CBT vs. Metacognitive Models

(ACT, DBT, MBCT, etc.)

CBT

Rationale=control

Cognitive restructuring

Breathing retraining

Interoceptive exposure to
lessen fear & avoidance

Situational
exposure to lessen fear
fear and avoidance

MC Models

Rationale=relinquish control

Thought Diffusion

Observe & accept

Interoceptive exposure with
acceptance of internal cues

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.

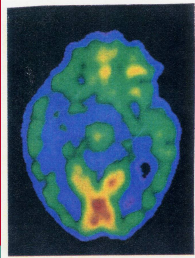
"E" is for exposure such as in scheduling an hour of worry time, allowing focused exposure to all your worries, and giving your higher brain a chance to work on developing the capability of dealing with the ambiguities inherent to life.

"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 (Beauch 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-vIPFC
- 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

- Do not reach out to others for comfort (withdrawl)
- Interpersonal trauma versus natural disasters, etc... “mistrust schemas”

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



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

Shifting Perspective to Speed Up the Slow Track

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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.

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 +

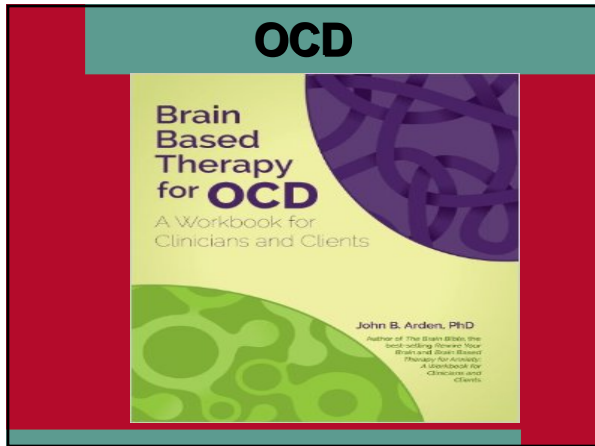
- There are a variety of interoceptive exercises including:
 - Running in place--- to increase heart rate and hyperventilation
 - Holding your breath--- to simulate sensations of suffocation
 - Spinning--- leading to dizziness
 - Hyperventilation or breathing through a straw---leading to light-headedness

BBT and Panic Disorder

- Desensitizing the Amygdala—
Avoiding avoidance
- Interoceptive exposure exercises—
Embracing body sensations
- Speeding up the slow track—Getting the pre-frontal cortex involved

BEAT Panic

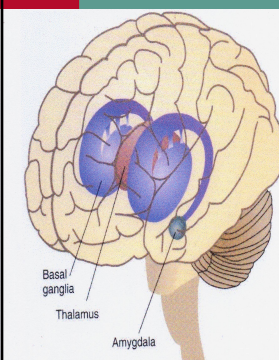
- "B" is for body. When you feel your heart race or breathe too fast just ride it out. Say, "I can befriend my own body!"
- "E" is for exposure. Through interoceptive exposure exercises you can regain tolerance to body sensations. Say, "this is not a heart attack but just my own body sensations that 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.



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



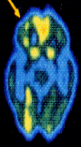
Cues: e.g. an emotional state, stress, fatigue, addictive cue

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

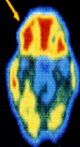
Flooded OFC in OCD

Obsessive Compulsive Disorder

High Orbital Glucose Metabolism



Normal Control

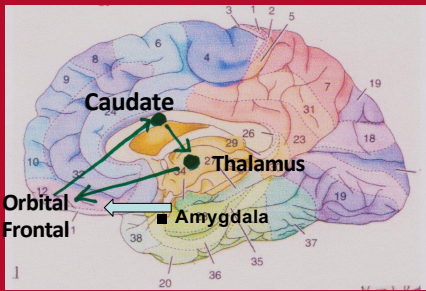


Obsessive Compulsive

UCLA School of Medicine

- 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”

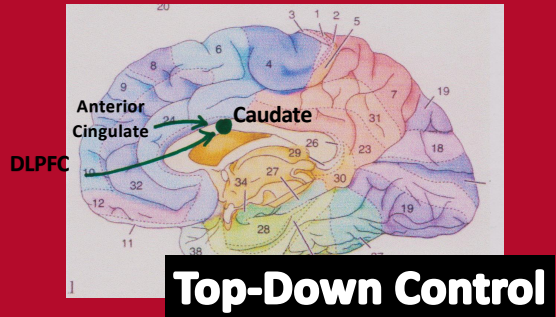
OCD: failure of top down control



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



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 system of practical and enjoyable behaviors through neuroplasticity.

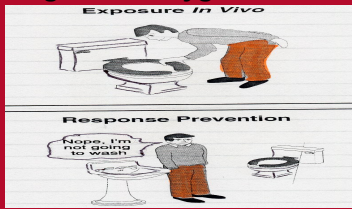
Client Education

- 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



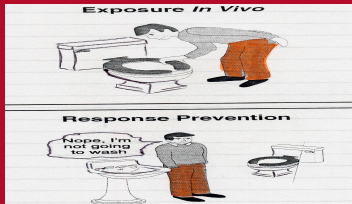
Client Education

- 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.”

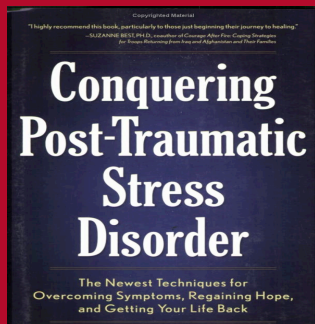
This step strengthens the inhibitory circuits



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

PTSD as a Worldwide Problem

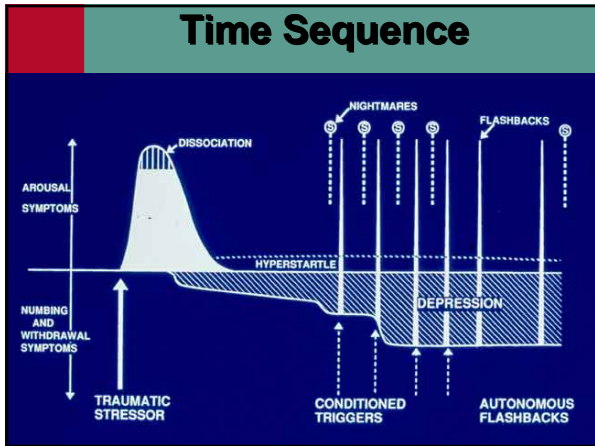
Germany	2.2%*
United States	7.8%
Ethiopia	15.8%
Gaza	17.8%
Cambodia	28.4%
Algeria	37.4%



Iraq, Syria,
Afghanistan?

Risk Factors for PTSD

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



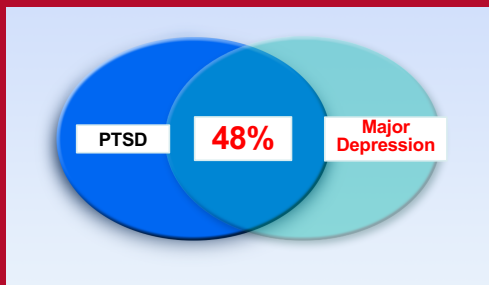
- ### Phylogenetic Responses to Stress
- 1) Trigger the social engagement system—the myelinated vagus
 - 2) Fight or flight—SNS and HPA axis arousal
 - 3) Immobilization—freeze, collapse, and feigned death:
 - 2 stages
 - Freezing in terror
 - Paralyzed—shut down—total submission, trance-like, dissociation

- ### 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, excitotoxicity, blocking of neurogenesis)

Most Common Acute Post-Traumatic Stress Response

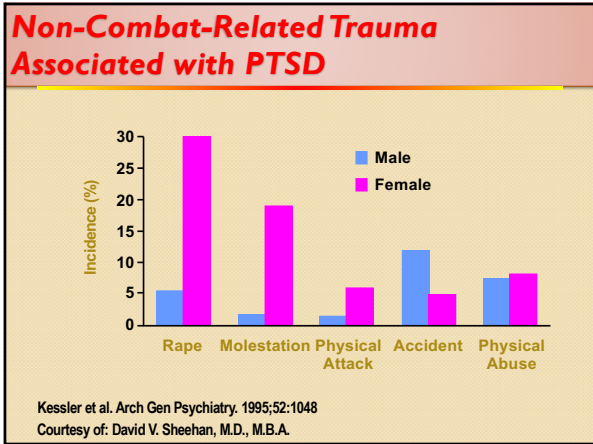
- Depression
- Anxiety Disorders
- Substance use / abuse
- Acute Stress (ASD) and PTSD
- Adjustment disorders
- Persistent complex bereavement

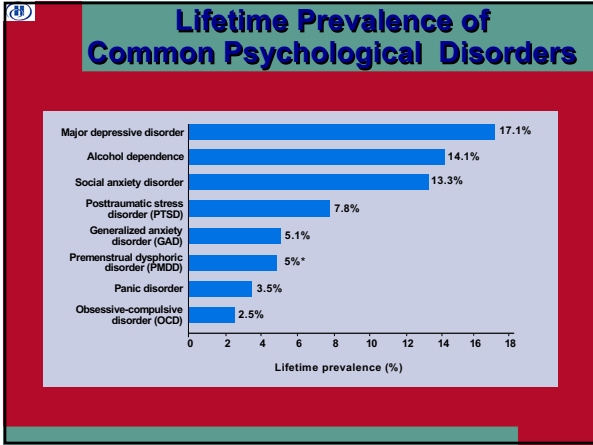
Common Occurrence of PTSD and Depression



A Big Problem: Reluctance to tell or seek out help

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



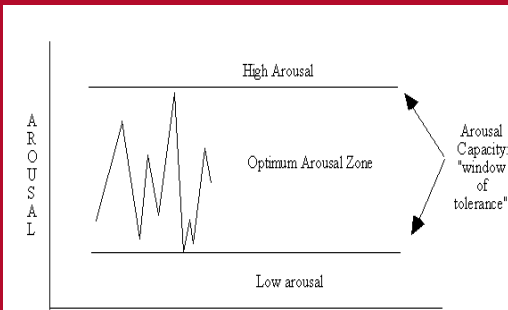


Predicting PTSD

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

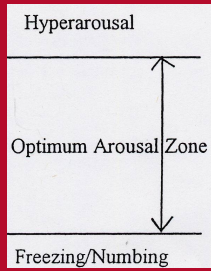
Window of Tolerance



Working the "Therapeutic Window"

Over-Shoot

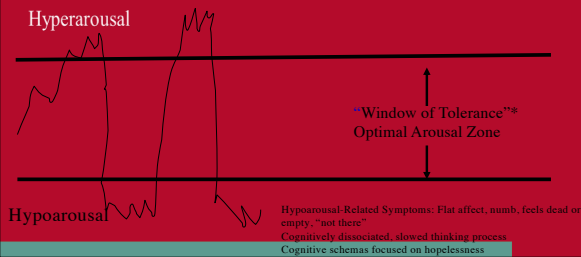
Under-Shoot



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



Client Education

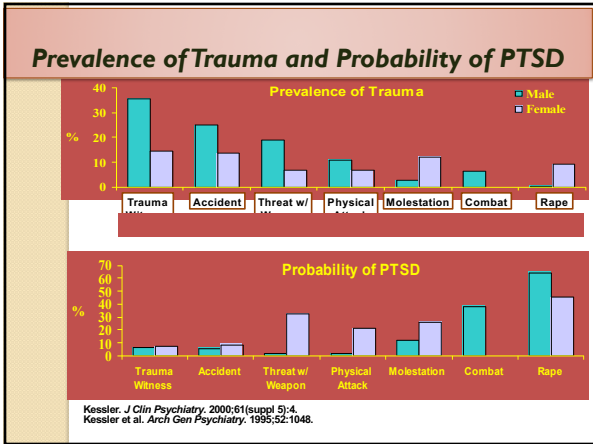
- Though your memory may be temporarily impaired, you can revitalize these areas of your brain by aerobic exercise followed by learning and goal oriented behaviors.

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.



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, 2000)
 - 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

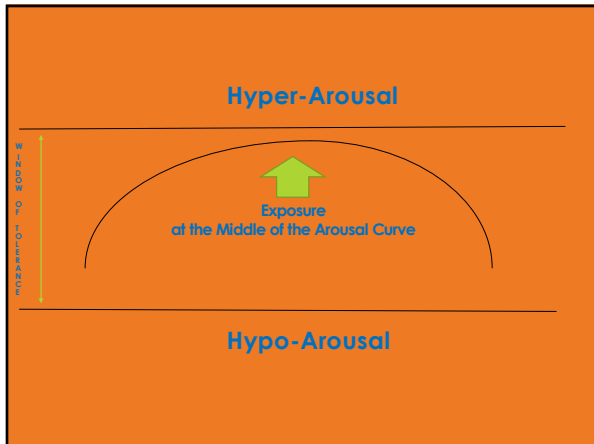
- Traumatic memories are fragmented and disorganized into “hotspots” which can spur flashbacks
- Hotspots occur where there is maximal functioning separation between SAMs and VAMs (i.e. less integration) (Brown, 2005)
- They need to be integrated and converted into a coherent and an organized form to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

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

Delaying 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
 - Counterconditioned

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 requires safety and positive attachment to the principle care givers, attention can be focused on internal awareness and introspection
- 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 (much like parents should have help promote)
 - Facilitating self-exploration and self-reference
 - Helping the client identify, label, accept feelings , and needs
 - Development of a coherent internal life and self-determination

“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 adaptive elevation
- Decreased PICs
- Recalibrated HPA

Orienting Response, REM, and Memory

- Somatic stimulation of the orienting response (i.e. via EMDR, EFT, acupressure etc.) involve:
 - *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
- The shift in attention involves:
 - The orienting response (Sokolov, 1960)
 - Induces REM like state
- Both facilitate cortical integration of memories (Stickgold, 2002)

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.

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.

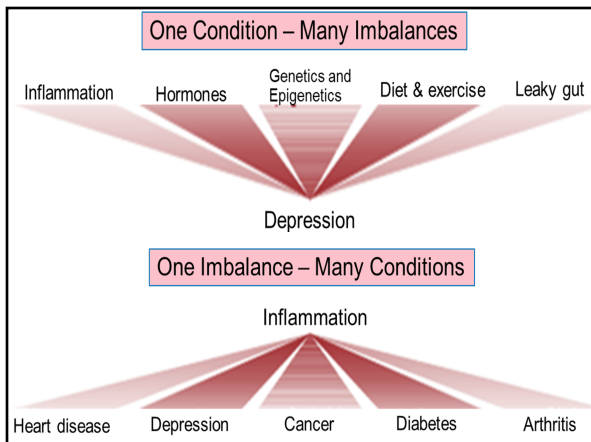
“A” is for acceptance of what happened. No victimization on one extreme or on the other of event(s) that occurred in the past.

“F” is for future. To visualize a hopeful posttraumatic growth.

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

Illness and Depression

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



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).

Pro-inflammatory Cytokines

- PICs the enzyme IDO, which depletes tryptophan
 - Thus, IDO indirectly lowers serotonin. IDO catabolizes tryptophan into kynurenine and its 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,
 - along with reduced ACC, amygdala, and hippocampal volumes, are associated with greater risk for depression

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

Hippocampus and Over-generalizing

- The dentate 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 dentate and CA3 results in black-and-white generalizations (Marenco & Belman, 2000)

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**

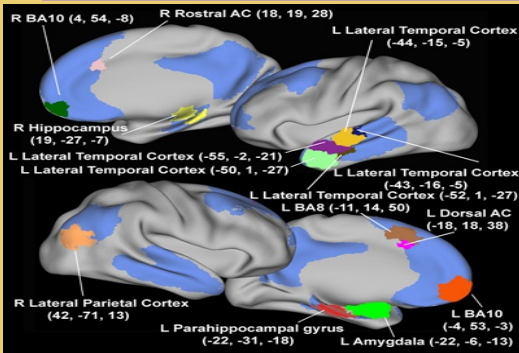
Exercise and Depression

- 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)

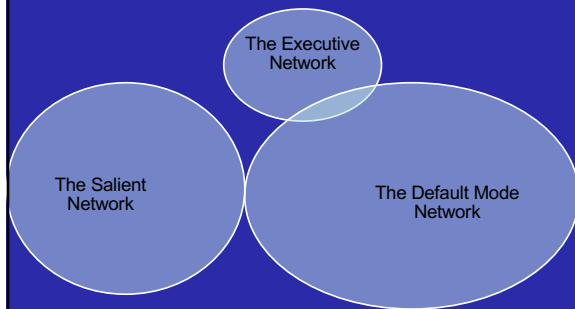
Exercise and Depression

- 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 (Babysak, 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 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 observation 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

Intentionality – breaking out of automatic thoughts and behaviors

Reducing Avoidance -- facing difficulties

Anti-ruminative – here and now focus not the past or future

Meta-Cognitive Awareness: Change your relationship to the thought.

Brain-Based Therapy

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

Working the M-B-G 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

Working the M-B-G Feedback Loops

Interventions that bolster under-active areas of the brain

- **Physiology**
 - 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

Transcendent Awareness

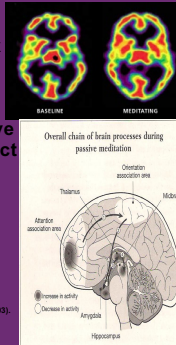
- Mindfulness
- Acceptance
- Forgiveness
- Gratitude
- Compassion

Balancing R-PFC and L-PFC

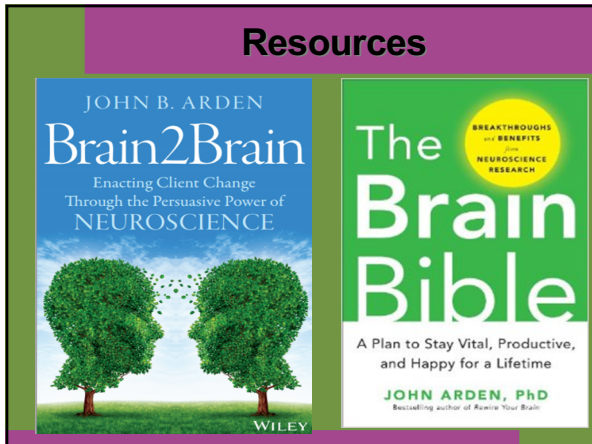
- The forest and trees together—not one or the other
- A symphony—all pieces in synch
- Not passivity—not mindless action but moving with purpose with time
- Mindful action—Zen is not like chopping wood. Zen *is* chopping wood.

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).



Resources



Transcendence

- Pleasure...often fleeting
- Engagement
- Meaningfulness
- Compassion
- Transcending suffering
- (bigger picture)
- The 9th!
-

Sustaining Positive habits

- 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
-

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** (Kabot-Zinn, 1990)

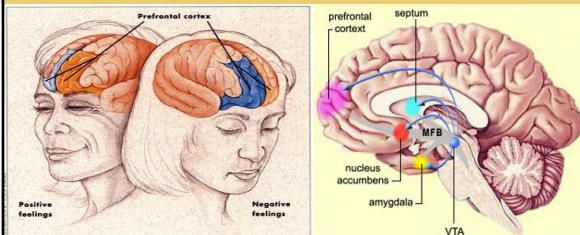
Mindfulness and Open Focus

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

Mindfulness: Brain Changes

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

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



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

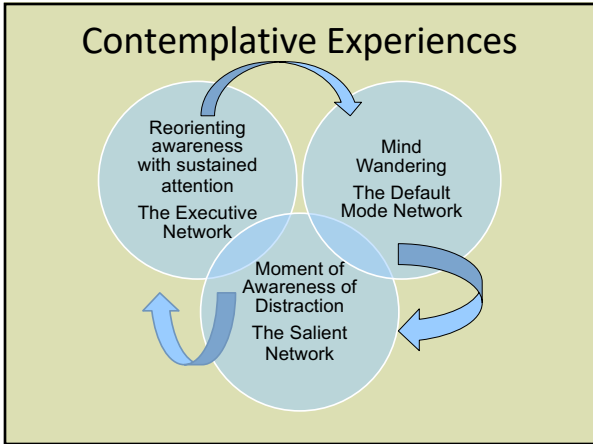
- 1) Breathing Rhythmically—deep, deliberate, and focused breathing allows you to slow your heart beat.
- 2) Focused attention—to the present moment can transform each experience into a rich and calm experience by turning on your brain's brain.

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)



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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
