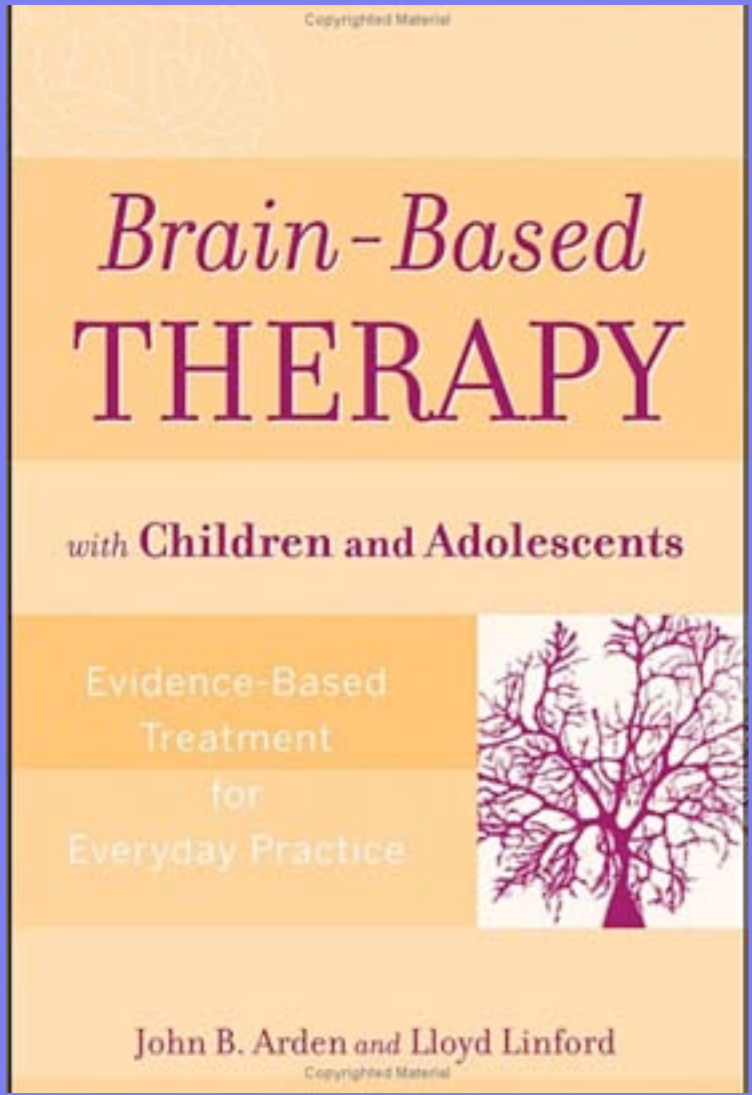
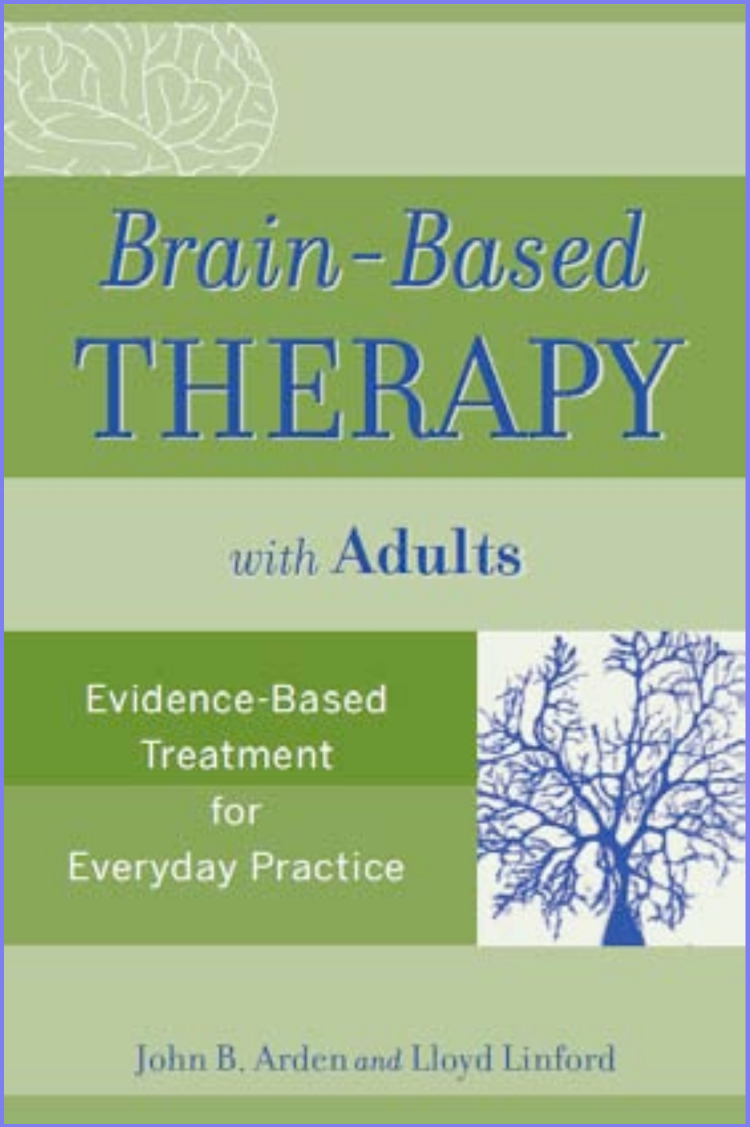
Brain-Based Therapy

John Arden, PhD

With CHILDREN



With ADULTS

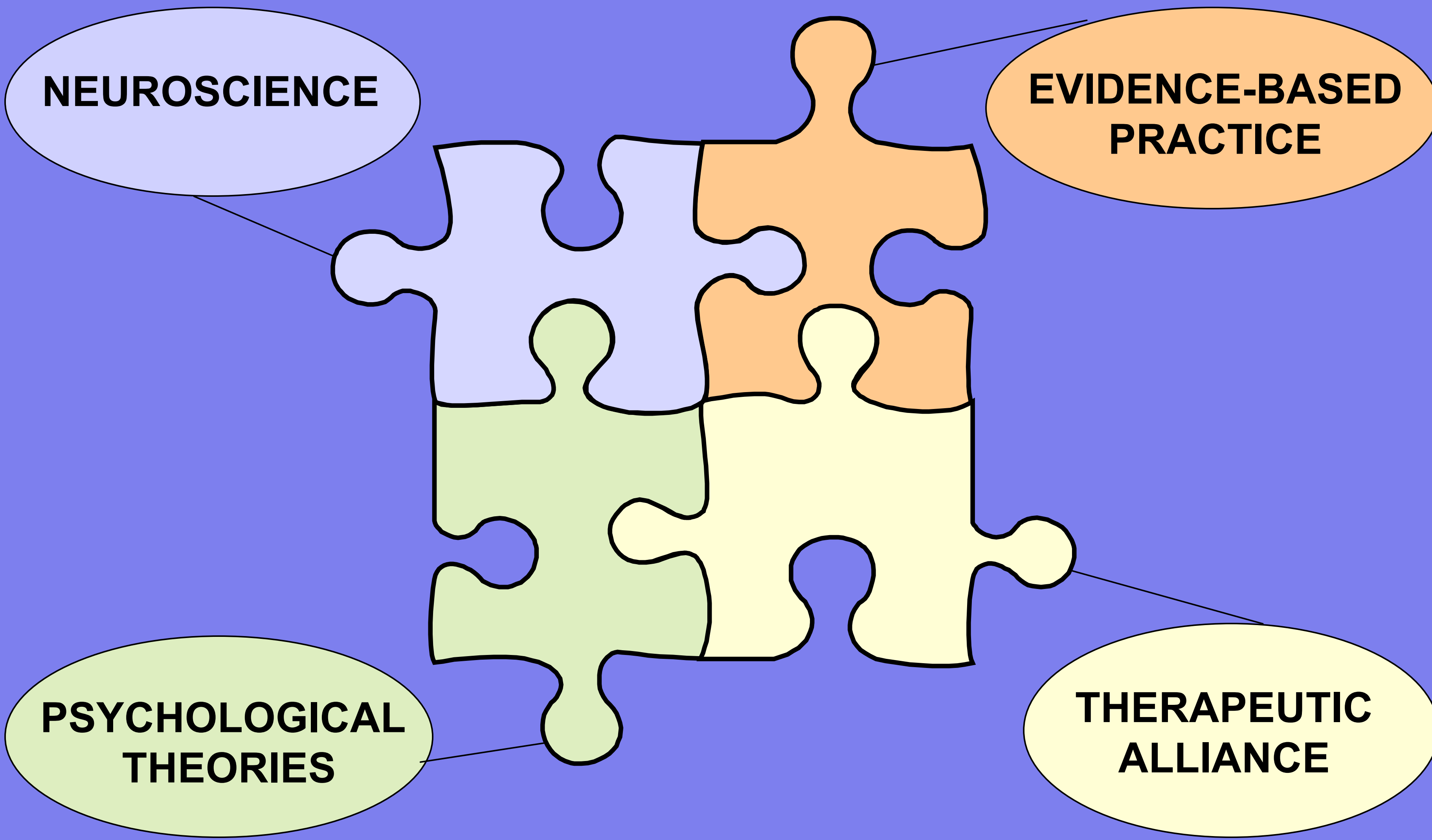

Brain-Based
THERAPY
with Adults
Evidence-Based
Treatment
for
Everyday Practice
John B. Arden and Lloyd Linford

The Day is Now

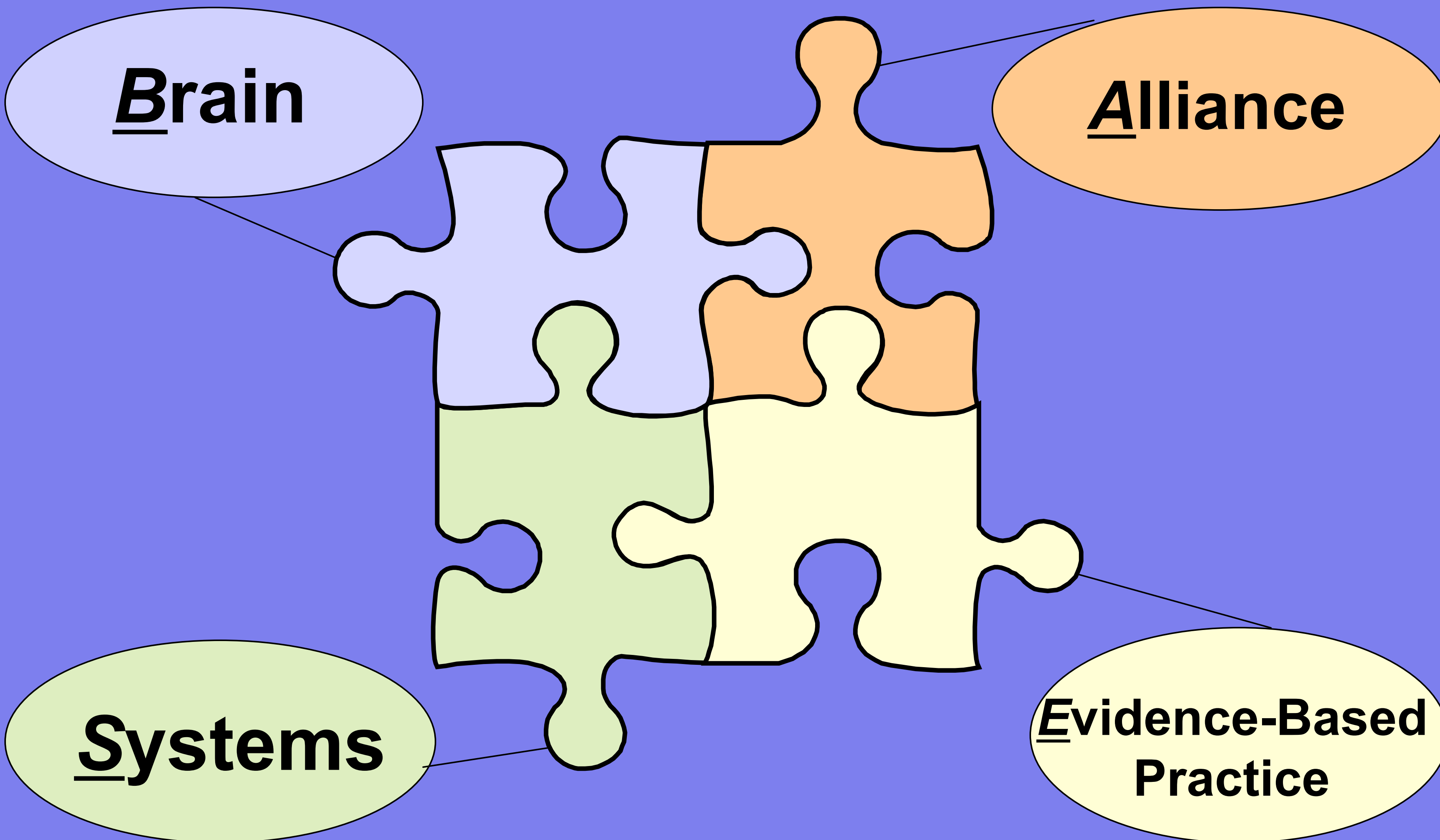
“We must recollect that all of our provisional ideas in psychology will presumably one day be based on an organic substructure.”

--Sigmund Freud

Brain-Based Therapy



The BASE of BBT



Brain-Based Therapy

Joins

- Psychotherapy Research
- Neuroscience
- Attachment studies
- Evidenced-supported treatment
- Developmental Psychology
- Memory research

Day 1: Foundations

1. The Sea Change in Psychotherapy
2. Neuroscience
3. Nurtured Nature
4. Life Span Development
5. Memory
6. SEEDS

Day 2: Applications

- Overview
- Stress, Trauma, and Change
- Panic
- PTSD
- OCD
- Depression
- SEEDS

The Sea Change in Psychotherapy

The “Pax Medica”

After the Cartesian area and Eysenck etc.

-80s brought us:

- **The DSM-III**
- **Prozac**
- **Evidenced-based psychotherapy**
- **The medicalization of psychotherapy**
- **Lots of money**

Pax Romana

Pax Medica: Side Effects

- **Medications removed psychology from psychiatry and moved psychology toward medicine**
  - ***Patients*** **receive** ***treatment***
  - ***Problems*** **became** ***diagnoses*** **per the DSM**
  - ***Diagnoses*** **determine** ***interventions***
  - ***Therapists*** **became** ***clinicians***
  - ***"Medical Necessity"***

Pax Medica

The Good News:

- **The *Pax* brought standards into Psychiatry**
- **It brought scientific rigor to the study of psychotherapy**

The Bad News:

- **A lot of the science wasn't very good**
- **One dimensional**

Pax Romana

Medicalization of Psychotherapy

- Based on DSM dxes, specific techniques
- Managed care
- British NHS/APA: Mandating ESTs
- Diagnosis determines “medical necessity”:
  - Who needs treatment
  - Treatment goals
  - Who gets paid
  - Who gets disability

Managed Dollar

I'm sorry, Mr. Jones, but your
HMO does not pay for enemas.
I'm going to have to slap
the shit out of you.

Cracks in the Empire

<u>SSRIs Revisited</u>

- **A re-analysis of all studies of antidepressant effectiveness revealed that while all 38 positive studies were published, only one of the 40 negative studies made it into print**
- **Positive studies *12 times more* likely to be published than studies finding negative results**

SSRIs

- Debuted in 1974
- Shift from meaning to pharmacology
- Correct “chemical imbalances in the brain”
- By 2005, antidepressants became the most frequently prescribed drug in the US
  - About 1:20 men and 1:10 women use antidepressants
  - 1:20 Americans sees a licensed mental health professional for any type of psychotherapy

Serotonin Revisited

- 50 to 60% of clinically depressed people improve on SSRIs or tricyclics (Quitkin, 2000)
- A meta-analysis of the placebo studies found 42 to 47% efficacy (Arnold, et. al., 2005)
  - That's just 10% less than antidepressants!
  - What about the percentage of antidepressant subjects actually experienced a placebo effect?
- In a re-analysis of the data from a landmark 1985 NIMH depression study, the best performing psychiatrist got better outcomes with placebos than the worst-performing psychiatrist got with imipramine. (McKay et al, 2006)

Serotonin Revisited

- Reducing trytophan from the diet (Delgato, 2000)
  - Didn't effect healthy people w/o a family hx of depression
  - One third of healthy people with a family hx of depression got more depressed (what about the other two thirds?)
  - Two thirds of people tx with SSRIs got more depressed in 5 hours!
  - The drug Trianeptine reduces depressive symptoms but it also reduces serotonin levels (Fuchs, 2002)

Cracks in the Empire

The War Over "Evidenced Based"

- **1980: "The Benefits of Psychotherapy"**
  - » (Smith, Glass and Miller)
- **1995: Barlow and "EBTs" (aka CBTs)**
- **2000: Lambert, Norcross, and Miller counterattack with outcomes**

Outcome Data

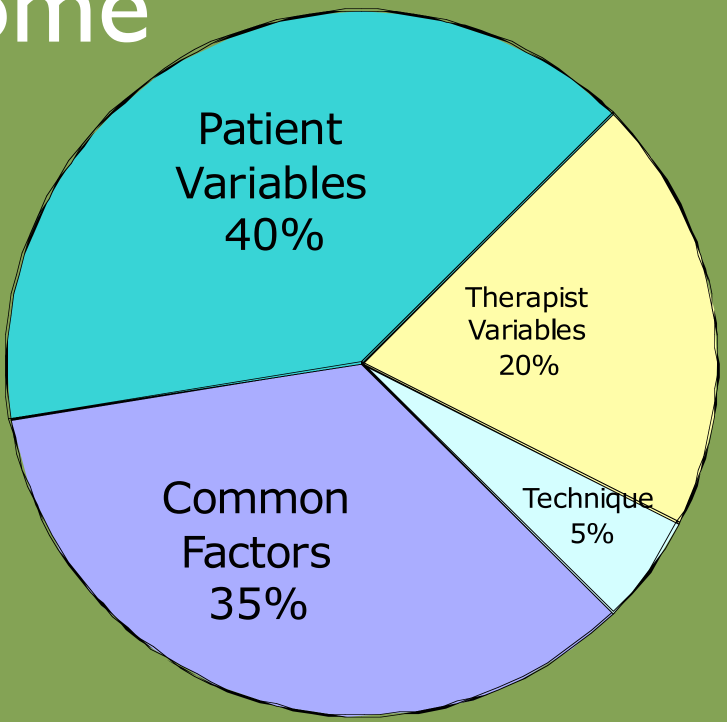
- 43% of patients recover without therapy
- Therapists are poor judges, not just of the outcome of a complete therapy, but even of a single session
- We overvalue our own competence and undervalue that of our colleagues:
  - 80% of the therapists consider themselves “better than the average” therapist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

__The Modern Era: 2000-2011__

Psychotherapy Research

Factors affecting outcome

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

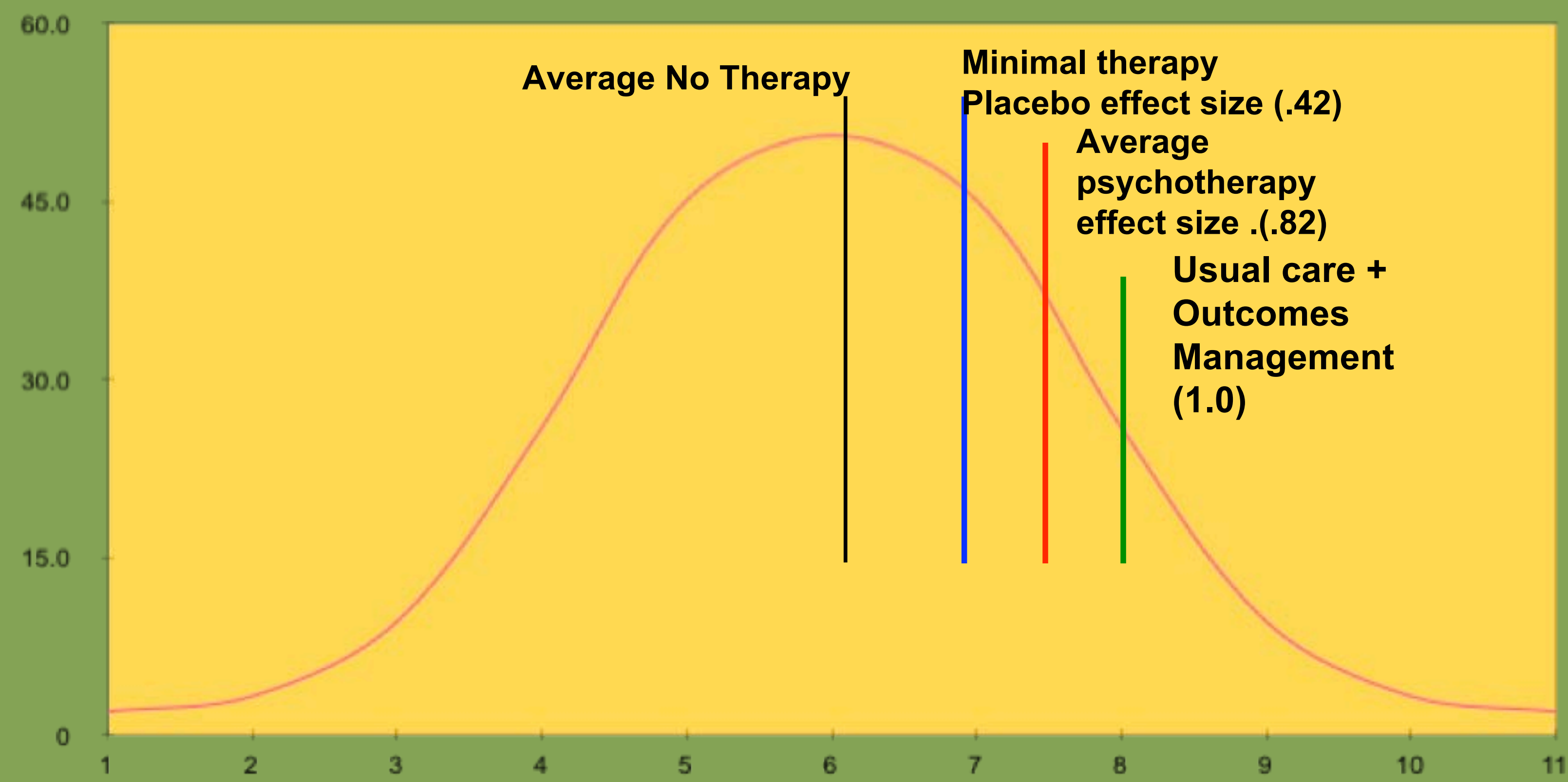


After Lambert and Ogles, 2004

“Common Factors”

- Client understands and agrees with treatment plan
- Consistency
- Trust and hopefulness
- Boundaries and confidentiality
- Positive regard

40 Years of Psychotherapy Research



- *-- After Lambert, Weber & Sykes, 1993*

Attachment and Psychotherapy

- **The therapeutic alliance challeges:**
  - The interaction of the attachment systems of therapist and client
  - Rewires the brain's emotional and attention-regulation systems
- **What makes the "talking cure" work?:**
  - When **firing patterns that have been established during attachment** are activated in **therapy by trust and hopefulness,** they can be **integrated and regulated**

Therapist Insecurity

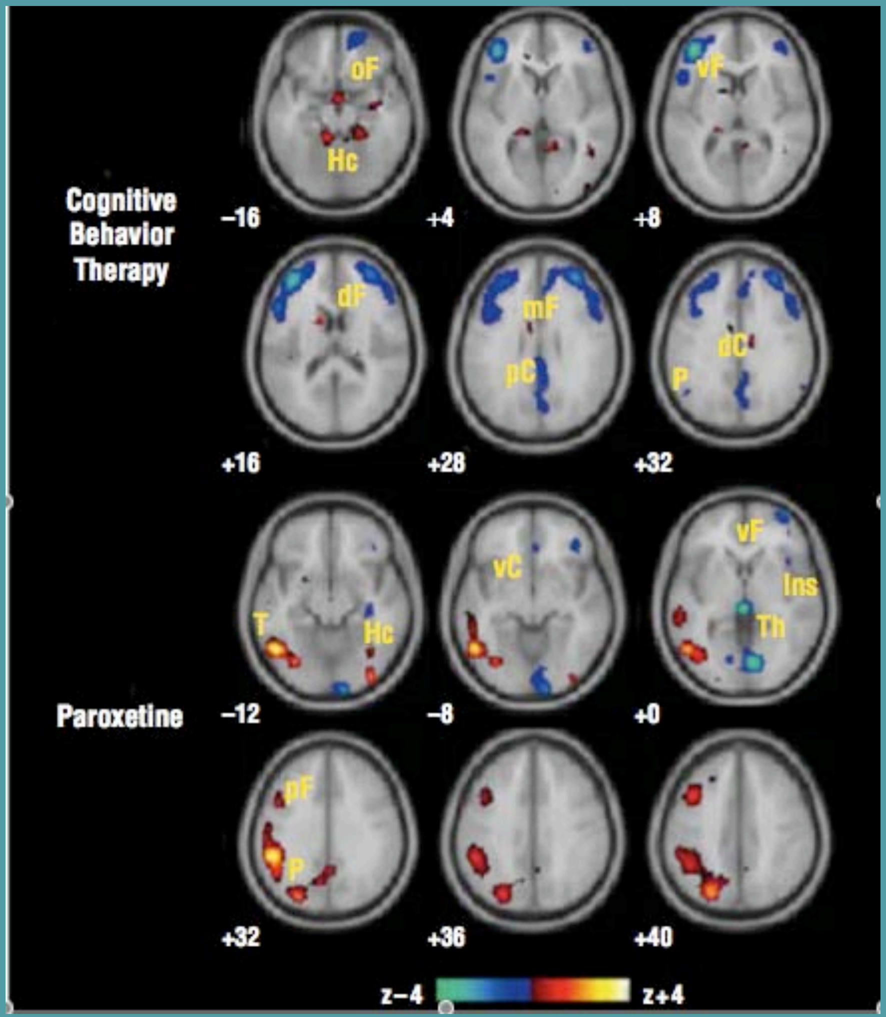
- Insecure therapists are likely to experience temporary breaches as failures or personal attacks
- They are more likely to misuse neutrality, misunderstand intersubjectivity, or hide behind cognitive or theoretically driven interventions
- Research shows they get worse outcomes

After the *Pax*

- **Demands for accountability will only increase**
- **We need a therapy that includes:**
  – The biological realities of human nature
  – The lessons of 40 years of psychotherapy research
  – The wisdom of major theories and interventions
  – Checks on subjective evaluations of progress and attunement

Worth a Thousand Words

Psychotherapy changes the brain



Goldapple, Segal, et al. (2004). *Arch. Gen. Psych.*, *61*, 34–41.

Psychotherapy and the Brain

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

- **Reduced amygdalar activity in treated phobics** (Straube, *et al.,* 2006), **panickers** (Prasko *et al.,* 2004), **and social phobics** (Furmark *et.al,* 2002)
- **Reduced frontal activity in treated depressives** (Goldapple *et al*., 2004)
- **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)

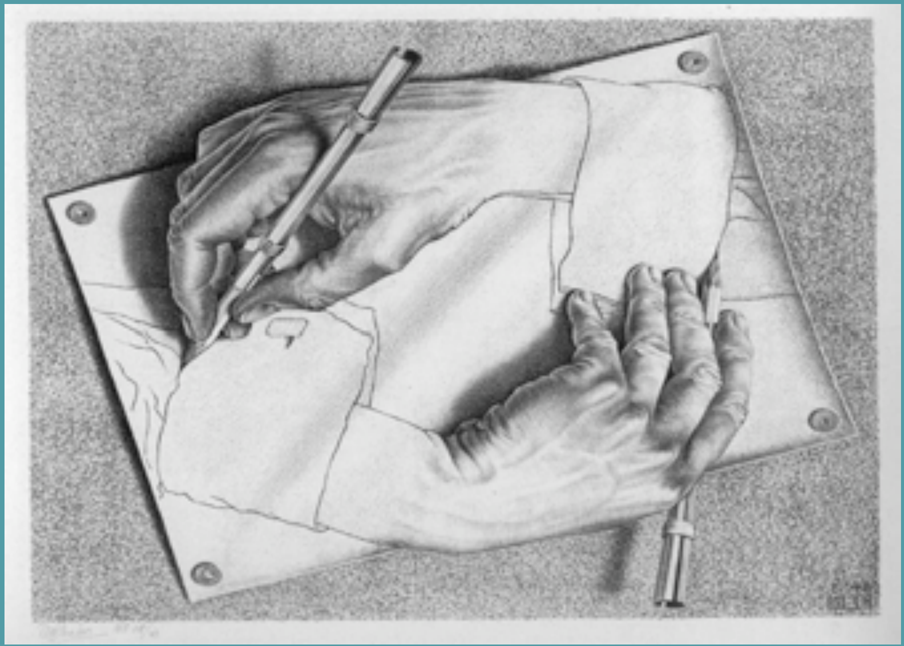
Brain-Based Therapy

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

Brain-Based Therapy

- Discriminates between what is therapeutic and what's not
- Includes techniques consistent with how the brain works
- Relies on the therapist's alliance with the client
- Employs <u>common denominator</u> methods of psychodynamic therapy, CBT, IPT, mindfulness, etc.

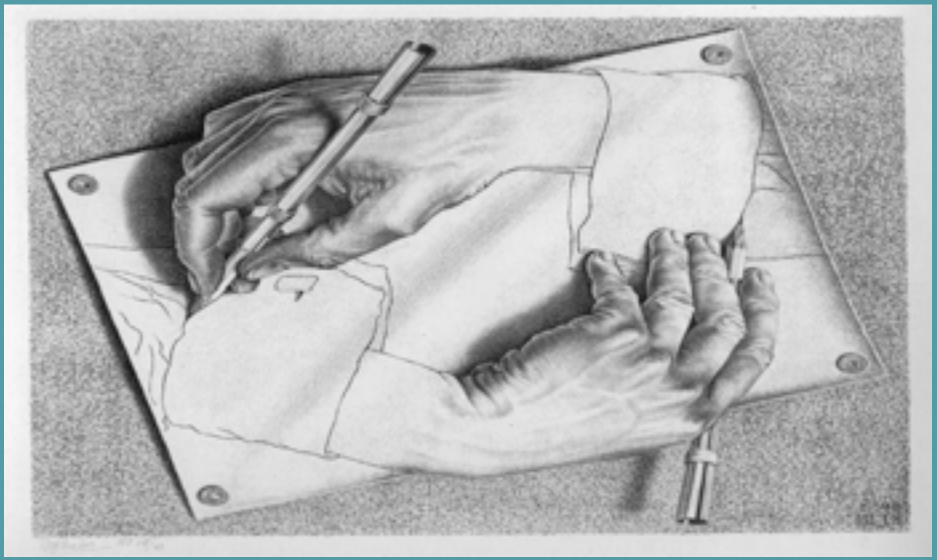
BBT: The BASE



- **B** is for Brain
- **A** is for Attunement
- **S** is for Systems of psychological theories and intervention
- **E** is for Evidenced-based Practice

The Future and Brain-Based Therapy

- Neuroscience
- Outcome Management
- Attachment/ Alliance

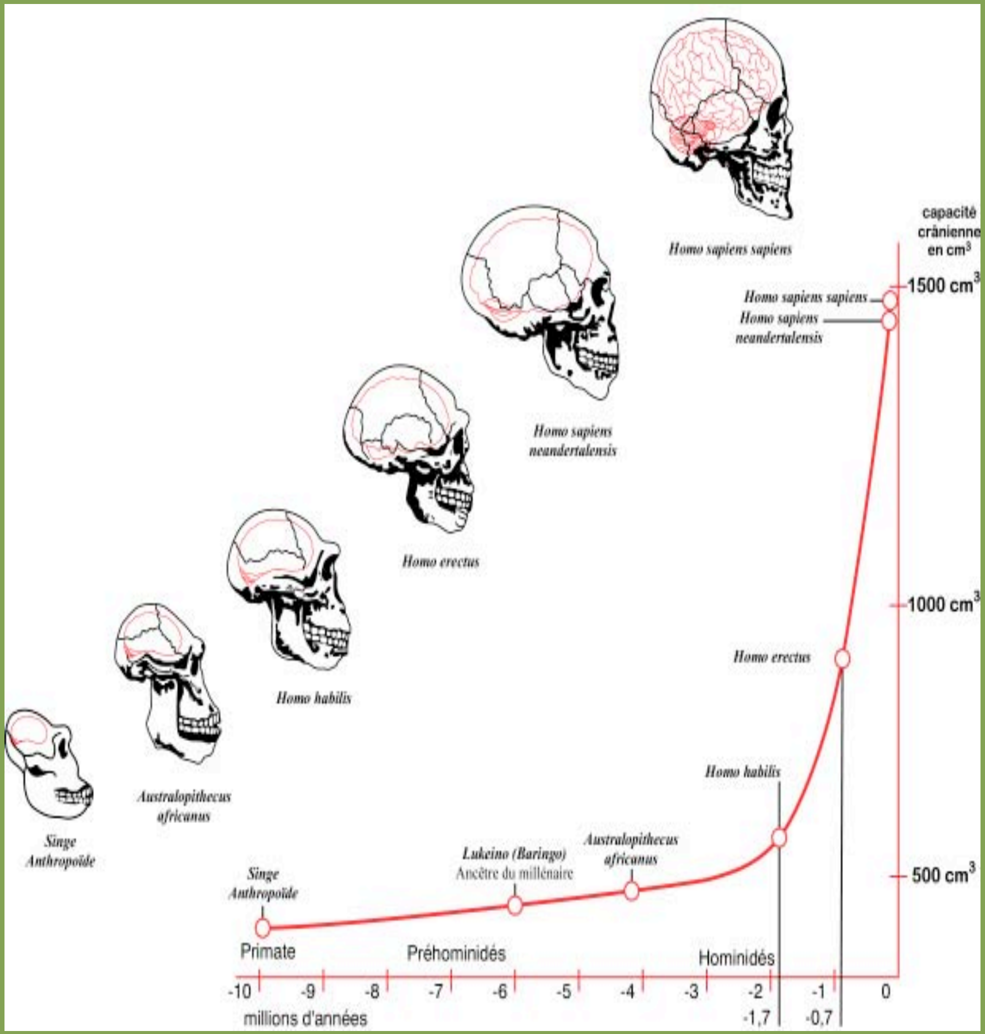


- Evidence-Based Practices
- S.E.E.D.S.

Brain Evolution

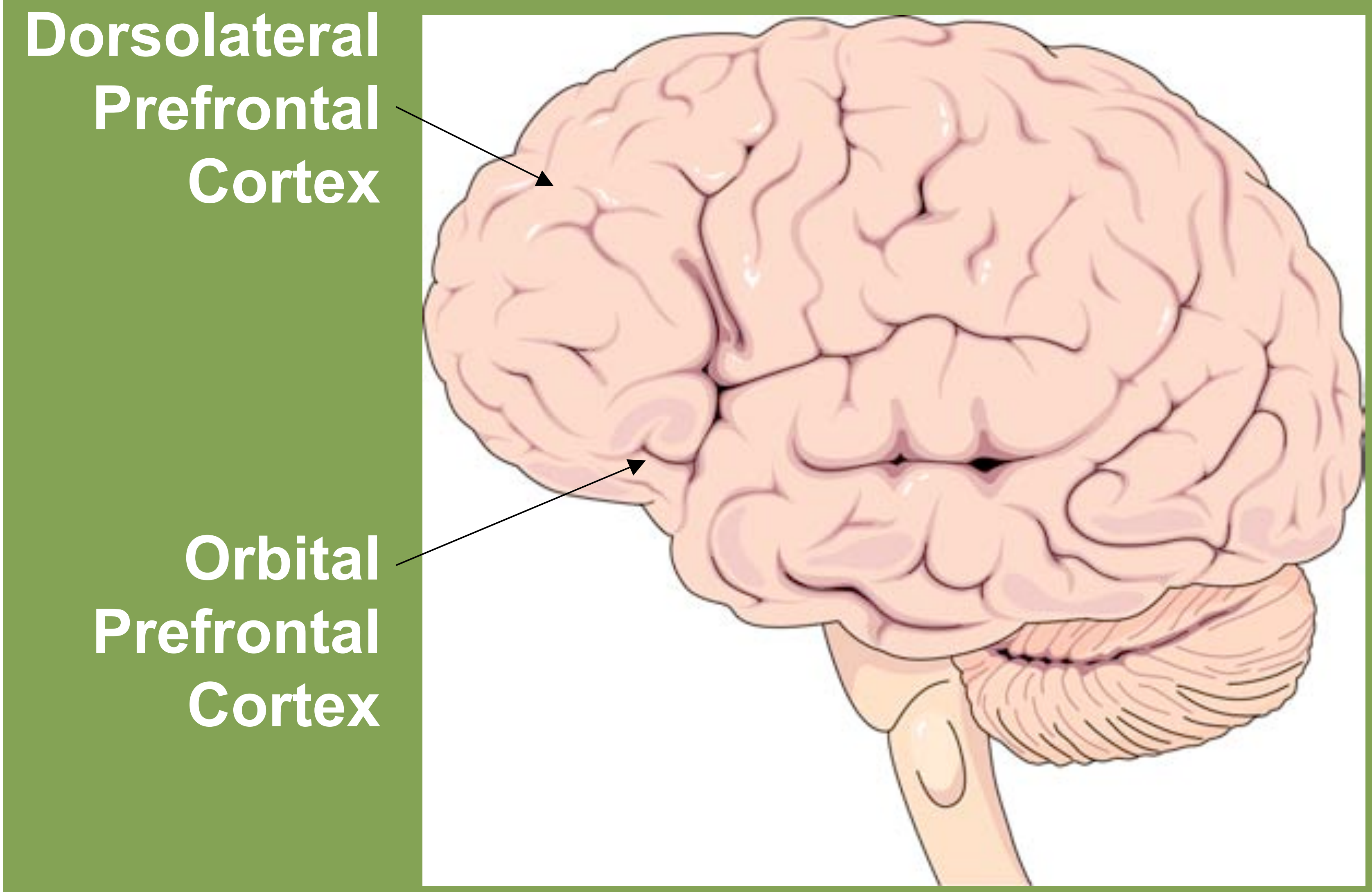
- Human evolution is the story of growth & increased complexity of the cortex

- PFC- 20% of the human brain is comprised of the frontal lobes
(FYI - 3.5% of the cat's brain is in the frontal lobe)



Pre-Frontal Lobes

- The "Executive" brain –Executive control center
- Motor pre-frontal lobes are last to myelinate – e.g., teenagers
  - Identity
  - Insight
  - Sense of Self
  - OFC part of the "limbic system"

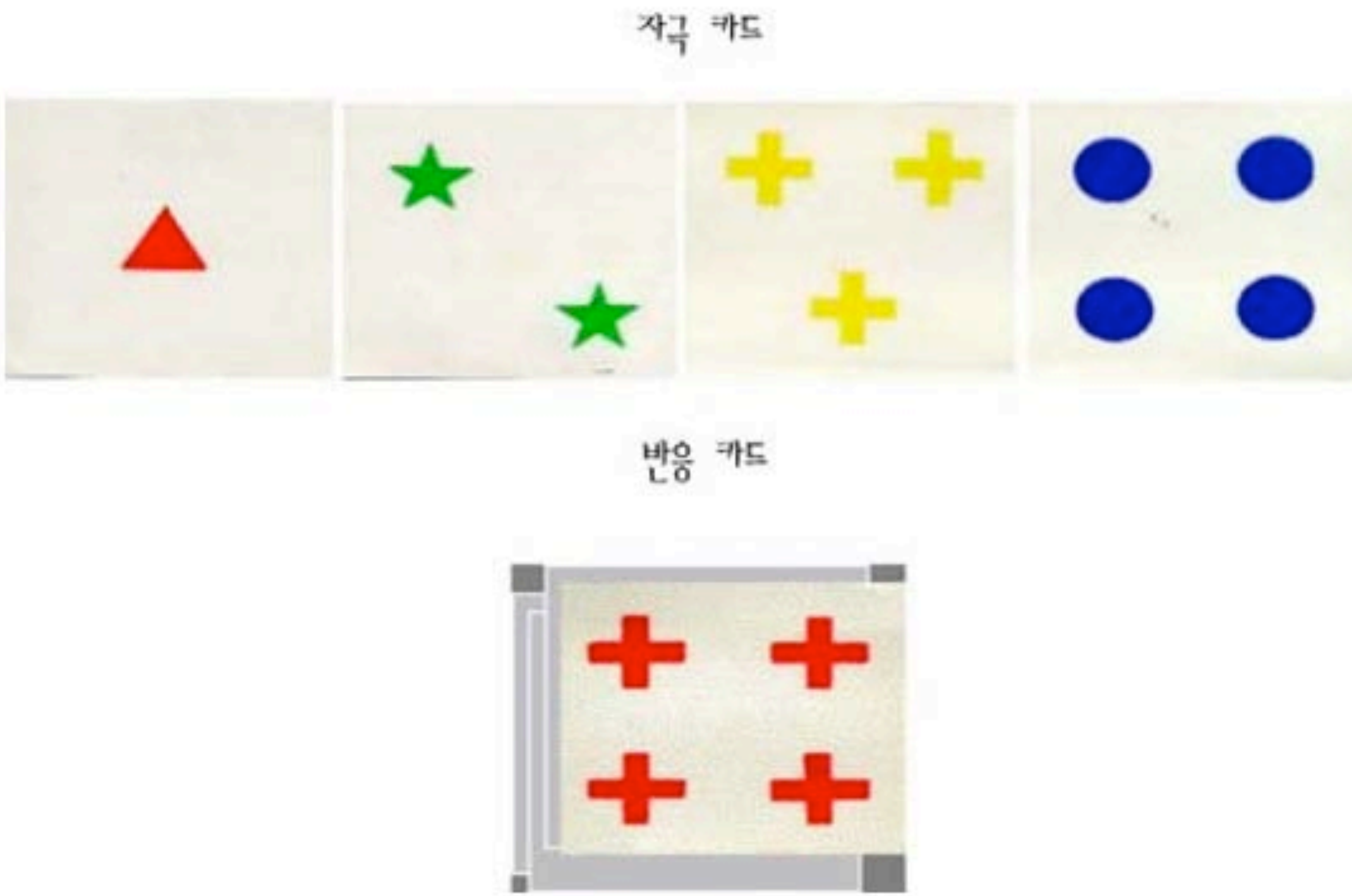


Dorsolateral Prefrontal Cortex
Orbital Prefrontal Cortex

Pre-Frontal Cortex

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

Wisconsin Card Sorting Test (WCST)



Phineas Gage

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)
- Reverse-learning tasks include :
  - Ability to evaluate, integrate, and act on environmental cues
  - To stop responding to something when it becomes unhealthy and shift back to

New Discoveries in Neuroscience

- Affect Asymmetry –set points
- The Amygdala—fast and slow tracks
- Default Mode Network
- Neuroplasticity
- Neurogenesis
- Mirror neurons
- Spindle Cells
- Nutritional Neuroscience

Affect Asymmetry

Set points

LEFT FRONTAL LOBE

- Positive emotions
- Approach behaviors
- Labeling thoughts and feelings and
- Developing new narratives (helps to alleviate anxiety and depression)

RIGHT FRONTAL LOBE

- Negative emotions
- Withdrawal behaviors
- Feeling overwhelmed

Alexithymic pts. have smaller right

Cs

larger right ACCs--more fearfulness

Neuroplasticity

- Donald Hebb (1904-1980)
  - Brought lab rats home for his kids to play with
  - Back at the lab they learned more quickly than cage-bound rats
  - They had developed bigger, heavier brains
  - *"Neurons that fire together, wire together."*

Neuroplasticity

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

Neuroplasticity

- Changes in synaptic efficacy
  - Increases in receptor density
  - Up-regulating their activity
  - Glial cell availability
  - Changes in the shape and structure of synapses

Examples of Neuroplasticity

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

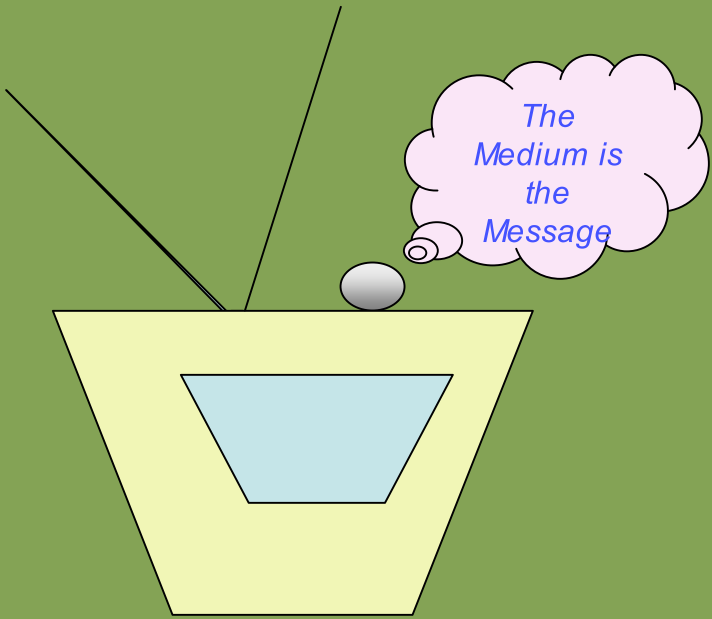
Examples of Neuroplasticity

- Musicians using specific fingers to play their instruments showed enlarged areas of their somatosensory strips associated with those fingers. (Pantev, et al, 2001)
- Blind Braille readers showed enlarged cortical areas associated with their reading finger compared to blind non-Braille readers and to sighted people. (Pascul-Leone & Torres, 1993)

Brain Environments

Enriched Environment

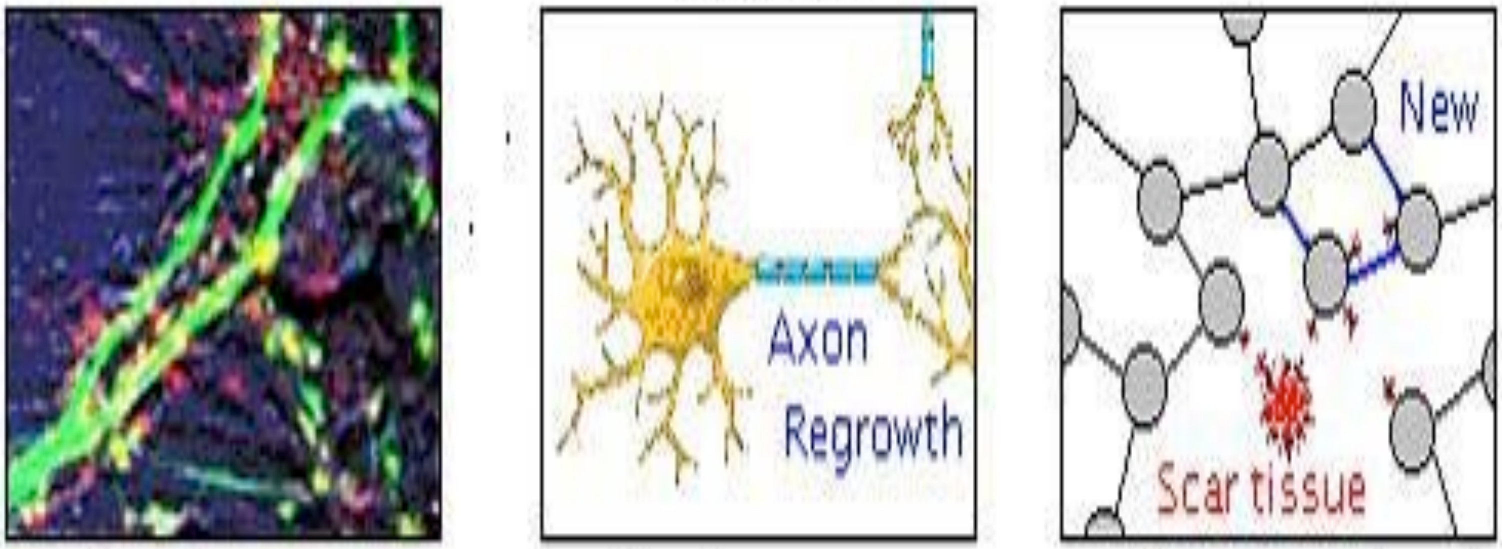
Impoverished Environment



"Your Brain on TV"

Examples of Neuroplasticity

Figure (iii)



a – Actual new synapse

b – Simple new synapse

c – New connections in Neural Network

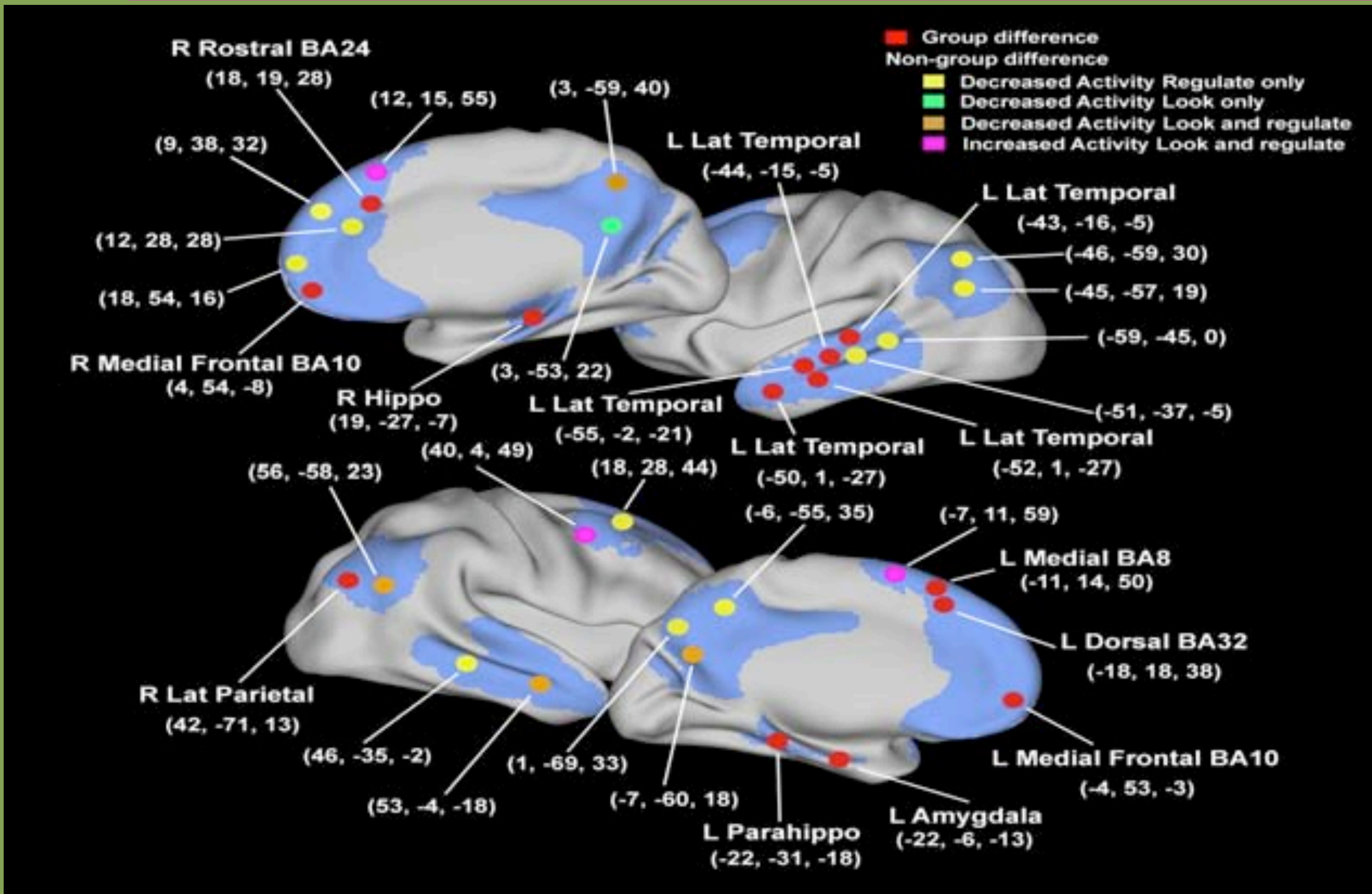
Default Mode Network (DMN)

- At work when the brain is "resting": ie. day dreaming etc
  - 30% of waking hours
  - Using 20xs as much energy as when you are paying attention to something
  - Only 5% more to pay attention above baseline (DMN)

Areas identified as part of the DMN

- – Medial parietal (including the posterior cingulate and adjacent precuneus) involved in remembering events in one's life
- – mPFC (including the ventral anterior cingulate cortex)—involved in imagining what others are thinking as well as our own emotional state
- – Critical for the sense of "self"

Task-induced activity in the default mode network



Sheline Y I et al. (2009)

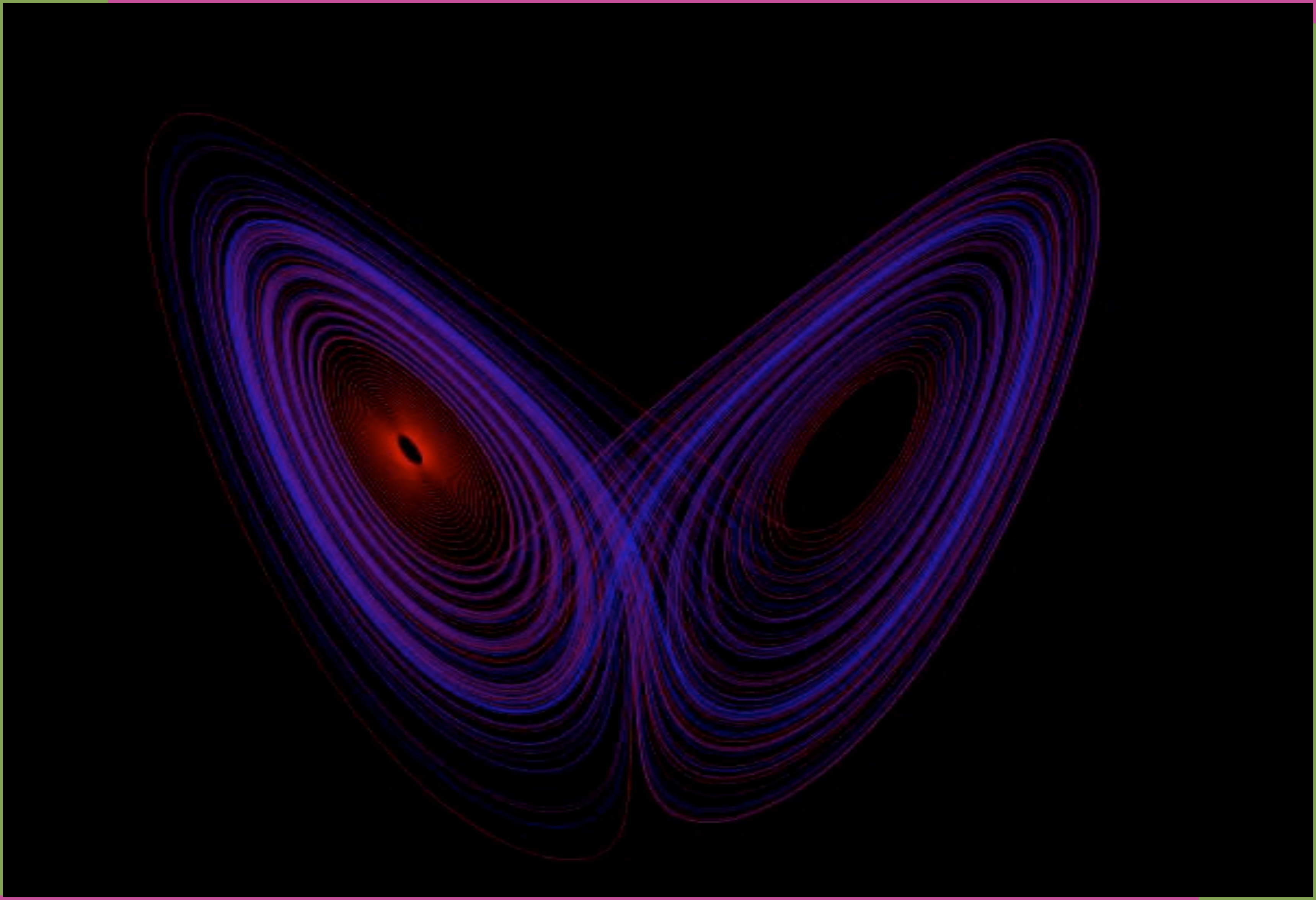
DMN Variations

- Increases when DLPFC is not engaged:
  - Stressed, bored, no novelty, or tired
- Malfunctions in the DMN:
  - Schizophrenia—defective mPFC—impaired self reflection—not sure where thoughts come from
  - Depression—obsessive ruminations over negative experiences
- Need meta-awareness for creativity

Neurodynamics

- The brain is a complex system characterized by nonlinear change
  - Pax Medica employs linear causes/effects
- Complex systems:
  - Tend toward increasing complexity, i.e., they are self-organizing
  - Maintain continuity *and* flexibility
  - Need new inputs to expand (a lake vs. a pond)

A Lorenz Attractor



Neurodynamics

- The brain dwells in a chaotic but stable state
- In far-from-equilibrium conditions
- Sensitive dependence on initial conditions
- Attractors:
  - Strong attractors require little energy
  - Weak attractors require energy and effort
- Networks that require the smallest energy-expenditure occur effortlessly
- Emotions act as attractors – “motivate”

BBT & Neurodynamics

- Affect regulation can be seen as a type of “self”-organization
- Look for periods of flux (readiness for change)
- A thought or feeling can trigger a ripple effect, leading to a change of plans
- States (weak attractors) become traits (strong attractors)

BBT Strives to:

- Induce repeated states (weak attractors)
  - (i.e. positive moods)
- Repeat often enough so they become traits – (or strong attractors)

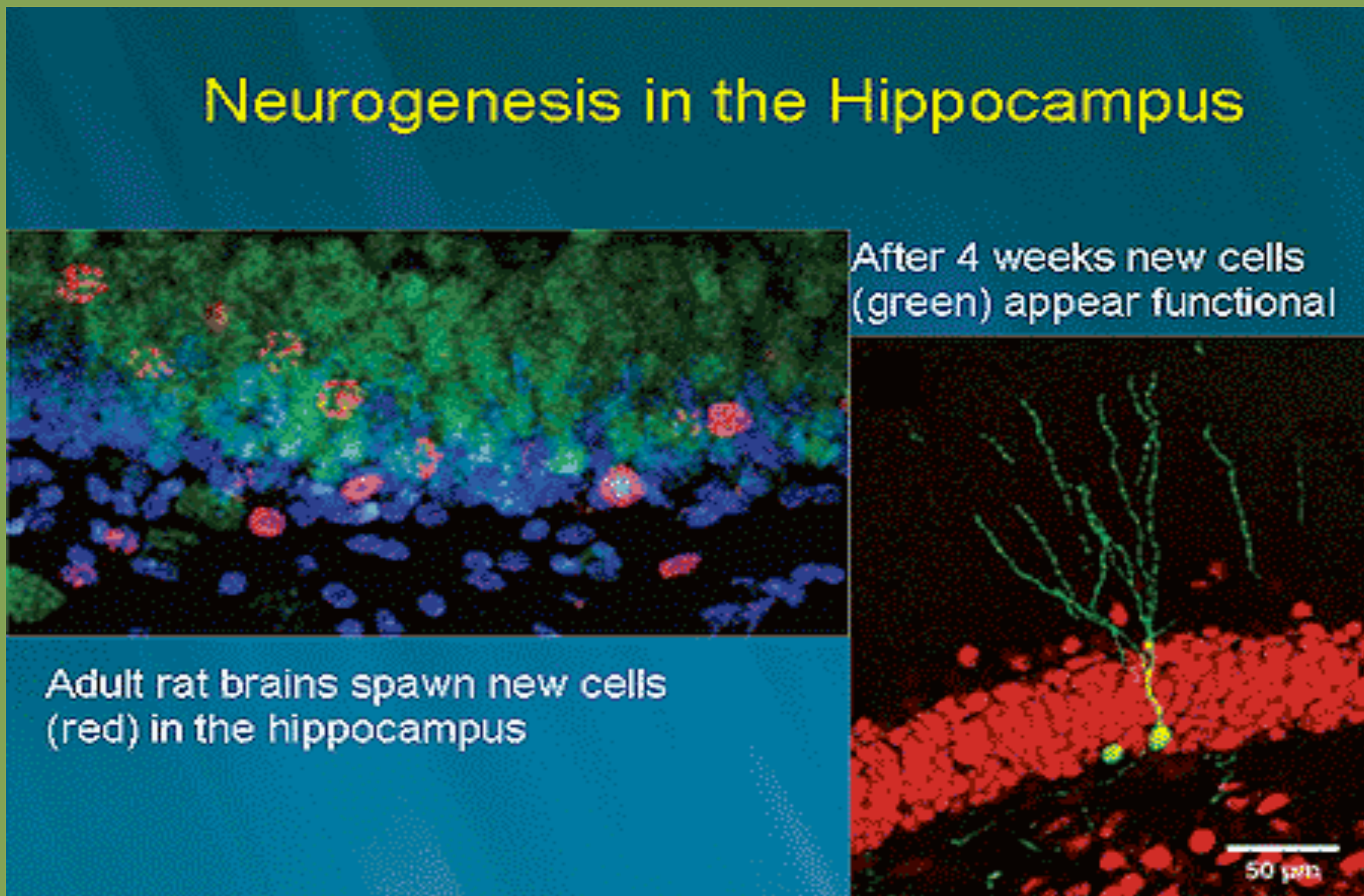
A Mnemonic "Recipe" for Feeding Your Brain

- Focus
- Effort
- Effortlessness
- Determination

Brain Derived Neurotropic Factor

- BDNF plays a crucial role in reinforcing neuroplasticity and neurogenesis.
- BDNF is like Miracle Grow to help:
  - Consolidate the connections between neurons.
  - Turn on the nucleus basalis to focus attention, deciding what's important for neuroplasticity
  - Promotes the growth of myelin to make your neurons fire more efficiently
  - Acts on stem cells in the hippocampus to grow into new neurons

Neurogenesis



Factors that Decrease Neurogenesis

- Aging
- Chronically high cortisol
  - Chronic stress
  - Recurrent depression
- Radiation
- TBI

Factors that Increase Neurogenesis

- **Exercise**
- **Fasting**
- **Fewer calories consumed**
- **Type of food content (Omega—3 from algae**
- **Antidepressants**

Regulatory Networks of the Social Brain

- Bonding/Attachment
- Affiliation
- Fear Regulation
- Affect Regulation
- Safety

The Effects of Social Medicine

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

Systems of the Social Brain

- Brain Structures
  - Orbital Frontal Cortex (OFC)
  - Amygdala
  - Insula
  - Cingulate
  - Mirror Neurons
  - Spindle Cells
  - Facial expression modules

Systems of the Social Brain

- Neurotransmitter systems include:
  - Oxytocin
  - Dopamine
- Central Nerve
  - Vagus Nerve

Close and Trusting Relationships

- Activation of excitatory and growth-enhancing neurochemicals
- Oxytocin and Vasopressin stimulate protein synthesis necessary for neuroplastic processes in networks of the social brain

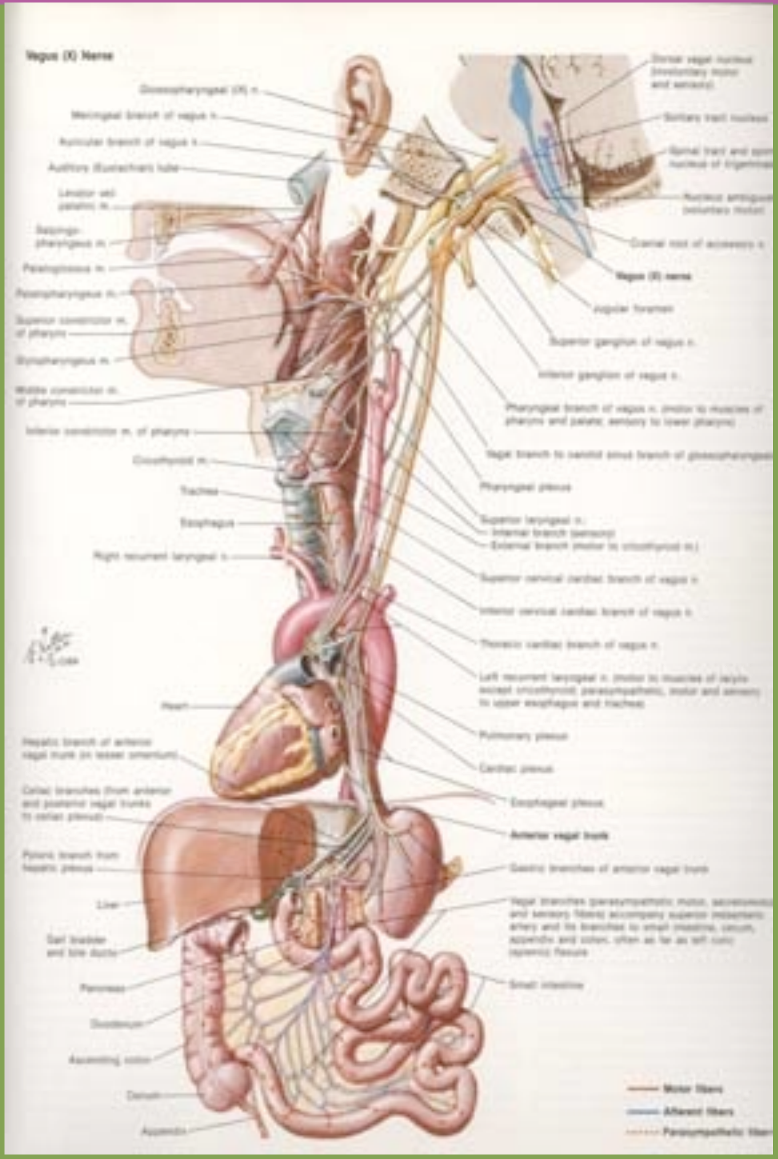
(Insel, 1997; Ostrowski, 1998)

The Vagus Nerve

• 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.

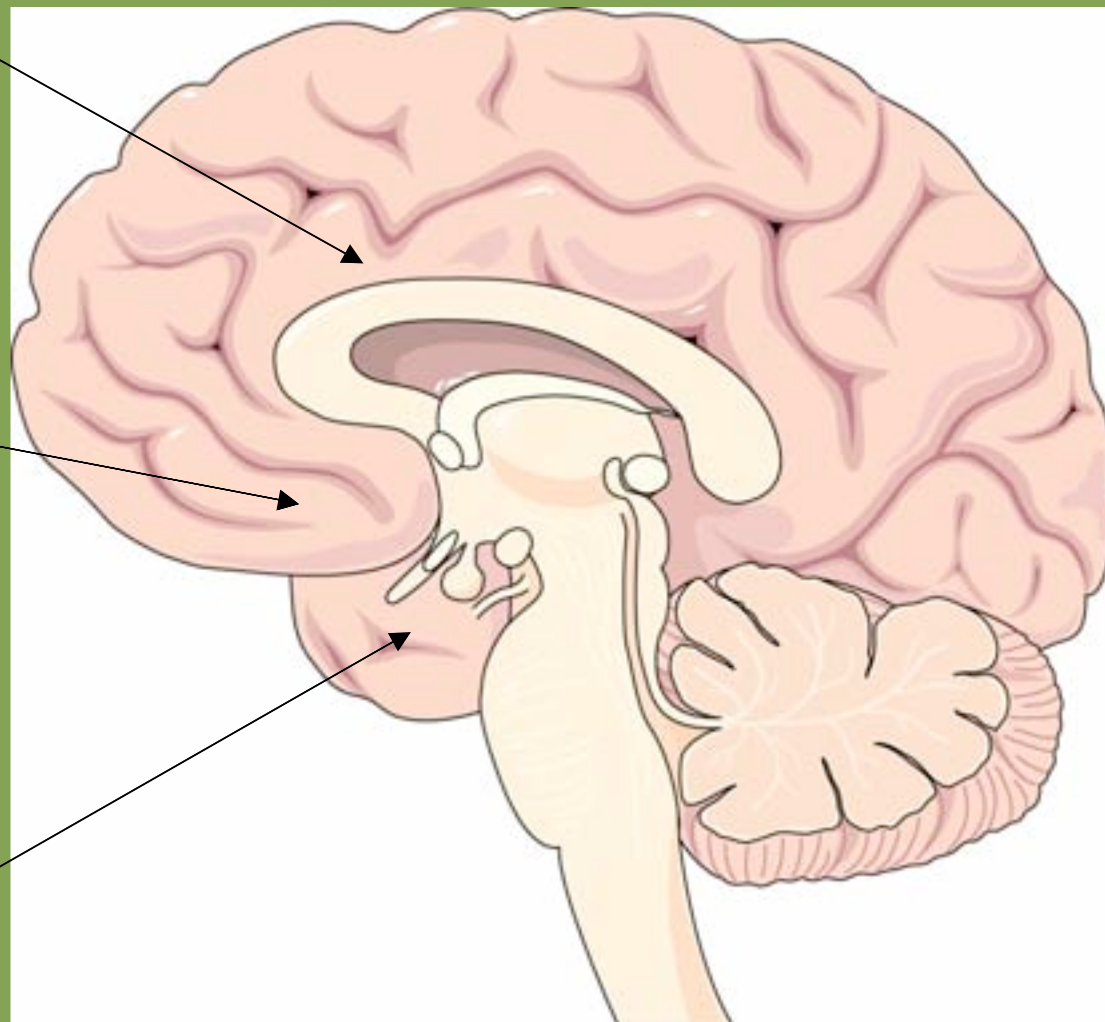


Variations in Vagal Tone (Porges)

- *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

Vagal Brake (Porges)

- Dorsal vagal complex extends down into abdominal organs (i.e. heart)
  - A mechanism to slow heartbeat
    - Acetylcholine and oxytocin
  - When brake is off:
    - ↑ heart rate (life feels like in a constant state of emergency)
    - ↑ allostatic load


Cingulate Cortex
Orbital Frontal Cortex
Fusiform Gyrus

Cingulate Cortex

- Active when detecting emotional signals from self and others (Critchley, et al., 2004)
- Part of neural basis for cooperation (Pilling, et al, 2002)
- ACC integrates cognitive and emotional information from cortex (Bush, et al, 2000)
- Damage results in reduced empathy and/or maternal behavior (Brothers, et al., 1996)
- Posterior cingulate: autobiographic memory and emotional processing (Critchley, et al, 2003)

Insula

- 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": serves as an intersection of body and cortex for experiencing empathy (Carr, et al, 2003)

Drug/Alcohol Cravings & Attention Deficits

- Cocaine addicts have smaller cingulates, insulas, and PFCs (Franklin, et al, 2002)
- Same reward system is active with flirting and bonding (Panksepp, 1998)
- The OFC and ACC activate when addicts crave, binge, and are intoxicated (Goldstein, 2002)
- The same system deactivates during withdrawal

Mirror Neurons

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

Theory of Mind

- Amygdala
- Insula
- Anterior cingulate (Siegal & Varley, 2002)
- The R-OFC -- decoding mental states
- The L-OFC -- reasoning about those states (Sabbagh, 2004).
- There may be three major nodes:
  - the medial prefrontal cortex for self-related mental states;
  - the superior temporal sulcus for goals and outcomes
  - the inferior frontal area for actions and goals (Frith & Frith, 1999)

- **Intersubjectivity** as "the sharing of subjective states by two or more individuals
  - in psychoanalytic therapy, the interrelations between analyst and analysand.
  - The non-verbal communication of infants, young children, and their parents. (Stern)
- **Mentalization** --the ability to understand the mental state of oneself and others.
  - Individuals without secure attachment have difficulties in the development of mentalization-abilities. (Fonagy)
  - Securely-attached individuals tend to have had a mentalizing primary caregiver, and resultantly have more robust capacities to represent the states of their own and other people's minds.

- **Metacognition** is defined as "cognition about cognition", or "knowing about knowing."
  - Includes knowledge about when and how to use particular strategies for learning or for problem solving.
- **Theory of mind** –the ability to attribute mental states—beliefs, intents, desires, pretending, knowledge of to others
  - to oneself and others and to understand that others have beliefs, desires and intentions that are different from one's own.

Spindle Cells

- Found in abundance in the insula and ACC
- Respond extremely quickly—“Behavioral Flexibility”
- Involved in making snap judgments, and solving complex problems in emotionally stirring situations
- Vulnerable to neglect, abuse, and trauma

Facial Expressions

Left Hemisphere	Right Hemisphere
• Controls expression on the right side of face	• Controls expression on the left side of face
• Is NOT adept at reading facial emotion expression (e.g. alexithymics)	• Is adept at reading facial emotion expression

Facial Expressions

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

D Smiles

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

Duchenne 1862 Stimulating Facial Muscles

Facial Expressions

- Therapists can model and influence the patient’s facial expressions and mood via the mirror neuron system
- Feedback system:
  - 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)


A
B
C

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)

Laughter is Good Medicine

- Improves cognitive function (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)

Kindling Laughter Circuits

Breathing out with laughter triggers the vagal nerve and the parasympathetic nervous system

↓heart rate

↓blood pressure

↑relaxation

Laughter module

Supplementary motor area (SMA)

From the SMA to the insula

To the amygdala

Through mirror neurons both experience mirth and shared understanding

Psychological Boost of Humor

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

EMOTIONS


anger
① eyebrows down and together
② eyes glare
③ narrowing of the lips


happiness
A real smile always includes:
① crow's feet wrinkles
② pushed up cheeks
③ movement from muscle that orbits the eye


sadness
① drooping upper eyelids
② losing focus in eyes
③ slight pulling down of lip corners


disgust
① nose wrinkling
② upper lip raised


surprise
Lasts for only one second:
① eyebrows raised
② eyes widened
③ mouth open


fear
① eyebrows raised and pulled together
② raised upper eyelids
③ tensed lower eyelids
④ lips slightly stretched horizontally back to ears


contempt
① lip corner tightened and raised on only one side of face

Brain-Based Therapy

- Close and Trusting Relationships (Attachment)
- Activation of Moderate States of Arousal (Challenge)
- Activation of Affect and Cognition (Multimodal)
- Co-Construction of New Narrative (reconsolidating memories)

The Therapeutic Brain

- Psychotherapy requires neuroplasticity
  - States to traits
- Keep brain bias toward PFC and hippocampal vs. amygdala learning states
  - Affect regulation -- “self”-organization
- Bumping the set point
- Making the DMN useful

Shift in Approach

BBT:

- Teaching people about their brains boosts confidence in therapy and externalizes the problem
- Encourages the alliance and discourages resistance
- “This is our common project”

Client --Take Home

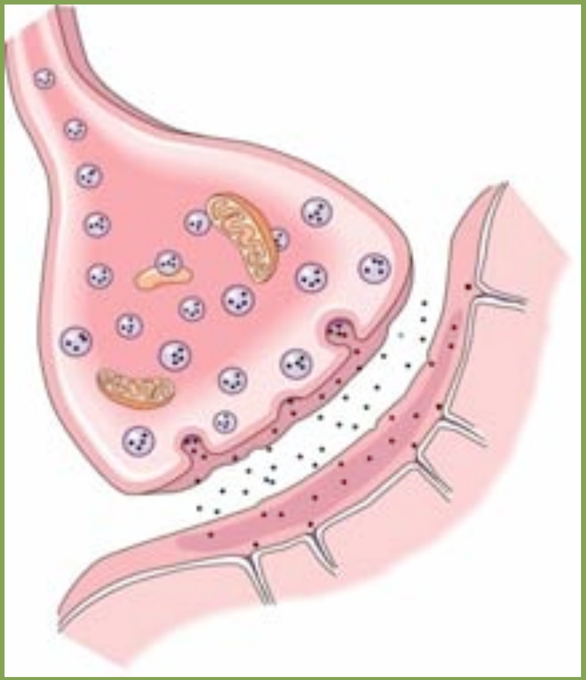
BBT:

- “To rewire your brain, you will need to do some things you don’t feel like doing….”
- Moderate anxiety is a good thing….it helps neuroplasticity
- “Don’t worry, I’ll be there with you as your partner.”

4. Developmental Neurobiology

The Developing Brain

- Born with twice as many neurons as mother (for redundancy) allowing for sculpting (pruning) --experience dependent learning during sensitive periods
- Apoptosis (programmed cell death). 50 percent of the neurons die --use it or lose it
- Myelination—first primary areas then back to front (Luria's 3X3)



Developmental Neurodynamics

- Neuroplasticity involves many forms of synaptic modifications:
  - 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)

Brain Growth Cycles

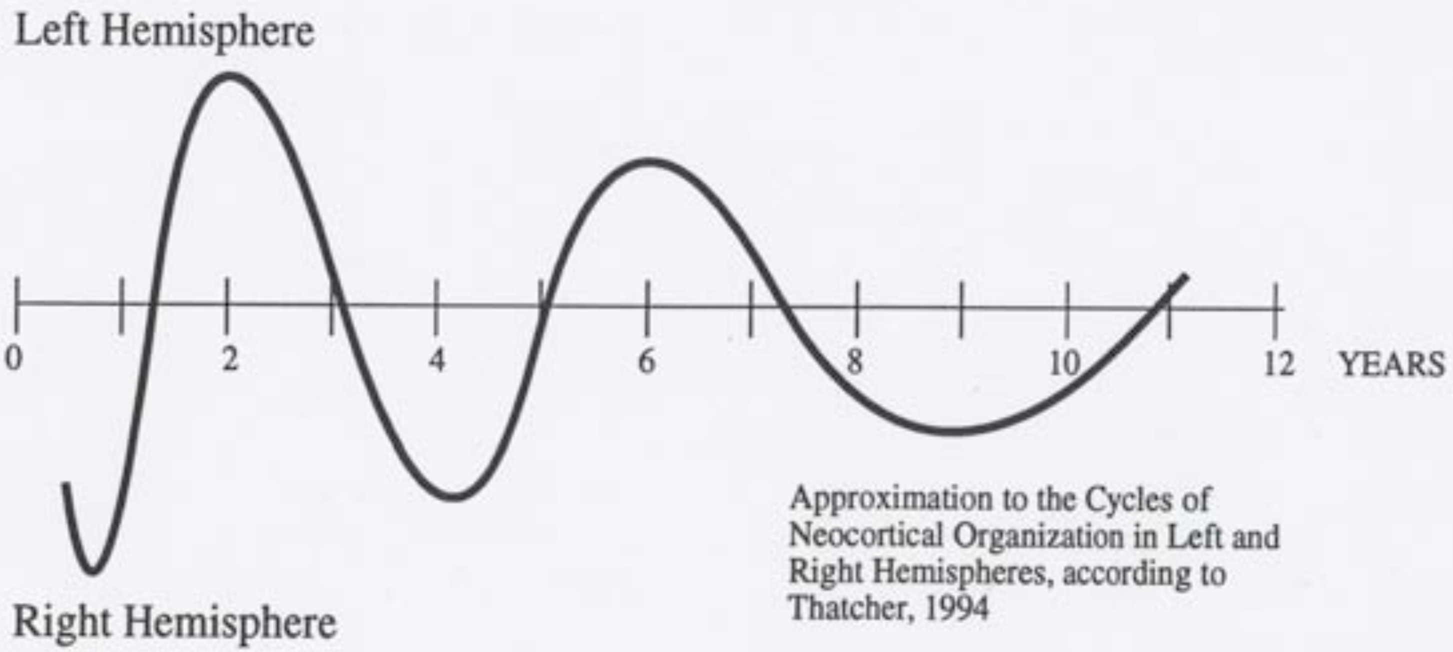


Figure 4: Brain growth cycles continue asymmetrically throughout childhood, correlated with changes in the balance of functions in the two hemispheres (25, 115).

Deprived Environment

- 150,000 children were found languishing in Romanian orphanages. They were malnourished and neglected.
- They missed human contact during critical periods (Kuhn & Schanberg, 1998).
- Sustained impairment if over one year Increased Cortisol
- Impaired OFC
- Cognitive impairments (i.e. ADD)

Child Abuse and Neuropathology

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

Enriched Environments

- Increased brain weight and density, more growth in dendrites, increased relative density of dendritic spines, and more synapses per neuron
- More granular cells in the dentate gyrus of the hippocampus (Kemperman, et al. 1997).
- As much as 85% of the dentate gyrus neurons are generated postnatally. These granule cells are excitatory and use glutamate as their primary neurotransmitter.
- Performed better on various tests of cognitive (memory) skills

“Nature”:Temperament

Temperament (Chess & Thomas, 1977)

- *Easy* - those infants that approach objects with an engaging mood and are regular in rhythmicity and respond well to new situations. They adapt well to the new situations and are cheerful. They comprise 40% of the population.

- *Slow to warm up* - they are generally shy, inhibited, and react to familiarity initially by withdrawal and occasional mild distress. They are hesitant to accept change. They comprise about 15% of the population

- *Difficult* - they are generally irritable, withdraw from unfamiliarity, and are poor in adaptation. They are irregular in feeding, elimination, and sleep. They comprise 10% of the population.

Variations in Vagal Tone

- 3 year olds with higher vagal tone made a more rapid adjustment to preschool than those with lower vagal tone (Fox and Field,1989) .
- Children with low vagal tone at age 5 showed a stronger correlation between marital hostility and problem behaviors at age 8 than those with higher vagal tone (Katz and Gottman, 1995) .
- Newborns with high reactivity to a heel stick procedure -- more crying, high cortisol, short heart periods, and low vagal tone showed lower scores on distress to limitations (a temperament measure) at 6 months (Gunar, et al., 1995).

Neurodynamics of Temperament

- Inhibited "Kagan babies" examined with fMRI at age 22 – they had overactive amygdalas (relative to controls) when exposed to novelty
- (Schwartz et al., 2003)

- Shy children show greater right frontal activity then left frontal activity. (Finman, et al., 1989; Fox, et al., 1994)

- *Goodness of fit* ---how the child's temperament fits the expectations of the parents or the demands of a family system. TOTS

Temperament Evaluated

- When the temperament traits were noted ***after age 3 or 4***, those described as "difficult" were less able to adjust to adult life then those categorized as "easy."
- When the activity level of a child ***under*** 12 months is used to project later behavior there is less consistency than when the measure of activity level is used ***after*** 12 months. (Rothbart and Bates, 1998)

“Nurture”: Attachment

Primed for Attachment

- Infants are born “premature”
  - Attachment schema
- Self Identity
  - Self-esteem/”Love-ability”

Affect regulation

  - Fear modulation/Approach-avoidance behavior

Smiling—Still Face vs. Visual Cliff

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

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)
- Maturing--new learning re: neutral faces and ambiguity are tolerated due to increased cortical processing (Casey, et. al., 2005)

"Still Face" and Depression

Infants of depressed mothers

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

Intergenerational Transmission

Infants of depressed mothers have:

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

- **Treating the mother's depression is as important as treating the child's and can contribute to the child's improvement**

Neurodynamics of Attachment

- Beginning in infancy mothers can be taught to massage their infants to re-establish bonding (Field, 1997).
- Despite being depressed, parents can learn to manage to show positive emotions and care for their children (Cumberland-Li et al., 2003).

D.W. Winnicott

- Analysand of Melanie Klein
- *Good-enough mothering*
- the *holding environment*
- *Impingements (major and (minor)*
- *mirroring*
- *transitional object*

“Good Enough” Parents

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

Good-enough mothering-the ANS

- **If the baby is matched by instantaneous soothing he will not develop brakes to the HPA (CRH—ACTH—adrenal) arousal**
- **Good enough mothering factors in time before the baby is soothed**
  - **To anticipate being soothed and activate his parasympathetic nervous system**
  - **builds in frustration tolerance**

John Bowlby (1907 – 1990)

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

Mary Ainsworth

Mary Ainsworth (1913–1999)

- **Set out to confirm Bowlby**
- **The classic attachment studies look at *reunion* behavior**
- **Infant Strange**

ISS/ Maternal Behaviors

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

Infant Strange

- The infant's reaction to four different situations is observed:
  - mother and infant alone together
  - when a stranger is introduced into the setting with the mother and infant
  - when the mother leaves the room for 3 minutes and the stranger stays with the baby
  - when both mother and stranger are absent and the baby is alone
- The key observations occur when the mother comes back
  - How well can the pair calm Lisa down and how quickly does Lisa return to play?

Major Attachment Types

- **Secure Attachment**
  - Bi-directional affect regulation (Bebee & Lachmann)
  - *Correction of mismatched attunement*
- **Insecure attachment**
  - via hyper-synchronous interaction and communication
  - absolutely asynchronous interaction

The Neuroscience of Attachment

- Autonomic Nervous Systems
- Endorphin & Benzodiazepine receptors
- Cortisol Regulation
- Positive Immunological Functioning
- ***Neural Growth and Plasticity***

Thermostat of Attachment

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

Love

Activation of the reward systems to see with rose colored glasses

- Medial insula, Caudate, Putamin and Ventral anterior cingulate

Deactivation of fear (i.e amygdala and R-PFC)---↑potential blindness to red flags

Oxytocin—the “cuddling hormone”

- Activating the vagus nerve
- ↓heart rate and ↑relaxation

↑ Dopamine “in love”

The Chemistry of Love

- Initial sight to remember - PFC says ‘pay attention she/he’s attractive’ triggering your VTA and SN to discharge dopamine
- Hippocampus codes in this important memory with the person again
- Nucleus Acumbus (pleasure and addiction center) gets activated from DA when separated too long - a crash or withdrawal
- Septal region (pleasure center) gets activated (as well as with orgasm) after dopamine triggers the excitement
- Partners run the risk of ‘tolerance’ of DA receptors down regulating (fewer in number because of the initial rush, now need more DA to get stimulated)
- Couples need to stimulate novelty to stimulate DA

Ethnic Attachment Styles

- Northern Germany-- a preponderance of *Avoidant* patterns of attachment. It is not uncommon for mothers to step out briefly from home leaving their infants unattended or outside of supermarkets. (Grossman, et al., 1981)
- In Japan – a preponderance of *Ambivalent* and hard to sooth infants. Mothers and infants are rarely separated. Babysitting is rare and when it occurs is generally with grandparents (Miyake, et al,1985).
- Among Kibbutzim in Israel infants have been reported to become *anxious* by the entry of strangers in attachment testing situations. Terrorist attacks creates a xenophobia. Strangers, therefore, are distrusted. (Saarni, et al, 1998).

Attachment and Temperament Longitudinally

- Secure attachment is correlated with a lower incidence of psychiatric disorders than in the general population (van IJzendoorn & Bakerman-Kranenburg, 1997).
- Disorganized attachment -- to dissociative problems
- Early temperament variation wasn't strongly associated with later psychiatric problems
  - Although maternal sensitivity and infant irritability interacted to predict security

Attachment Longitudinally

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

The Move to Representation

Ainsworth:

- Parental insensitivity to baby's attachment signals produces infant insecurity

Mary Main:

- The infant's attachment style at 12 months informs how the child at age 6 will narrate stories of loss

The Adult Attachment Interview

Mary Main

- 18-question interview about attachment history
- Primes the attachment system in adults
- Adult attachment powerfully predicts the attachment style of the offspring
  - If you know the child's attachment style you can predict with 80% accuracy the parents' style
  - Predict the attachment style of unborn children

Child & Adult Attachment Categories

Child (ISS)		*Adult (AAI)*	
(B)	- secure	(F)	- free/autonomous
(A)	- avoidant	(DIS)	- dismissing
(C)	- ambivalent	(E)	- preoccupied
(D)	- disorganized	(U)	- unresolved

Attachment & Adult Intimacy

- Attachment to parents predicts adult capacity for intimacy
- Attachment to peers predicts adult capacity for conflict resolution (Sroufe)
- A meta-analysis of the AAI studies--insecure attachment is correlated with anxiety and mood disorders later in life.

Security and Attention

- Secure kids and adults flexibly shift the focus of their attention, depending on changing circumstances
  - Distressing things happen, but aren't dwelled on
  - With kids, sad stories tend to have a happy ending
- Insecure kids focus attention inflexibly on one aspect of the environment
- Therapists can help clients achieve "earned" security

The AAI: Preoccupied

- Ambivalent babies have Preoccupied parents
- Preoccupied adults are obsessed with love and loss
- These clients are *under-regulated* and prone to be chaotic

The AAI: Dismissing/Avoidant

- Avoidant babies learn to deal with parental insensitivity by shifting attention away from their attachment system and emotions
- When they grow up to be dismissive adults they know little about their own feelings or those others

–**Dismissing adults are over-regulated and rigid**

–But separations still provoke spikes in their levels of cortisol

The 4th Category: Disorganized

- The attachment figure inspires fear
  - Profound conflict between wired-in attachment programs and learning
  - Child both approaches and avoids contact
  - Trauma shows up in disorganized breakdowns
- If the parent is unresolved there is an 80% chance the baby will be disorganized

Attachment Spectrum

Down regulate | Flexible | Up-regulate

Avoidant/Dismissive | Secure | Ambivalent/Preoccupied

Security's "Common Factors"

- **Main found that attachment profoundly shapes how the mind represents reality**
- ***Security in adulthood is based on***
  - **TOM**
  - **The capacity for intersubjectivity**
  - **Metacognition**
  - **Mentalization**

Attachment and Attention

- **Insecure attachment styles are characterized by *inflexibility* of behavior and attention**
  - They remain organized under stress by concentrating on only one aspect of the surround
  - This inflexibility of attention appears again in the narratives of their parents when asked to discuss their own attachment experiences

6 Executive Functions impaired withADD

1. Activation—organizing, prioritizing, and activating to work (vs. impulsive or procrastinating)
2. Focus—Sustaining and shifting attention to tasks (Jame's spotlight)
3. Regulating alertness--sustaining effort, and processing speed (vs. drossiness and running out of energy)

6 Executive Functions impaired with ADD

4. Managing frustration—affect regulation and modulating emotions (vs. affective liability)
5. Memory—utilizing working memory and accessing recall
6. Action—monitoring and self regulating action (acting w/o sufficient forethought

Changing Attachment Style

- **Alicia Leiberman**
  - Working vulnerable moms changing their mentalizing capacity with goal of promoting children's security
- **Peter Fonagy**:
  - Promotes TOM and empathy with borderlines
  - Reflective Parenting Program

Therapist Insecurity

- When therapists are insecure or unresolved,

  alliances with clients are impaired
- Therapists intervene in ways that
  - Fail to challenge the client's ingrained style
  - Aggravate unresolved problems
  - Produce poorer outcomes

Rewiring Attachment

- Attachment schema are largely stable
- Where change occurs:
  - Insecure > Secure
    - positive relationships & moderate levels of stress
  - Secure > Insecure
    - sustained environmental and familial stressors
    - negative changes in caretaking, marriage
    - loss & bereavement
    - chaos
    - decreased resources

Therapeutic Extrapolations

- How does the client responds to “good enough” interventions?
  - Use outcome management protocols
  - Be aware of nonverbal communications
- Negative affects and reactions are a plus!
  - Utilize negative reactions for repairing ruptures
  - Avoiding premature terminations and idealized transferences

Adolescent Brain Changes

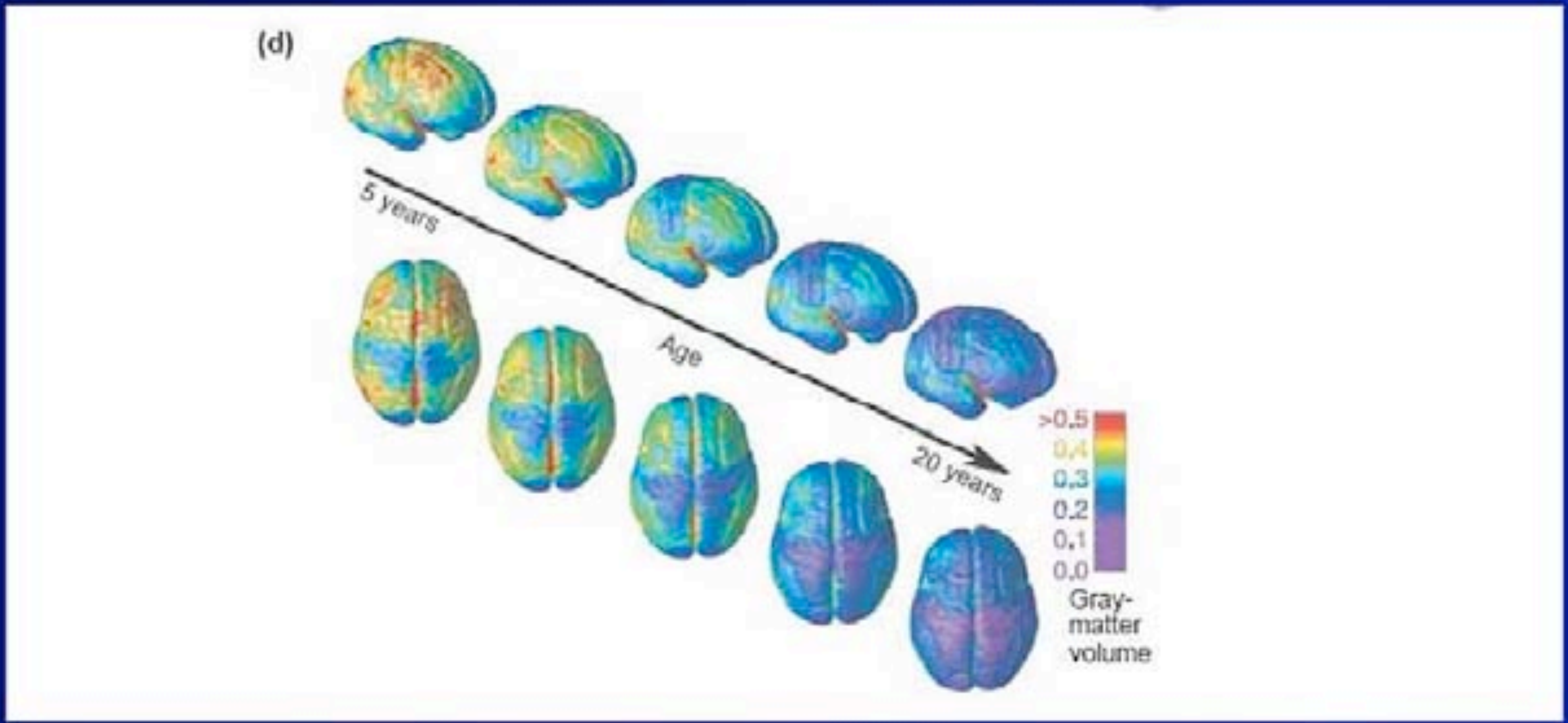
- Between ages 10-12 frontal lobes go through a growth spurt with new connections and branching.
- Major synaptic pruning (loss of 50% of synaptic connections)
- Increased myelination (15x faster)
  - Early 20s myelination of the PFC (especially the DLPFC)

The Adolescent Brain

- Relative to adults:
  - Heavy reliance on the amygdala
  - While relatively less reliance on PFC
  - Less activity in the nucleus accumbens
  - Less DA
  - More oxytocin
- As a result they feel that they need to:
  - Seek excitement to get enjoyment
  - Seek affiliation and the feeling of belonging

Adolescent Brain Changes

- Density decrease from 5 to 20



Not "Good Enough" Parenting

- Over-controlling parents have been found to be associated with exacerbating child inhibition (Wood, et al, 2003).
- Parents can paradoxically encourage their child's fearfulness by controlling his activities or solving his problems (Rubin, et al, 2003).
- Adolescents who have indulgent parents tend to be irresponsible, immature, and/or conforming to peers.

“Good Enough” Parents

- **Adolescents with indifferent parents tend to be impulsive and can develop conduct disorders and engage in early alcohol, and sexual experimentation.**
- **Work with an adolescent’s parents to enhance an authoritative/inductive parenting---to be “good enough.”**

brain changes during aging

- Loss of gray matter in:
  - the DLPFC
  - the temporal lobes
- Decrease of myelin in the frontal lobes
- Loss of volume in the temporal lobes
- Degeneration of white matter in the PFC
  - in the hippocampus
- Loss of large neurons in the frontal lobes

brain changes during aging

- Shrinkage of the cerebellum
- Preservation of the OFC
- Shrinking of the striatum
- Decrease in length of white-matter fibers
- Loss of diameter in white-matter fibers
- Decrease in cerebral glucose metabolism

Aging and Testosterone

- By age 50 men use 50% of their adrenal testosterone
  - 60% of their testosterone produced by testes
- Women lose:
  - 70% of their testosterone
  - 90% after menopause

Gender and Aging

- Older men who are social ↑ brain regions associated with pleasure and reward
  - Ventral tegmental area-- ↑ DA
  - Nucleus accumben
- Men ↑ health after retirement if married but not for women
  - Men live 1.7 years longer
  - Women live 1.4 years fewer years

Age Related Memory Decline

- Preserved
  - Semantic memory (factual and conceptual knowledge)
  - Procedural memory
  - Language abilities
- Declines beginning in your late 20s
  - Episodic memory (recall of experience and events)
  - Spontaneous recall (of names)
  - Processing speed
  - Selective attention (difficulty ignoring irrelevant info)
  - Working memory
  - Ability to multitask

Older have Nicer Pasts

- Older people tend to see the past through rose colored glasses
- They remember fewer negative images than younger people
- They have reduced interactions between the amygdala and the hippocampus when shown negative images
- Scans show that older people had increased interactions between the amygdala and the DLPFC
- They are able to regulate emotion better than younger people and are less effected by negative events.

Pattern Recognition

- As we age we accumulate an increasing number of cognitive sets
- This process involves more emphasis on pattern recognition instead of problem solving
- An increased emphasis on LH and decreased emphasis on RH
- Patterns are like attractors representing the activation of particular constellations of neural networks
  - A broad range of inputs can activate the attractor enabling the person to capture the essence of a large number of pertinent experiences
- This capacity forms part of wisdom

Reverse aging: Woody Allen

- "In my next life I want to live my life backwards.
- You start out dead and get that out of the way.
- Then you wake up in an old people's home feeling better every day.
- You get kicked out for being too healthy, go collect your pension, and then, when you start work, you get a gold watch and a party on your first day.
- You work for 40 years until you're young enough to enjoy your retirement.
- You party, drink alcohol, and are generally promiscuous, and then you are ready for high school.
- You go to primary school, you become a kid, you play, you have no responsibilities, you become a baby, and then...
- You spend your last 9 months floating peacefully in luxurious spa-like conditions with central heating and room service on tap, larger quarters every day, and then *voila*...
- You finish off as an orgasm!"

3. Memory

Memory and Movie Mistakes

- TBI resulting in profound retrograde amnesia with intact new learning.
  - The exact opposite of neurological reality (anterograde amnesia and little retrograde)
- 2 head injuries are better than one. A common “cure” is another head injury.
- Most films show memories are temporalily inaccessible. Recovery of memory is possible through various unlikely means

Two Memory Systems

Implicit

Non-declarative

- Procedural
- Emotional
- Generalized
- Classical conditioning

Amygdala and BG-driven

Explicit

Declarative

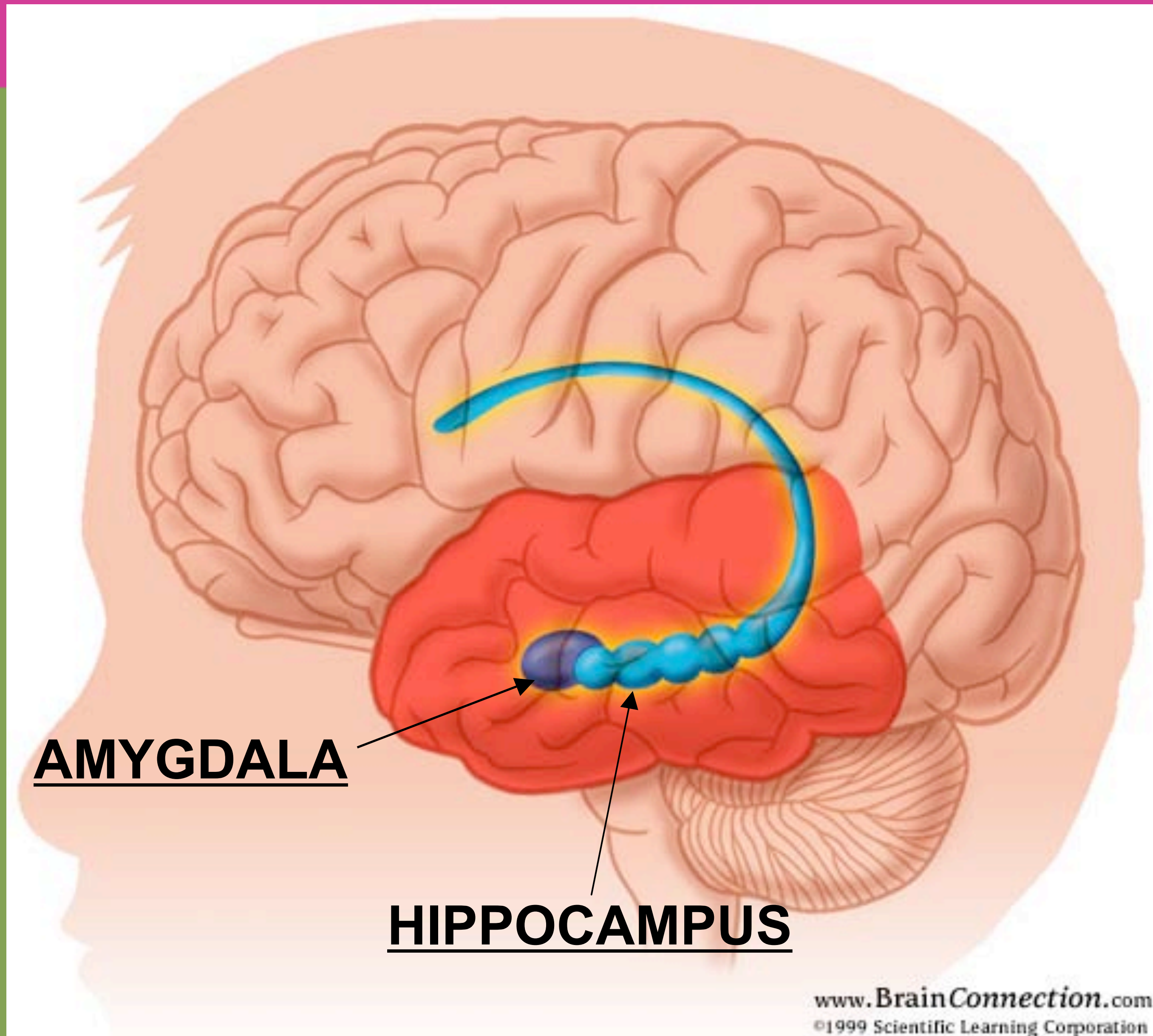
- Episodic
- Autobiographical
- Semantic
- Context Specific

Hippocampus-driven

"Explicit" Memory Test

- Thread
- Pin
- Eye
- Sewing
- Sharp
- Point
- Prick
- Thimble

- Haystack
- Thorn
- Hurt
- Injection
- Syringe
- Cloth
- Knitting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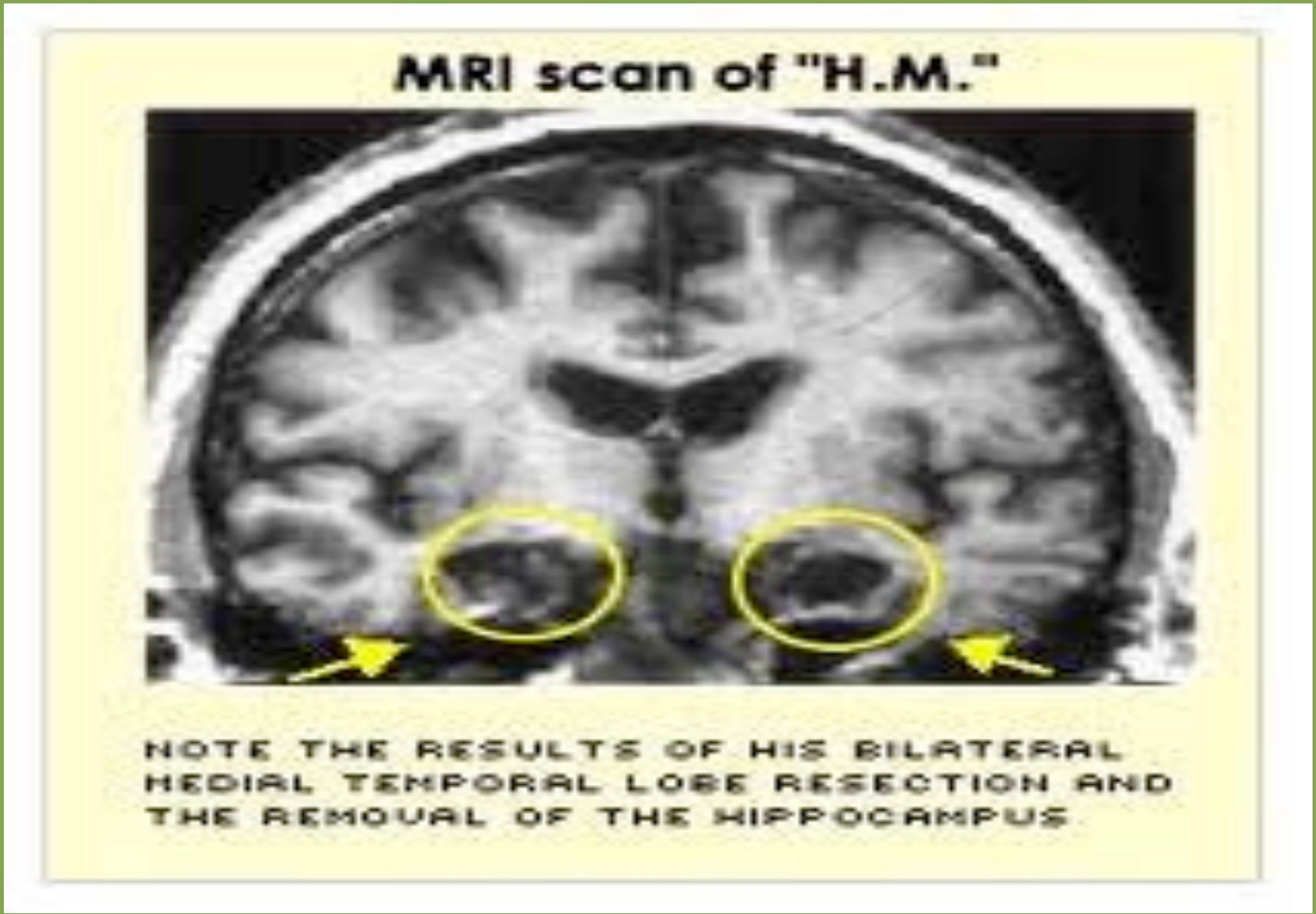
• Fear Conditioning • Emotional Valance • Generalized • Cortisol Heightened Sensitivity (Hypervigilence) • Matures Early • “Little Albert”	• Many Cortisol Receptors • Context Specific • Heightened Cortisol leads to atrophy • Matures Later • Infantile Amnesia • “H.M.”

Henry's Brain



Memory Consolidation

- Consolidation takes place over a period of time—from hours to years (McGaugh, 2004)
- Emotional effects of consolidation are often not detectible immediately after the event, but evolve gradually and are labile and vulnerable to disruption
- Adrenergic and cortisol effects which began during the event continue to modulate the consolidation of the memory trace after the event (Haman, 2009)
- Some consolidation of emotional of

Memory Consolidation

- Some consolidation of emotional of memories occurs during REM (Holland & Lewis, 2007)
- During waking consciousness cognitive processes including rehearsal of, rumination over an emotional event reinforces and strengthens emotional memories (LaBar & Cabeza, 2006)

Functional connectivity between the amygdala and hippocampus

- emotional arousal ↑ amygdala
- modulating activity in the medial temporal lobe system through the up-regulation of activity of the entorhinal cortex and hippocampus (McGaugh, 2004)
- neurochemical enhancements to this system
- EEG studies indicate increase synchrony between neural firing in the amygdala and the hippocampus at the theta frequency which enhances memory-related

The amygdala, affect asymmetry, and gender

- Pts with right amygdala lesions recollect more high-intensity pleasant autobiographical memories and fewer high-intensity unpleasant memories
- Pts with left amygdala lesions recall fewer high-intensity positive memories and more high-intensity negative memories (Buchanan, et. al., 2005)
- Men right lateralize amygdala activity that later predict emotional memory
- Women left lateralize amygdala activity

Amygdala

- A relevance detector
- Retains motivational value of events
- Orchestrates a wide range of physiological reactions
- Aids in the facilitation of attention toward emotionally significant stimuli (Vuilleumier, 2009)

The Role of the Hippocampus

- Needed temporarily to bind together distributed sites in neocortex that together represent a whole memory
- Index to database of memory
- Novelty detector: compares incoming info to stored knowledge; if difference, triggers dopamine increase
- Specialty is binding new to old information
- Ceases to play a role in the retention of a specific memory after about 2 years.

Source Memory

- Ronald Reagan often tearfully told the story of a WWII bomber pilot who ordered his crew to bail out but stayed in the plane when the gunner was too wounded to bail-- the pilot said “Don’t worry we’ll ride it down together.” It actually was a 1944 movie –”A wing and a Prayer.”
- A woman accused memory expert Dr Donald Thompson of having raped her. She had seen the program just before being raped.
- Piaget claimed that his first detailed memory was saved from nearly being kidnapped at age 2 by a nurse who concurred. But 13 years later the nurse wrote his parents to confuses she had made it up.
- Studies by Marcia Johnson et al. have shown that the ability to distinguish memory from imagination depends on the recall of source info.

Genetic variations—amygdala

- 5-HT transporter gene influences the transport of 5-HT from synaptic cleft
  - 5-HT has variations in the transcription control region, which results in either short (S) or long (L) variants, --alleles.
  - We all carry 2 alleles of any gene (one from each parent)—thus, 3 categories, those with:
    - 2 long alleles—L/L
    - 2 short alleles—S/S
    - 1 short and 1 long—S/L
  - The S/L and S/S—in **"S"** group-- ↑ in anxiety "neurotism" and ↑ amygdala resting activation amplified by life experience

Genetic variations—amygdala

- Variation in the tryptophan hydroxylasc-2 (TPH2) gene modulates amygdala processing of emotional stimuli regardless of value
- $TPH2_T$ allele were found to have greater amygdala activation in response to happy, fearful, and sad faces (Canli, 2009)

Positive or Negative Emotion and Memory

- Negative emotion narrows attention and limits memory for peripheral details
- Positive emotion promotes memory not so constricted
- Recalling positive memories -- “reminiscence bump” with an excess of positive memories from early adulthood (Bertsen & Rubin, 2002)
- During positive experience we may want to “take it all in”

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)
- Amygdala can trigger the release of epinephrine and norepinephrine (“fight, flight, or freeze”)
  - And the second phase—the HPA axis response and release of cortisol

Flashbulb Memories

- A particular type, not class
- During emotional peaks, NE dramatically sensitizes synapses by adding phosphate molecules to receptor –GluR1
  - Increasing the ability of receptors to be recruited to synapses
  - Primes neurons by increasing their sensitivity

Neurochemistry of Memory

- NE and amygdala: inverted U function
- Oxytocin: inhibits some memory consolidation; enhances encoding of positive social memory (happy faces)
- Estrogen: improves memory
- Cortisol: high levels inhibit, sustained hippocampal death
- DA: working memory

Negative Memories

- Negative emotion narrows attention, limits memory for peripheral details
  – to threat—i.e. “weapons focus”
- Thus, less accuracy for peripheral stimuli (i.e. color of the car or person’s hair) more to the object of threat (gun, knife, etc.)

Amygdala and aging

- Amygdala atrophy between 2-20% depending on the study
- For healthy adults MRI studies average of 7% reduction compared to healthy young adults
- Reduction is the greatest after age 60
- Pts. with AD 14-60% reduction
  - along with the hippocampus and entorrhinal cortex—significant plaques and tangles

Negative Emotion and Memory

- Positive emotion promotes memory not so constricted
- Recalling positive memories -- "reminiscence bump" with an excess of positive memories from early adulthood (Bertsen & Rubin, 2002)
- During positive experience we may want to "take it all in"

Inhibition vs. extinction

- Extinction doesn't erase fear learning
  - After "extinction" a conditioned fear can return in a range of circumstance including:
    - because they are fragmented and disorganized
    - Simple passage of time via spontaneous recovery
    - Exposure to the US
    - Exposure to the CS in a novel context
- Inhibition of fear involves new learning (via the mPFC and hippocampus) to inhibit the expression of conditioned fear rather than eliminating the fear

Genetic variations—amygdala

- 5-HT transporter gene influences the transport of 5-HT from synaptic cleft
  - 5-HT has variations in the transcription control region, which results in either short (S) or long (L) variants, --alleles.
  - We all carry 2 alleles of any gene (one from each parent)—thus, 3 categories, those with:
    - 2 long alleles—L/L
    - 2 short alleles—S/S
    - 1 short and 1 long—S/L
  - The S/L and S/S—in **"S"** group-- ↑ in anxiety "neurotism" and ↑ amygdala resting activation amplified by life experience

Genetic variations—amygdala

- Variation in the tryptophan hydroxylasc-2 (TPH2) gene modulates amygdala processing of emotional stimuli regardless of value
- $TPH2_T$ allele were found to have greater amygdala activation in response to happy, fearful, and sad faces (Canli, 2009)

The Dynamics of Fear

- Amygdala memories are hard to forget ("Stone tablet")
- Hippocampal circuits tell us what to fear and in what context ("Etch-a-Sketch")

The Fast Circuit to the Amygdala

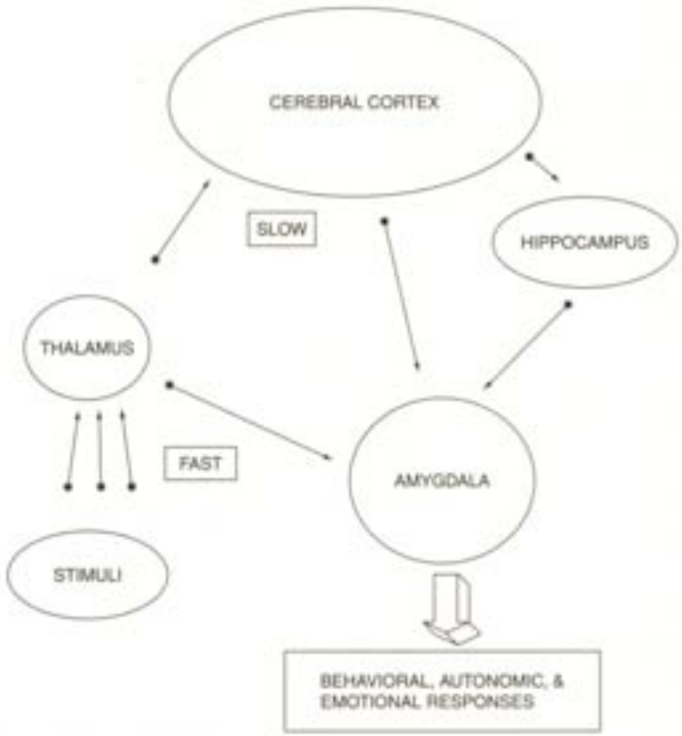
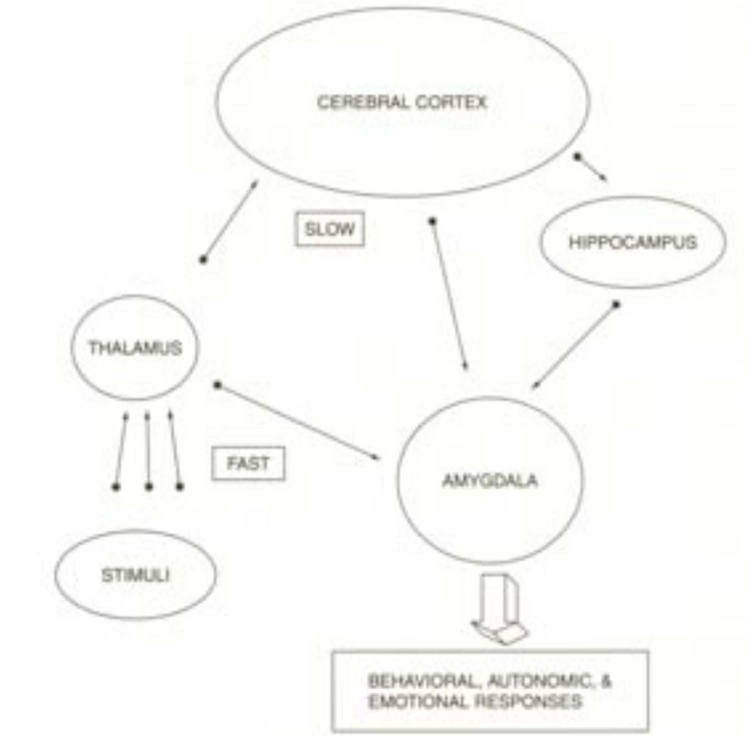


Figure 11.1 Fast and slow fear circuits

A depiction of the two pathways of information to the amygdala—one directly from the thalamus and the other through the cortex and hippocampus (adapted from LeDoux, J. Emotion, memory, and the brain. *Copyright © 1994 by Scientific American, Inc. All rights reserved).*

- Goes from the Thalamus directly to the Amygdala
- Fight or Flight: HPA activation
- Emotional Learning
- Fear Conditioning
- PTSD, Anxiety, etc.

The Slow Circuit to the Amygdala



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A depiction of the two pathways of information to the amygdala—one directly from the thalamus and the other through the cortex and hippocampus (adapted from LeDoux, J. Emotion, memory, and the brain. Copyright © 1994 by Scientific American, Inc. All rights reserved).

- Goes from the Thalamus through the Cortex and Hippocampus to the Amygdala
- Worries and GAD
- Fears and Phobias
- Taming the Amygdala
- Exposure, New Thinking (cortex) and Reconditioning

Memory (summary)

- Attention is critical to the coding of new memory
- 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

Memory Test

“Needle” Critical Lure

- Thread
- Pin
- Eye
- Sewing
- Sharp
- Point
- Prick
- Thimble

- Haystack
- Thorn
- Hurt
- Injection
- Syringe
- Cloth
- Knitting

Neurochemistry and Memory

- Estrogen—improves memory
- Oxytocin—inhibits some memory consolidation and enhances encoding of positive social memory (happy faces)
- Cortisol—high levels inhibits memory: sustained ↑ -hippocampal atrophy
- CRH—sustained release—dendritic spines in the hippocampus retract
- NE—high and low impair memory function
- DA—required for normal working memory
- ETOH, MJ, Cocaine—impair memory

Source Memory

- Ronald Reagan often tearfully told the story of a WWII bomber pilot who ordered his crew to bail out but stayed in the plane when the gunner was too wounded to bail-- the pilot said “Don’t worry we’ll ride it down together.” It actually was a 1944 movie –”A wing and a Prayer.”
- A woman accused memory expert Dr Donald Thompson of having raped her. She had seen the program just before being raped.
- Piaget claimed that his first detailed memory was saved from nearly being kidnapped at age 2 by a nurse who concurred. But 13 years later the nurse wrote his parents to confuses she had made it up.
- Studies by Marcia Johnson et al. have shown that the ability to distinguish memory from imagination depends on the recall of source info.

Grocery Store Effect

- Driving home from work you forget to stop at the store
- This minor error in memory is evidence of two competing parts of the brain, on that creates habits, the other involved in novel learning
  - Driving home from work is a habit, done on autopilot –the striatum
  - Stopping at the store is comparably a novel task—hippocampus

Maximizing Memory

- Pictures are remember better than words
- Memory is better the second time you learn something
- Concrete information remembered better than abstract information
- Positive information is remembered better than negative (Pollyanna effect) except if sudden or negative trauma
- Memory is better for frequent information for recall testing, but better for rare information for recognition

Recall is better if

- Actions more than thoughts
- Memorable events better then random
- Rare more than frequent actions
- Read—recite—review—read again
- Chewing gum 35% improvement—raises heart beat, increases blood to the brain
- Doodlers recalled 7.5 names and places—29% more than the average of 5.8 remembered by controls

Memory and Sleep

- **Only with more than 6 hrs of sleep improved did memory improve over the 24 hrs. following a learning session** (Strickgold, 2000)
- **Sleep changes memory, making it more robust and resistant to interference in the coming day—stabilizing memory**
- **During sleep the brain dissects memories and retains only the most salient details—helps to remember aspects of a negative even**
- **Plays a crucial role in retaining emotional memories**

Memory and Sleep

- REM improves implicit (procedural) learning
- Non-REM improves explicit (declarative)
- Sleeping during a retention interval leads to better memory than wakefulness: i. e. consolidation
- A single night of sleep deprivation produces a significant deficit in hippocampal activity during episodic memory encoding, resulting worse subsequent retention

Kandel and the Neurochemistry of LTP

- **STP/STM = functional change in existing synapse: transient strengthening of communication between two neurons**
- **LTP/LTM = change in the number of synaptic connections via gene activated of protein synthesis.**
- **LTP = Serotonin → C-AMP → PKA → CREB**
- **CREB = transcriptional control protein, increases in # of synaptic connections**
- **CREB 1 activates genes; CREB 2 represses genes**

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Gender and Memory

- Women superior in episodic memory
- Women excel in verbal episodic memory tasks, such as remembering words, objects, faces, pictures or everyday events
- Men outperformed women in remembering symbolic, visuospatial processing
- Sex differences favoring women on tasks such as both verbal and visuospatial processing
- Women are better than men at remembering faces, especially of females
- Women better in tasks requiring little to no verbal processing such as recognition of familiar oders, and that the female episodic memory advantage decreases with visuospatial abilities

Maximizing Memory

- Elaborative rehearsal better then rote memory
- Intensional learning better then incidental memory
- Memory is better if mental image is formed
- Information that you generated is learned better than if you must read or hear it
- Memory is better if you perform a task rather than watch someone else do it or read about it.

Maximizing Memory

- Attention
- Emotional engagement
- Novelty
- Associations

Recovered Memory Therapy?
Be Careful!

- 183 claims of repressed memories of childhood abuse:
- 100% report torture/mutilation (no evidence)
- 100% in therapy 3-5 years after first memory
- 10% SI before therapy—67% after therapy
- 83% employed before therapy—37% after therapy
- 23% lost parental custody
- 100% estranged from families

Trauma and Memory

- Research indicates that spontaneously recovered memories may reflect real memories of abuse
- There is no support for abuse memories recovered through suggestive therapy
- Not possible to distinguish repressed memory from fake memory without some form of corroborating evidence.

Memory Summary

- Memory is not an exact copy—ie. Not one neuron, not byte on a hard drive.
    - Distributed network of associations located in multiple locations coding in the various sensory networks
- Memory is constructive process that can be reconstructed
- Therapy involves the reconstruction
    - Especially of the integration of implicit

Break a Fast

Skipping Breakfast contributes to:

↓ problem solving

↓ working memory

↓ attention

↓ concentration

↑ Mood swings

↑ depression

↓ energy

↑ stress reactivity

↑ anxiety

Hydration

- Dehydration contributes to:
  - Brain cells shrivel up
  - Enlarging ventricles
  - Brains work harder with poor results
  - Impaired cognition
    - Attention
    - Forgetfulness
    - Speech problems

Nutrition

1) The food is absorbed in your gastrointestinal track.
2) Amino acids and other nutrients including vitamins and minerals are carried through your bloodstream to your brain.
3) Enzymes convert the substances such as the amino acid precursors into neurotransmitters. Or the conversion takes place indirectly by causing insulin to be released from your pancreas, which draws amino acids from your blood and tissues.

Nutrition

4) The neurotransmitters are stored in synaptic vesicles
5) After the neurons fires (through an action potential) it releases the neurotransmitter from the pre-synaptic membrane into the synapse.
6) The neurotransmitter either finds the right membrane like a “key” fits into a “lock” on a post-synaptic membrane making it fire or it gets reabsorbed back into the pre-synaptic membrane.

Blood Sugar

- If their blood sugar drops below 50 milligrams per milliliter people may develop symptoms that include:
  - Free-floating anxiety
  - Shakiness
  - Lightheadedness
  - Irritability
  - Rapid heartbeat
  - Difficulty concentrating

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Glycation (excess glucose)

- Blocks protein from moving freely
- The body's membranes become "gunked up"--blocked, which slows down neural communication
- Interferes with synaptic transmission
- Causing structural damage to the mitrochondria (the energy factories in each cells that produce ATP)
- Lead to free radicals
- Causes inflammation.

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

- The higher the GL of a food
  - the greater the adverse insulin effects of the food.
  - Long-term consumption of foods with a high GL leads to a greater risk of:
    - Obesity
    - Diabetes
    - Inflammation.
    - A form of free radical damage to fatty acids is called *malondialdehyde* (MDA). ↑ GL and ↑ MDA.
    - Another form of free radical products of damaged fatty acids is called *isoprostanes*

Glycemic load leads to:

- A form of free radical damage to fatty acids is called *malondialdehyde* (MDA). ↑ GL and ↑ MDA.
- Another form of free radical products of damaged fatty acids is called *isoprostanes*,
  - Mild isoprostane elevation is associated with Alzheimer's disease.

Advanced glycosylated end products (AGEs).

- AGEs acts like a chemical glue that attaches molecules to one another
- AGE causes what has been referred to as a *cross-link*. (like overcooked meat)

Amino Acids

Amino Acid	Neurotransmitter	Effects
L-Trytophan	Serotonin	Improves sleep and calmness and mood
L-Glutamine	GABA	Decreases tension and irritability
L-Phenylalanine	Dopamine	Reduces anger and increases feelings of pleasure
L-Phenylalanine	Noreprinephrine	Increases energy, feelings of pleasure, and memory

Deficiencies of B Vitamins

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

Omega 3 Fatty Acids

- Alpha-linolenic acid (ALA) in foods such as walnuts, flax seeds, and green leafy vegetables.
- Stearidonic acid (STD)
- Eicosatrienoic acid (ETE)
- Eicosatetraenoic acid (ETA)
- Eicosapentaenoic acid (EPA)
- Docosapentaenoic acid (DPA, Clupanodonic acid)
- Docosahexaenoic acid (DHA)
- Tetracosapentaenoic acid
- Tetracosahexaenoic acid (Nisinic acid)

Omega 6 Fatty Acids

- Linoleic acid (LA) -- used in the biosynthesis of arachidonic acid (AA) and thus some prostaglandins. It is found in the lipids of cell membranes. Abundant in many vegetable oils, especially poppy seed, safflower and sunflower oils. Competes with *n*–3s for positions in cell membranes
- Gamma-linolenic acid (GLA)
- Eicosadienoic acid
- Dihomo-gamma-linolenic acid (DGLA)
- Arachidonic acid (AA) One of the most abundant fatty acids in the brain, and is present in similar quantities to DHA. The two account for approximately 20% of its fatty acid content.
- Helps to maintain hippocampal cell membrane fluidity.
- Protects the brain from oxidative stress by activating perioxisomal proliferator-activated receptor-y.
- Activates syntaxin-3 (STX-3), a protein involved in the growth and repair of neurons
- disturbed metabolism of AA may be associated with neurological disorders such as Alzheimer's Disease and Bipolar Disorder]. --(overexpression or disturbances in the AA enzyme cascade).
- A higher increase of AA that is implicated in depression.
- Docosadienoic acid
- Adrenic acid
- Docosapentaenoic acid (Osbond acid)

Omega 6 -- DHA

- High concentrations of DHA in synaptic membranes and mitochondria.
  - critical for synaptic transmission and membrane fluidity.
  - critical in keeping cell membranes soft and flexible
  - important for holding receptors in place-- Soft and flexible membranes are capable of alternating the shapes of the receptors

Eicosapentaeonoic acid (EPA)

- Membrane fluidity affects function of enzymes such as adenylate cyclase and ion channels such as calcium, potassium, and sodium, which in turn affects receptor numbers and functioning.
- Used to manufacture more synapses with more nerve endings
- Involved in the conversion of L-tryptophan to serotonin and the control of its breakdown.
- treatment with omega-3 supplementation shows benefit for depression as well as

Eicosapentaeonoic acid (EPA)

- found throughout the body
- associated with support for the activities of neurotransmitters such as serotonin and dopamine
- anti inflammatory effects
- helps lower triglycerides (fats in the blood)
- lower blood pressure

Eicosapentaeonoic acid (EPA)

- reduce the risk of blood clots and reduce the amount of arterial plaque
- required for the production of prostaglandins
- inhibits AA conversion into the thromboxane-2 and prostaglandin-2 families

Essential fatty acids and Cytokines

- Essential fatty acids balance the influences of cytokine activity. *Cytokines* are proteins, peptides (a derivative of amino acids), and glycoproteins (proteins with carbohydrates). When EFCs are not balanced:
- cytokines can cause inflammation
- and turn an immune system against its own cells, attacking and killing them.
- An increase in cytokines has been associated with depression, anxiety, and cognitive problems.

Myeline

- Myelin is composed of:
- Essential fatty acids
- Phospholipids
- Cholesterol (HDL)

trans-fatty acids

- Formed when an unsaturated fat is heated for a long time in a metal container, (ie. deep frying) in fast-food restaurants, are formed.
- These are altered fats. While essential fatty acids are curved and flexible and thus help the nerve cell membranes to maintain their electrical properties, trans-fatty acids are straight
- tend to be solid at body temperature, and act like saturated fat. This makes them more rigid and inflexible, which makes them interfere with the normal functional properties of the nerve cell membranes.

The vast reduction in omega-3 fatty acid consumption because:

- The reduction of cereal germ (which contains essential fatty acids) by current milling practices
- Decreased fish consumption
- A 2,500 percent increase in trans-fatty acid consumption (which interferes with essential fatty acid synthesis)
- A 250 percent increase in sugar intake (which interferes with the enzymes of essential fatty acid synthesis)
- An increase in the consumption LA oils (corn, sesame, safflower, sunflower)
- The hydrogenation of oils in commercial processing

trans-fatty acids

- Cookies
- Doughnuts
- Potato chips
- Candy
- Mayonnaise
- Vegetable shortening
- Crackers
- Cake
- Deep-fried foods
- Cheese puffs
- Margarine

trans-fatty acids can:

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

trans-fatty acids

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

Belly fat

- Belly fat generates inflammation.
- releases inflammatory cytokines
  - Cytokines are associated with inflammation and depression,
    - they lower the level of BDNF, the protector of nerve cells and the promoter of neuroplasticity.

Stress and Fatty Acids

- Stress can have a destructive effect on fatty acids. Those effects include:
  - Inadequate replacement of lost fatty acids
  - Destruction (rancidity) of long-chain fatty acids in the brain
  - Depletion of long-chain fatty acids in the brain contribute to depression (Hibbeln, 1995)

  The imbalanced ratio between Omega-6 and Omega-3 has been correlated with depression.

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

Deficiencies of Fatty Acids

- What symptoms of fatty acid imbalance might you look for? :
  - Dandruff
  - Dry skin
  - Dry, unmanageable hair
  - Brittle, easily frayed nails
  - Excessive thirst

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Stress and Fatty Acids

- Dry eyes
- Soft nails
- Increased thirst
- Learning problems
- Attention problems
- Weakness
- Frequent infections
- Poor wound healing

Omega-3 Fatty Acids

Foods That are Rich in Omega-3 Fatty Acids

- Fatty Fish such as Salmon, Sardines, Mackerel, Herring, Trout and Pilchards, Bluefish, Tuna, Halibut
- Canola Oil, Flaxseed Oil, Hemp Oil, Soybean Oil, Walnut Oil
- Walnuts, Flaxseeds, Pumpkin Seeds
- Soy and Tofu
- Green Leafy Vegetables
- Venison and Buffalo
- Some eggs are enhanced with omega-3s

Phospholipids

- A family of brain fats. They are both fat and mineral.
  - Phospho represents the mineral phosphorous
  - lipid means they contain fat molecules.
- Important in forming and protecting nerve membranes from toxic injury and free radical attack. (Amaducci, Crook, Lippi, et al, 1980)

Phospholipids: phosphatidylcholine (PC)

- PC is an important part of the nerve cell membrane
  - the choline portion manufactures acetylcholine
    - Lecithin (choline) is found in eggs and soy
  - Helps keep the level of the amino acid homocysteine in check which:
    - Is associated with degenerative diseases.
    - Sets the stage for the clotting of the blood vessel linings and plaque in the arteries
    - Blocks the synthesis of neurotransmitters
    - Trigger metabolic changes that injure the neurons

Phospholipids: phosphatidylserine (PS)

- PS--formed when the phospholipid complex combines with amino acid serine.
- PS is one of the structural molecules of nerve cell membranes.
- Influences the fluidity of nerve cell membrane
  - helps with the binding of neurotransmitters critical to electrical activity in the brain.
  - A good source of PS is soy.

Phospholipids

- If the structures of the phospholipids and the fatty acids are damaged or are poorly formed (changed in shape), the receptor can’t receive the neurotransmitter.
  - It’s partly for this reason that fatty acids supplements have been shown to improve the action of antidepressant medications

Phytonutrients (antioxidant abilities)

- The polyphenol group.
  - Within this family are the flavonoids:
    - catechins: (high amounts in green tea)
    - flavonols: (found in apples)
    - isoflavones: (found in soy).
    - anthocyanins (found in blueberries, elderberries, and cherries)

Phytonutrients (antioxidant abilities)

- highest oxygen radical absorbed capacity (ORAC) include:
  - blueberries, blackberries, strawberries, raspberries, and plums. In that order.
  - diets enriched with blueberries, strawberries, and spinach are correlated with improved cognition and motor functions. (Joseph, Shukitt-Hale, Denisova, et al, (1999)

Flavonoids

- 6000 different types found in fruits, vegetables, cocoa, soy, tea, etc.
- Act as antioxidants—protecting cells from free radicals
- Bolster the brain by interactions with proteins integral to structures
- Help regulate enzymes called phosphatases
  - the correct balance of phosphatases critical for maintaining the integrity of synapses & transmission

Flavonoids

- Blueberries-- ↑ enzymes called kinases essential for learning & memory
- People over 72 drank 2 cups of blueberry juice daily for 12 weeks
  - ––30% better at recall of words and objects than controls

Flavonoids

- Soy isoflavones—act like weak estrogens that bind to and stimulate estrogen receptors
  - They trigger modifications in neuron shape and neurochemistry of the hippocampus
- Flavonoids may stimulate neurogenesis in hippocampus
  - May also ameliorate the neurotoxic effects of excess glutamate by preventing it from binding to its receptors
  - May also oppose the action of enzymes called secretases that are involved in the destruction of neurons and that may be elevated in neurogenesis

Flavonoids

- Sage—high in a flavonoid “hispidulin”
  - —shown to interact with GABA
- Oregano and Thyme—containing the flavonoid “carvacrol”
  - having antidepresant effect in mice, interaction with DA
- Horney Goat Weed—high in the flavonoid “icariin”
  - Prevents protein clumps from causing neurons to suicide

Vitamin D

- Vitamin D receptors (VDR) are located in the human cortex and hippocampus, which are key areas for cognition.
- Vitamin D deficiency is common in older adults and has been implicated in psychiatric and neurologic disorders.
- In a cross-section of older adults, vitamin D deficiency was associated with low mood and with impairment on two of four measures of cognitive performance.

Omega 3

- 20% of the brain is made up of essential fatty acids
- ↓ Omega 3 = ↓ serotonin
- Current American average: 130 mg
- International Recommendations: 650 mg
- Omega 3 inhibits cytokine synthesis

Meal Size

- Large meals stress the GI track and create adverse systemic effects:
- Causing rapid rise in triglyerides
- ↑ blood sugar
- Risk factors for cardiovascular disease and diabetes

Diet and Aging

- Aging slows the production of antioxidants
- Making us less resistant to inflammation
- Sugar ↑ inflammation
- Cytokines ↑ inflammation

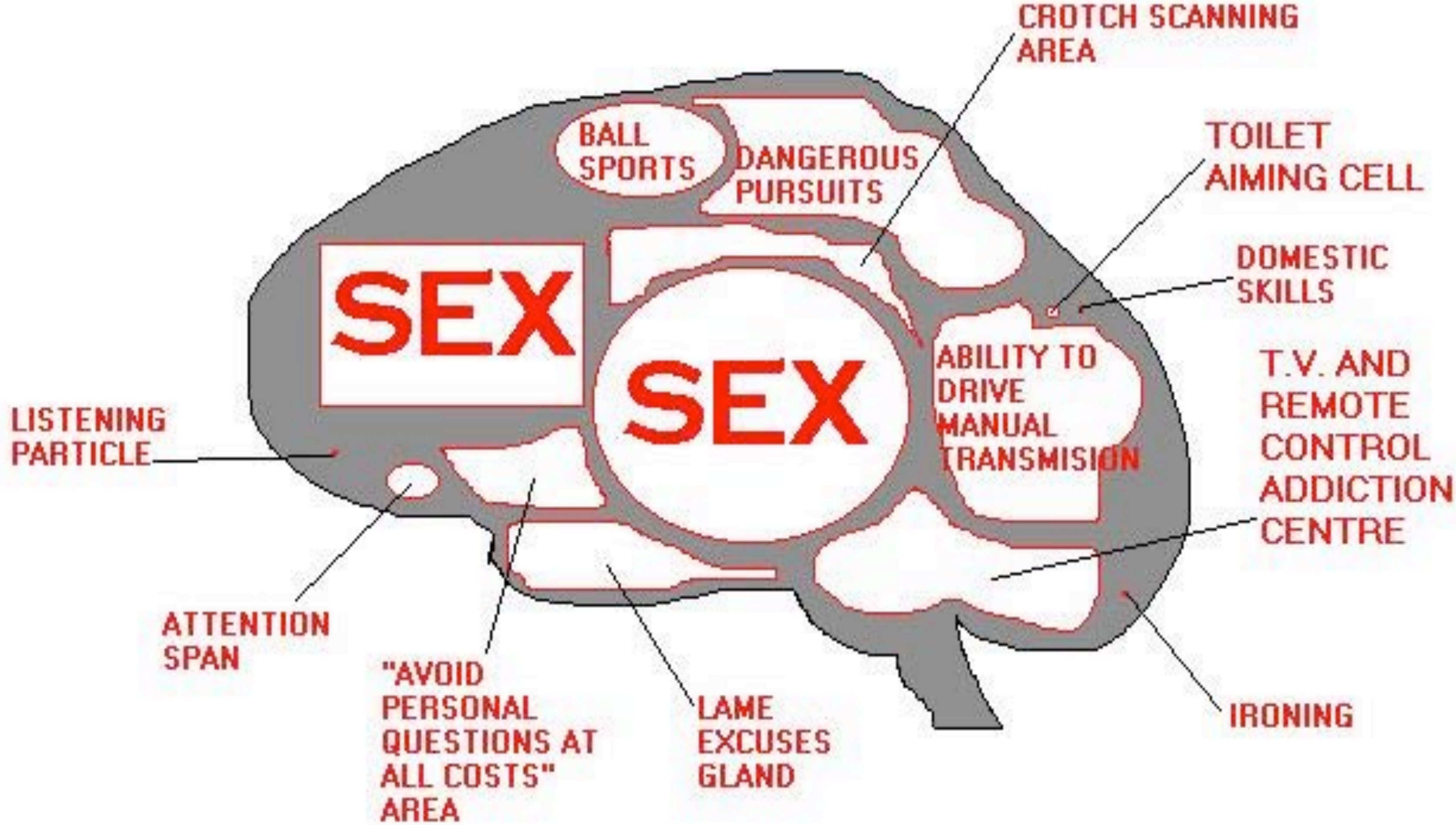
Snacks and Energy

- Protein snacks boost energy
  - –Via tyrosine which ↑ DA and NE
- Complex Carbos snacks calm (w/o protein)
  - –Via trytophan—serotonin
  - –Cause the release of insulin—changes blood chemistry
- Simple Carbos-- ↑ then ↓ energy

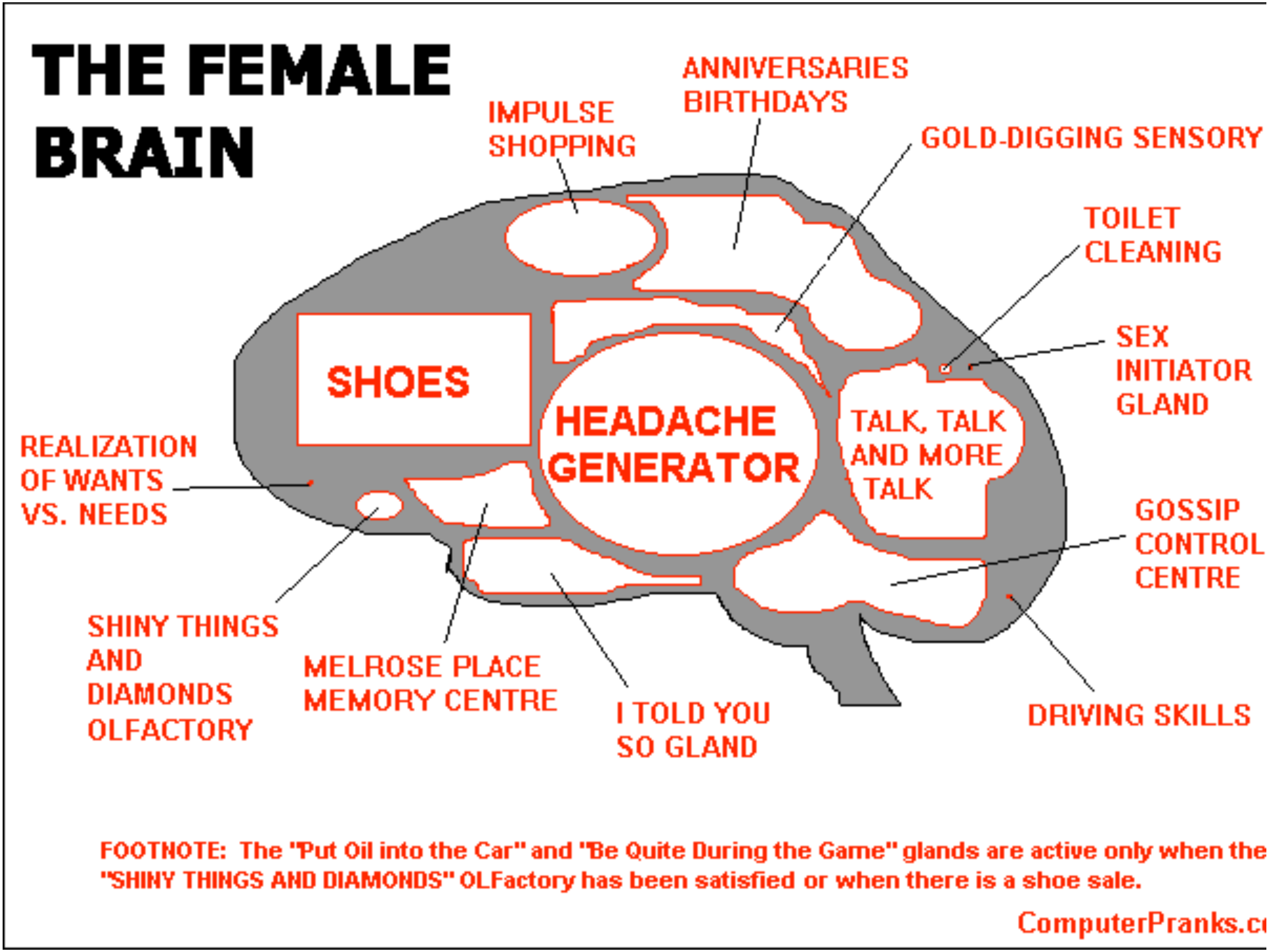
Gender Differences

- Girls develop language earlier than boys
- Boys develop upper body strength and visual perception earlier
- Girls score higher in grammar, speed of articulation, verbal memory, and verbal fluency
- Boys score higher on Block Design, and Maze performance (Hampson, 2008)
- Women have less lateralization and greater inter-hemispheric flexibility
- Women have thicker corpus callosum
- Women have greater bilateral blood flow

THE MALE BRAIN



FOOTNOTE: the "Listening to children cry in the middle of the night" gland is not shown due to it's small and underdeveloped nature. Best viewed under a microscope.


THE FEMALE BRAIN
IMPULSE SHOPPING
ANNIVERSARIES BIRTHDAYS
GOLD-DIGGING SENSORY
TOILET CLEANING
SEX INITIATOR GLAND
SHOES
HEADACHE GENERATOR
TALK, TALK AND MORE TALK
REALIZATION OF WANTS VS. NEEDS
GOSSIP CONTROL CENTRE
SHINY THINGS AND DIAMONDS OLFACTORY
MELROSE PLACE MEMORY CENTRE
I TOLD YOU SO GLAND
DRIVING SKILLS
FOOTNOTE: The "Put Oil into the Car" and "Be Quite During the Game" glands are active only when the "SHINY THINGS AND DIAMONDS" OLFactory has been satisfied or when there is a shoe sale.
ComputerPranks.c

Sex and Gender

- men have 2 ½ times greater area in their hypothalamus devoted to sex drive
  - ↑ sexual thoughts
- Men use their visual systems to a much greater degree
- Men make 10xs more testosterone than women
  - When testosterone levels drop, so does libido

Perimenopause and Menopause

- Perimenopause
  - Erratically cycling estrogen, progesterone, and testosterone
  - Fluctuating libido, erratic sleep, fatigue, hot flashes, and irritability
- Monopause
  - ↓ estrogen and no progesterone
- Postmenopause
  - Low steady estrogen & testosterone—lower oxytocin
  - Calmer

Gender Spectrum

- The superachiasmatic nucleus (SCN)—part of the hypothalamus is twices as large in gay men then straight
  - Caused by a difference in the way testosterone reacts to the developing brain
- The anterior commissure (part of the corpus callosum) is larger in gay males—as it is with women
  - Associated with greater verbal ability (Swaab, 1985, 2009)
- Less asymmetry of the two hemispheres with gay men (like women) than straight men (Savic, 2008)
- Hypothalamus in gay men more responsive to pheromones in male sweat then straight men (Savic, 2001).

Gender and Responsivity to Facial Expressions

- Men consciously suppress emotions but react more to microexpressions (Sonnby-Borgstrom)
- Women consciously exaggerate emotions but unconsciously react less
- After 2.5 seconds (the amount of time for conscious processing) men's facial muscles become less responsive then women's

Mirror Neuron System (MNS) and Gender

- Women recruit more of the MNS in emotional processing
- Young adult women—larger grey matter volume of MNS (Schulte-Ruther, 2008)
- Men make more accurate judgments when sable or moderately negative emotion is expressed (Yuan, 2009)
- Women perform better in empathy, interpersonal, sensitivity, and emotional recognition (Cheng, 2009)

Empathetic Systems and Gender

- Mirror Neuron System (MNS)
  - –emotional empathy
  - –more extensive in women
- Temporal-parietal Junction (TPJ)
  - –cognitive empathy
  - –increased activity in men

Gender and Spatial Perception

- Males
  - parietal lobes engaged automatically
  - use both parietal lobes
  - rotate objects holistically
- Females
  - parietal lobes on standby
  - use one hemisphere for spatial tasks
  - analytical and piecemeal more when rotating objects

Andropause

- Slow decreasing activation of testosterone and vasopressin
  - Less "must have sex now"
- Increasing role of oxytocin

Gender Neurohormones

- Androstenedione—mother of testosterone in ovaries
  - Dies with the ovaries during menopause
  - Adds to the high spiritedness during youth
- Allopregnenolone—mellowing, calming
  - In withdrawal as in it sudden departure in PMS, leads to irritability

Gender Neurohormones

- Mullerian Inhibiting Substance (MIS)—the defeminizer which strips away all the is feminine.
  - Builds brain circuits for exploratory behavior
- Oxytocin—calming and trust building
  - More available in women
  - For men the "down boy" calming and settling (blame for postcoital narcolepsy)
  - Sister of vasopressin
  - Friend of DA

Gender Neurohormones

- Progesterone—sometimes storm clouds and other times a mellowing agent (via allopregnenolone)
  - Increases irritability when estrogen is low and progesterone is dropping
  - Prunes hippocampal connections
- Vasopressin—involved in monogamy, gallantry, aggressively protecting, and defending turf, family, mate and children
  - ↓ vasopressin & ↓ estrogen==↓ serotonin

Gender Neurohormones

- Estrogen—dominant in premenopausal women
  - Associated with the activity of DA, oxytocin, NE, and acetylcholine
  - Conducive to ↑ hippocampal connections
  - For midlife men it plays a greater role as testosterone decreases increasing the desire to cuddle and relate by stimulating oxytocin

Gender Differences

- The medial preoptic area (MPOA—in the hypothalamus) is 2.5 larger in males
  - Related to sexual pursuit
- Temporal-parietal Junction—cognitive empathy
  - The solution seeker—fix it quick
- Dorsal Premammillary Nucleus (DPN)—deep inside the hypothalamus
  - Larger in males
  - Circuitry for instinctual one-upmanship, fear, territorial defense and aggression

Gender Differences

- Anterior Cingulate Cortex (ACC)—weighs and detects conflict
  - Smaller in men
  - The worrywart center
- Rostral Cingulate Zone (RCZ)—registering social approval and disapproval
  - Important for processing social errors
  - Helps reset and hide facial expressions
  - Particularly important for post puberty males

Gender Differences

- PFC—puts the brakes on the amygdala—executive control center
  - Larger and matures earlier in females (by 1-2 years)
- Mirror Neuron System (MNS)—helpful in reading faces and body language
  - Larger and more active in females
- Septum—associated with suppressing anger
  - Smaller in men

Gender Differences

- Periaqueductal Gray (PAG)—involved in pain and pleasure
  - During intercourse it is the center for pain suppression and Intense pleasure
  - More active in the male brain
- Amygdala—fired up to fight by testosterone, vasopressin, and cortisol
  - Calmed by oxytocin
  - Larger in males

Gender Differences

- Insula—center of “gut feelings”
  - Larger and more active in females
- Hippocampus—explicit memory
  - Larger in females
- Male brains 9% larger after correcting for body size but same number of neurons

Gender and Emotion

- Women tend to use both hemispheres to respond to emotional experiences
  - Connections are also more extensive (Wagner, et. al., 2003)
  - In response to emotional images women tend to light up 9 different regions, while men only 2 (Canli, et. al, 2002)
- Men tend to use one hemisphere

Gender and Aging

- Older men who are social ↑ brain regions associated with pleasure and reward
  - Ventral tegmental area-- ↑ DA
  - Nucleus accumben
- Men ↑ health after retirement if married but not for women
  - Men live 1.7 years longer
  - Women live 1.4 years fewer years

Gender and Aging

- Married older Men ↑ social support
  - "take your meds…. Go to doctors"
  - Differential effect effect of how both genders deal with the stress of a bad marriage

Language and Gender

- Female brains 10% ↑ neurons in areas of the brain associated with language and hearing
- Men use roughly 7,000 words a day
- Women roughly 20, 000 words a day

Hormone Fluctuations

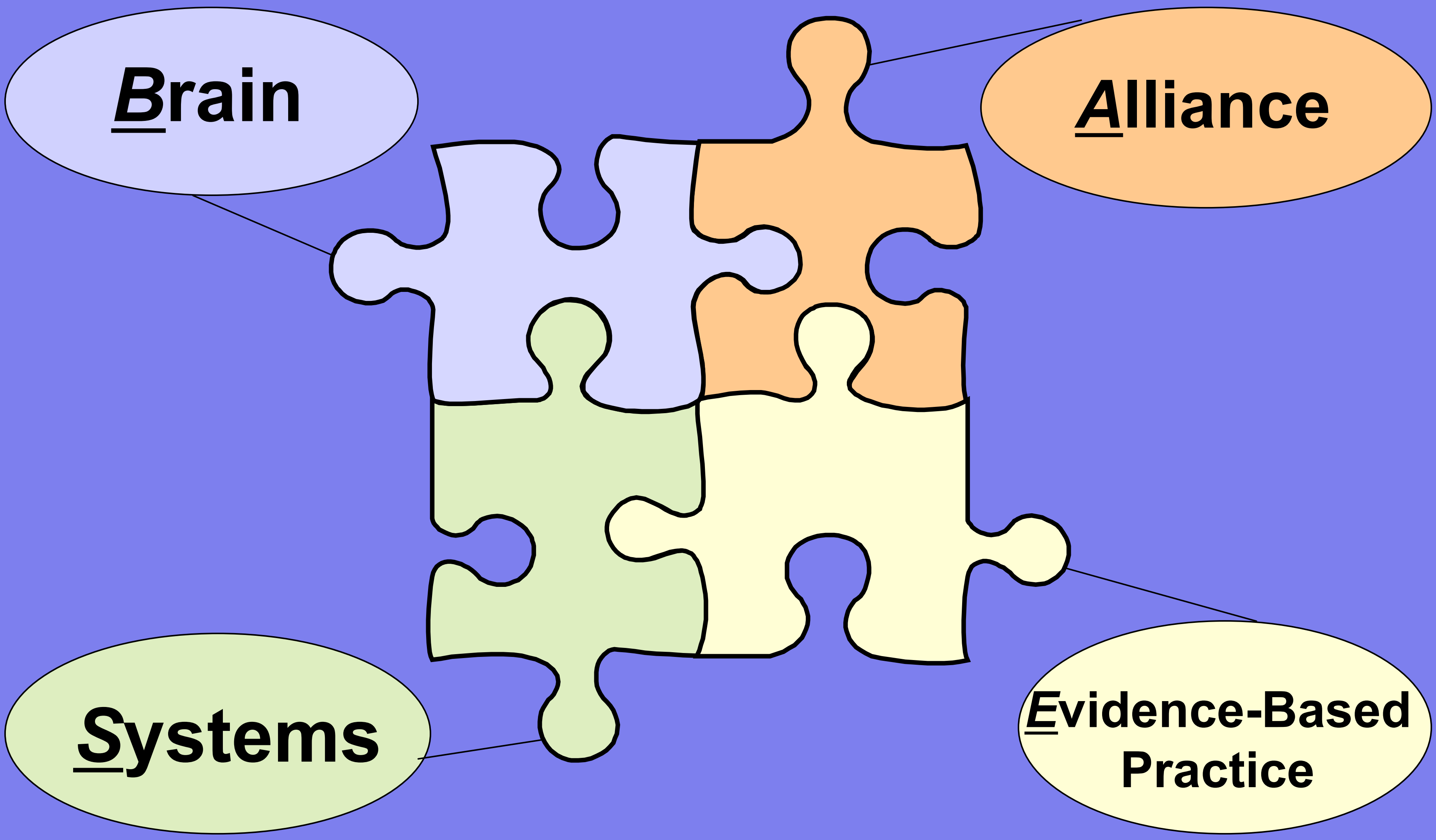
- Most women mildly affected
- 10% experience mood swing and ↑ stress intolerance
  - Ovaries make less estrogen and progesterone
  - ↓ serotonin
  - Diagnosis of premenopausal dysphoric disorder (PMDD)

Day 2: Applications

- Overview
- Stress, Trauma, and Change
- Panic
- PTSD
- OCD
- Depression
- SEEDS

1. Review

The BASE of BBT



Working from the BASE

The acronym BASE corresponds to each of the four dimensions:

B – Brain---the neurodynamics

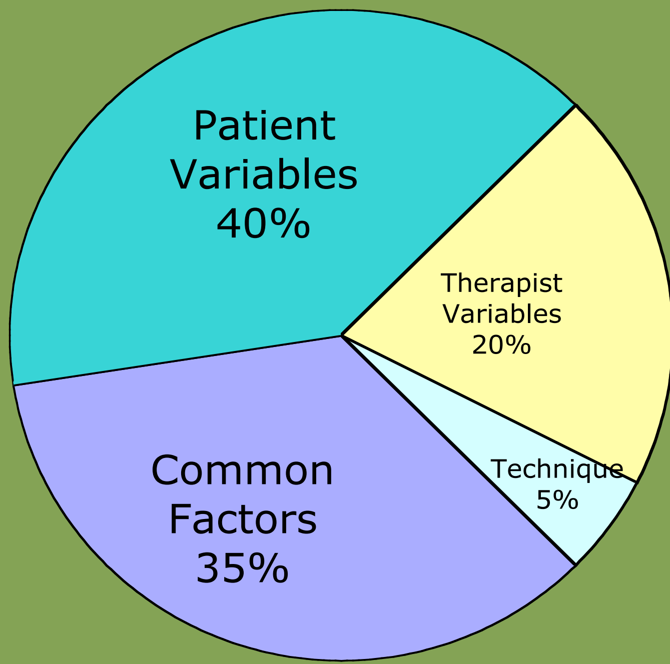
A—Attunement---the quality of the therapeutic alliance i.e. attachment dynamics

S---System---the system of psychological theories and diagnosis

E---Evidence-Based Practice---what research has shown works

The Waning of *Pax Medica*

- **Doubts about the medical model**
- **The fading of the "theoretical schools"**
- **The emergence of an integrated BASE model**
  - **Biopsychosocial**
  - **"Self"-organizing**



Developmental Dialectics

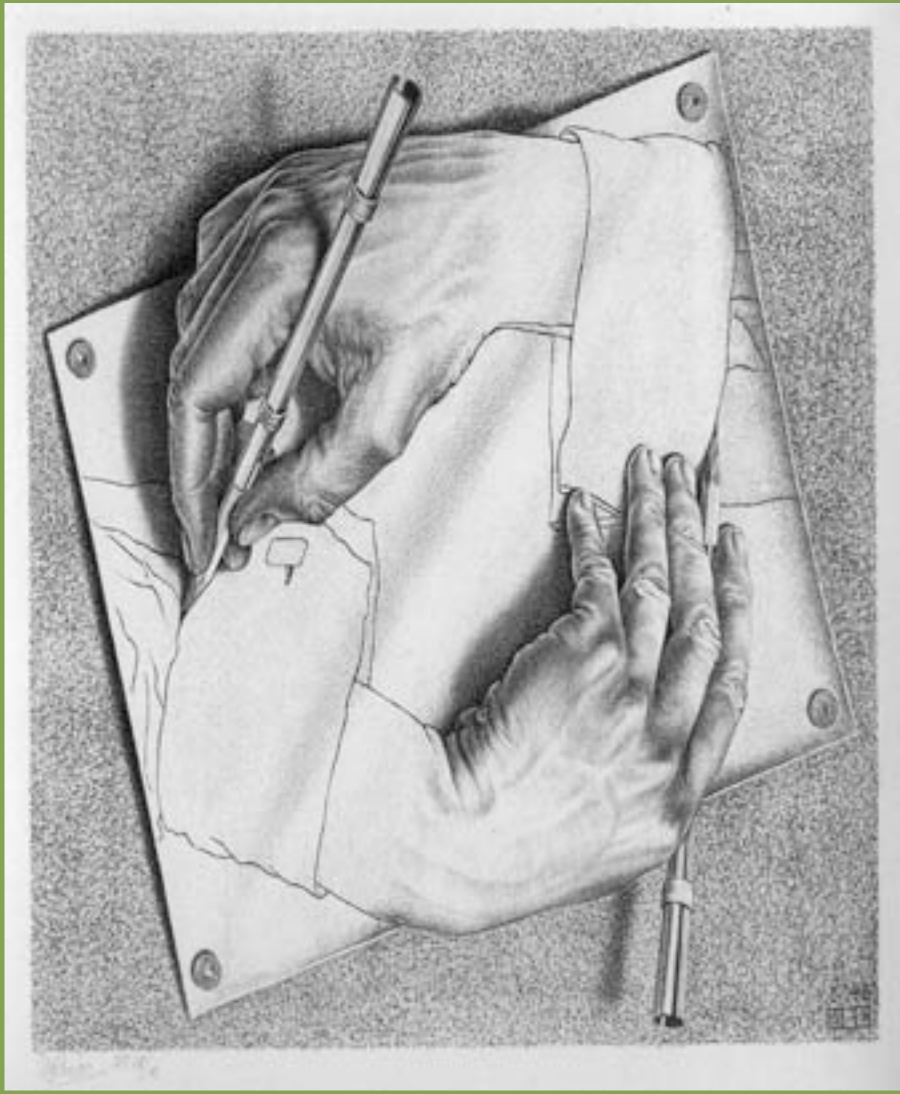
- **Nature/neurodevelopment**
  - –Early development of the social brain networks including the vagel system
  - –Myelination
  - –Pruning
- **Nurture/Attachment/Experience**
  - –Determines the individual's affect and stress regulation patterns

Child & Adult Categories

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

Neuroscience Breakthroughs

- Neural networks that mediate formative relationships
- PFC and executive functions
- Affect asymmetry
- Amygdala and fear networks
- Neuroplasticity
- Neurogenesis
- Default Mode Network
- Nutritional Neuroscience



A Mnemonic "Recipe" for Feeding Your Brain

- **F**ocus
- **E**ffort
- **E**ffortlessness
- **D**etermination

Two Memory Systems

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

Planning for a good alliance…

- **Connect attachment schema to the therapeutic relationship**
  - **Preoccupied =** idealization of therapist, splitting
  - **Dismissing =** overt denial of distress & symptoms
  - **Unresolved =** fearful of therapist / trust avoidant/ intermittently chaotic
  - **Disorganized =** lack of recall / intrusion / dissociation / magical thinking

AAI and Planning

- Preoccupied clients forget about the working relationship and get caught up in emotional memories
- Avoidant clients: “I don’t remember much about my childhood” and are puzzled about feelings and motives
  - **Don’t assume emotional memories haven’t been encoded until you’ve tried everything to evoke them (i.e. implicit reactions)**

Planning Therapy

<u>Matching/mismatching</u>

Down regulate **Flexible** **Up-regulate**

Avoidant/Dismissive **Secure** **Ambivalent/Preoccupied**

Attachment and Therapy

We help our clients earn security

- Re-visiting their attachment narrative
- Increasing the client's ability to attend to either the relational or external world, as needed
- Developing their metacognitive and mentalizing capacities
- The hope: Protecting their offspring from insecurity and tramatization

Insecurity is Inflexible

Preoccupied clients:

- Build affect regulation (meditation, DBT)
- Behavior activation
- Mentalizing

Avoidant clients:

- Increase exposure to affect (“how did you feel?”, groups)
- Focus on the transference and counter-transference
- Thought records

The BBT Alliance

- Holding a memory in awareness means energizing the neural nets that “remember” it
- When re-activated in a relationship characterized by trust and hopefulness, firing patterns that were previously segregated can be integrated, making the pain tolerable

Therapist Security

- Preoccupied therapists likely to experience temporary breaches as failures or personal attacks
- A dismissing therapist is more likely to misuse neutrality, misunderstand intersubjectivity, or hide behind cognitive interventions
- Disorganized or unresolved therapists are more likely to do harm
- The real “best practice” may be therapy and supervision

BBT Case Formulation

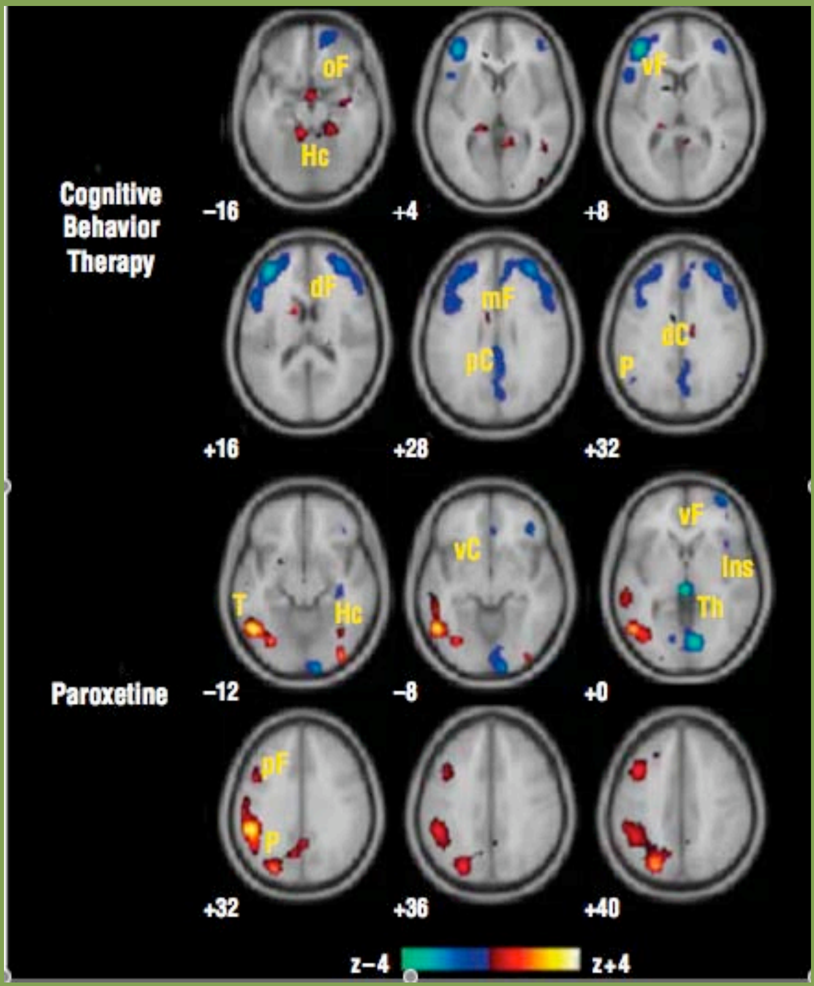
On-going assessment of progress and the alliance

- **How does the client respond to interventions?**
  - Outcome management protocols
  - Be aware of nonverbal communications (facial expression, action, rhythm)
- **Negative affects and reactions are a plus!**
  - Opportunities for repairing ruptures
  - “Good enough” is better than perfect!

Brain-Based Therapy

- *Both* medication and psychotherapy alter the brain
- Psychotherapy works "by producing changes in gene expression that alter the strength of synaptic connections…"

  --Eric Kandel, MD



The BASE: Case Formulation

- **B is for Brain**
- **A is for Alliance/Attachment**
- **S is for Systems**
  - –Theories of intervention
  - –Diagnosis
  - –Cultural factors
- **E is for Evidenced-based Practice**

Passive Pete: A Case in Point

- **The B: The Brain**
  - MJ complicates neurodynamic systems
  - Emotional regulation problems
  - R-PFC
- **The A: Attachment**
  - Passive dependent attachment (getting from people what he wants; doing as he pleases)
  - He wants to be cheered up

Passive Pete: A Case in Point

- **The S: Systems**
  - Passive-aggressive Dx
  - Dysthymia
  - relationship problems
- **The E: Evidence-based practice**
  - Group treatment for alcoholism;
  - Behavioral activation
  - Paradoxical approaches

BBT provides support for:

- **Psychodynamic theory**
  - Mentalizing (ToM and metacognition)
  - Good enough objects (integration)
  - Intersubjectivity (the "we")
- **CBT**
  - Cognitive schemas
  - Exposure
  - Behavior activation
- **Mindfulness (attention training)**

Psychodynamic Therapy

BBT supports:

- Focus on the alliance
- Implicit memories of early experience
- The bi-directional nature of dyadic relationships
- Good for highly resistant clients
- The interaction of affect or impulse arousal and defensive measures

Psychodynamic Concepts

- Freud's Project for a Scientific Psychology
  - "Contract barriers" – prelude to Sherrington's "synapses"
- Law of Association --When two neurons fire simultaneously this firing facilitates their ongoing association
- Jung's: Free Association – links in memory networks

Psychodynamic Concepts

- Early experiences can leave permanent memory traces
- Memories can be altered by subsequent experiences and retranscribed.
- Reliving past experiences through transference (secure attachment)
- Reliving past trauma can be altered through insight (attention) and working through (new adjustment)

Psychodynamic Therapy

BBT doesn't support:

- Passive ideas about "therapeutic neutrality"
- Lack of intervention/interaction can deepen client's tendency to perseverate
- Elitist roots
  - Can be authoritarian rather than authoritative
  - Encourages transferences ~ of a child to a narcissistic or depressed parent
- Privileges "the internal world" over the external one; the "mind" over "behavior"

Psychodynamic Extrapolations

Exploring emotions—the full range and contradictions

Examining Avoidance—using a little motivational interviewing

Identifying Reoccurring Patterns—codependency etc

Discussing Past Experiences—attachment styles

Focusing on relationships—including transference

Valuing fantasy life--DMN

CBT

The good

- Attention training elucidates affective bias
- Power of behavior to change the brain
- Good for low-resistance clients who like structure and follow instructions
- Develops collaborative alliance and treatment-based evidence
- Gives clients tools to take with them when therapy ends

CBT

The bad

- **Therapeutic alliance unexamined**
- **Emotions often *don't always begin with thoughts***
  - Origin in body sensations (James)
  - In nonconscious changes in brain state (Damasio)
  - In old and nonconsious emotional memories
- **CBT relies on the hippocampal record**
  - Constantly being remodeled
  - We forget facts and events and trains of thought much more readily than basic emotions

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)

Therapy and Brain Change

Direct, observable links between successful therapy and brain changes

- **Reduced amygdalar activity in treated phobics** (Straube, *et al.*, 2006), **panickers** (Prasko *et al.*, 2004), **and social phobics** (Furmark *et.al,* 2002)
- **Reduced frontal activity in treated depressives** (Goldapple *et al*., 2004)
- **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)

Planning Therapy

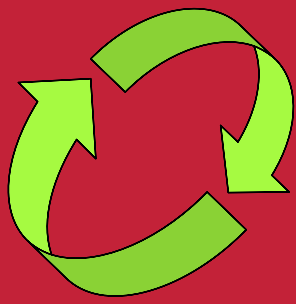
- Does the client have a DSM diagnosis for which a “best practice” has been identified?
- If the problem is primarily generalized distress, unhappiness, life events or relationships, the primary concerns may be attachment-based

BBT and EBT

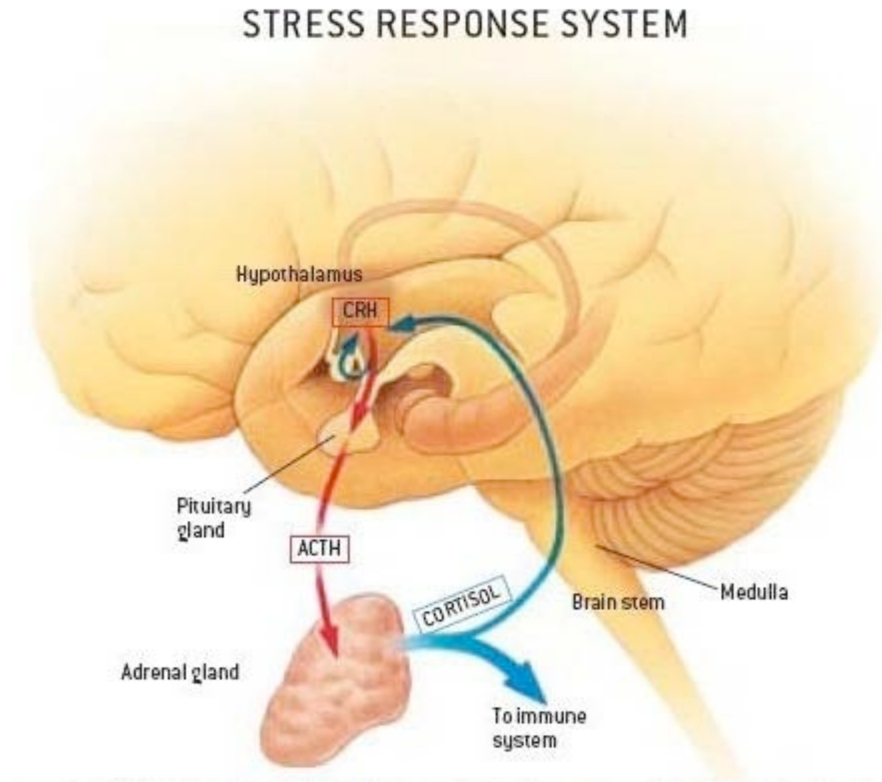
- Problems/disorders for which there is strong evidence that specific methods are indicated:
  - Panic
  - OCD
  - PTSD
  - Depression

Stress

- Fight-Flight mechanisms were designed for rapid action – not sustained stress
- Stress hormones damage brain structures
- When stress is early and prolonged, the resultant damage impacts stages of development
- The expanded cortex results in a brain that can create its own stress

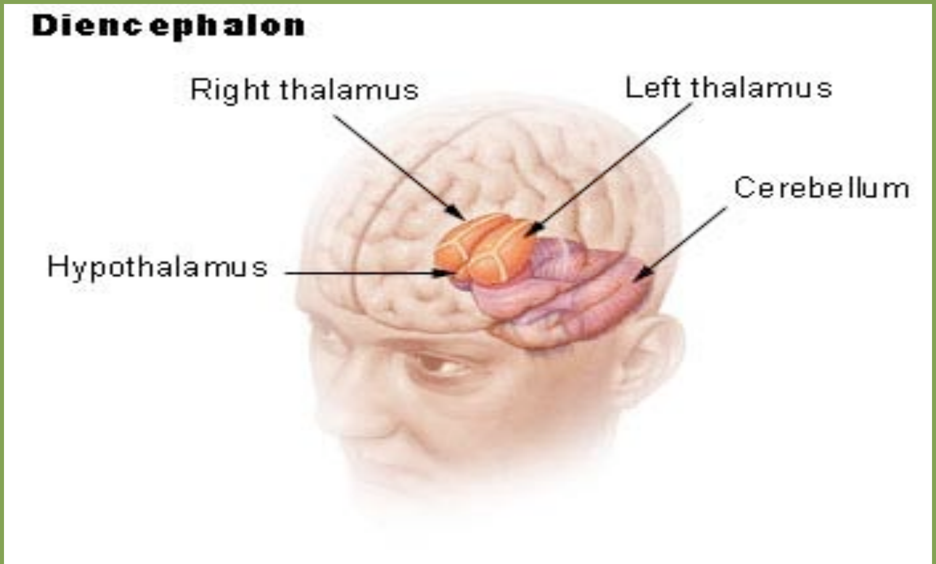


Hypothalamo-Pituitary-Adrenocortical (HPA) Axis: Cortisol Levels



Alice's Restaurant

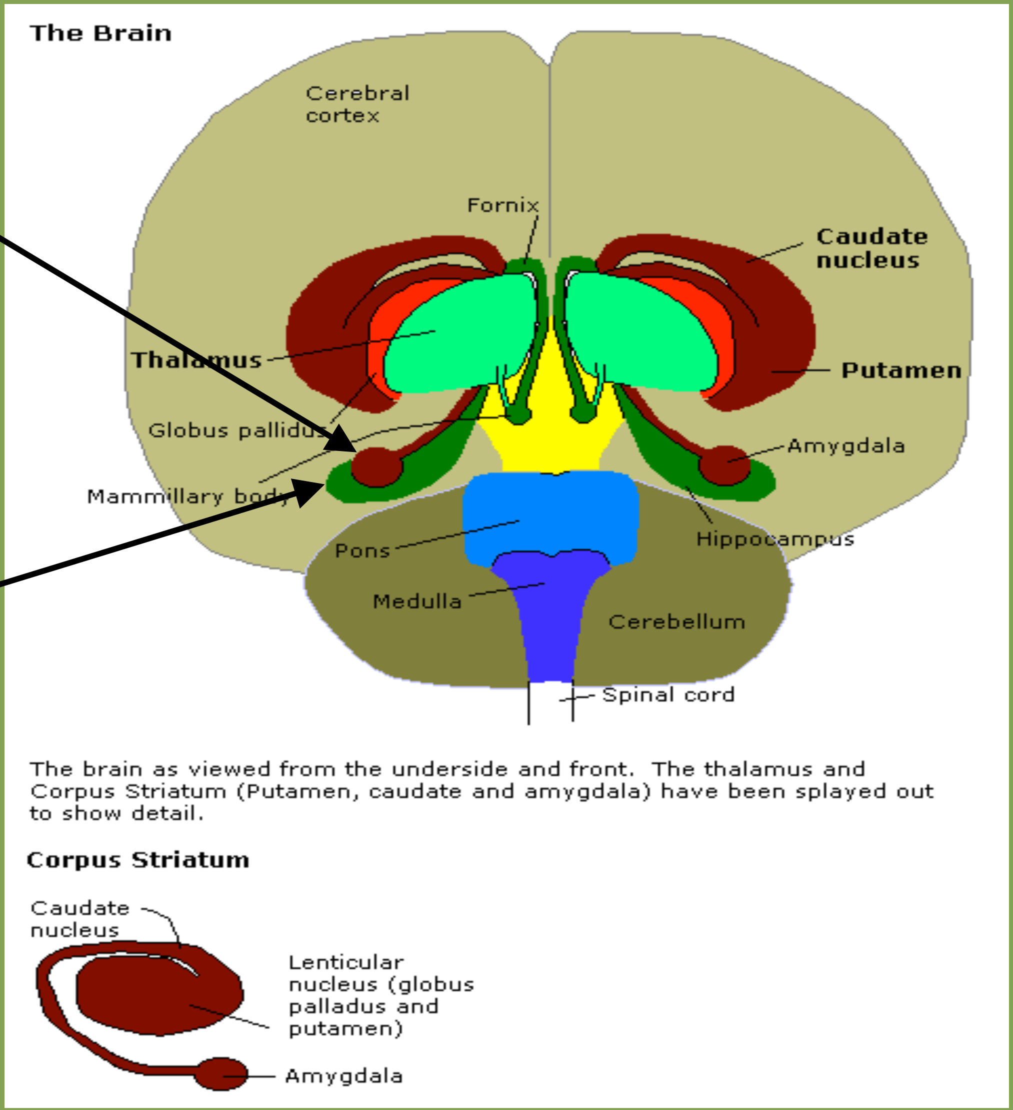
- **Many brain systems try to influence the hypothalamus**
  - **turns on the parasympathetic ("purr") circuits and also the sympathetic ("scream") circuits**
  - **The 3 "Fs"—fight, flight and sex….**



The Seahorse and the Almond

Amygdala *turns up* the HPA axis and the sympathetic NS

Hippocampus *turns down* the HPA but may get overwhelmed



Stress—Bottom Up or Top Down?

- **William James—bottom up--"My hands are shaking –I must be nervous"**
- **Walter Cannon—top down—emotions decided by the brain.**
  - **HPA axis**
  - **The 3 "Fs"—fight, flight and sex….**
- **Schacter and Singer (1962) 2 Factor Theory**
  - **Injection of epinephrine—arousal**
  - **Social situation with happy or sad "accomplice"—appraisal**
- **Paul Ekman—support for James**
  - Moving facial muscles changes emotions

Long-Term or Traumatic Stress

Cortisol Cascade Hypothesis:

- Stress causes production of cortisol
- Excessive cortisol causes dendrites in the hippocampus to shrivel up (Sapolsky, 1996)
- This feedforward loop leads to heightened reactivity of amygdala
- The hippocampus is essential for turning off HPA axis, damage to it leads to even more cortisol release as time passes
    - PTSD patients with smaller hippocampi (Bremner, 1999)

5-HT and NE Interplay

- ↑ or ↓ 5-HT effects the intensity of activation of NE
- Tryptophan depletion then the consumption of yohimbine (an alpha2 adrenergic agonist – ↑ NE activity)
- Healthy subjects with tryptophan depletion result in an increase in a subjective nervousness (Goddard, et. al., 1995)
- Yohombine alone to healthy subjects—no effect
- Yohombine alone to PD pts.-- ↑ symptoms

The neurochemical switch (mechanism for the inverted "U")

- NE has high affinity for the alpha2A receptors
- Moderate release of NE (i.e. alert wakefulness)
  - Facilitating PFC regulation of behavior and suppressing the amygdala

The neurochemical switch (mechanism for the inverted "U")

- Excessive release of NE (i.e. stress) engages the alpha1 and beta adrenorecptors
  - Impairs PFC functions and disinhibits the amygdala
- Thus the amygdala can serve to flood the PFC with NE and take it "off-line" which promote irrational behavior

The neurochemical switch (mechanism for the inverted “U”)

- NE and epinephrine play a central role in encoding and consolidating memories by the amygdala
- A moderate level of catacholamines – the inverted “U” is optimal for full spectrum memories
- Too little (i.e. boredom) –not enough attention—no consolidation of memories
- Too much activation narrows attention to the threat (at best)

Neurochemistry of less stress

- Dehydroepiadrosterone (DHEA)
- ↑ DHEA ↓ less intense emotional response to stress
- ↑ DHEA – more resilient
-
- Neuropeptide Y (NPY)
- People with PTSD noted to have ↓ NPY
- Injection of NPY in the rat amygdala ↓ anxiety symptoms

Dehydroepiandrosterone (DHEA)

- A natural steroid hormone--product of the adrenal glands
  - serves as precursor to male and female sex hormones
  - Levels in the body begin to decrease after age 30
- higher levels associated with a buffer to stress (Morgan, et. al., 2000)
- low levels associated with depression
- DHEA can cause higher than normal levels of androgens and estrogens in the body
  - theoretically may increase the risk of prostate, breast, ovarian, and other hormone-sensitive cancers

Neuropeptide-Y (NPY)

- NPY -- a neurotransmitter which binds to receptors on neurons in the prefrontal cortex
  - Alters their response to NE, and acts as a break to its accelerator pedal.
  - The best performers dealing with stress have NPY levels that are ⅓ higher than peers and quickly return to healthy baseline once the stress is over.
  - Less resilient individuals seem to have lower capacity for NPY production as well as NPY levels dropped to below baseline 24 hours afterwards . (Morgan, et. al., 2004)

Neurochemistry of stress

- The amygdala and 5-HT
- ↓ or 5-HT in amygdala associated with ↑ firing (decrease threshold)
- 5-HT acts through GABAergic interneurons which modulate glutamatergic input (Morgan, Krystal, & Southwick, 2003)
- ↑ of 5-HT associated with increased threshold of amygdala

NE and 5-HT Interplay

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- Yohombine alone to PD pts.-- ↑

Fear conditioning and the amygdala

- Convergence of US and CS leads to neuroplasticity in the lateral amygdala (LA)
- When the CS occurs alone synaptic firing flows to the medial part of the central nucleus which control condition fear responses (LeDoux & Schiller, 2009)

Fear conditioning and the amygdala

- Fear conditioning involves the release of glutamate in the LA which binds to excitatory amino acid receptors AMPA and NMDA:
  - when the magnesium block is removed sufficient calcium enters the cell and it activates protein kinase
  - which translocate to the cell nucleus and trigger gene expression and protein synthesis

vmPFC and amygdala inhibition

- Connections between infralimbic cortex (IL)—a subregion of the vmPFC and the intercalated cells (ITC)—within the amygdala form a pathway for inhibition
- The ITC are inhibitory neurons that connect the basal nucleus (B), lateral nucleus (CE)
- During recall of extinction the CS related response in the IL lead to:
  - Extinction of the ITC which in turn:
  - Inhibit communication between the LA (where fear memories are stored) and the CE (output of the fear response) (Quirk, et. al., 2000)

vmPFC and amygdala inhibition

- Stimulating the IL results in decreased excitability of the CE and the expression of conditioned fear (Quirk, et. al., 2003)
- If communication between the LA and the CE is disrupted the expression of fear expression is inhibited
- Projections from the vmPFC and the LA region play a role in the inhabitation of fear (Rosenkranz, et. al., 2003)

Neurodynamics of modulating fear

- The hippocampus projections to the vmPFC modify the PFC's inhibition of amygdala activity during the recall of extinction learning so that it is only expressed in the appropriate context (Phelps, 2009)
- DLPFC --involved in the effortful manipulation of or interpretation of the stimulus
- Then the vlPFC and mPFC—emotional interpretation

“Priming”—sensitization

- When response to repeated stress increases in magnitude via kindling the neurocircuts underlying the memories of the trauma
- Hormones such as arginine, vasopressin, and the catecholamines act synergistically with CRH
- When an emotional stresses is experienced the amygdala—HPA axis function are enhanced through higher ACTH and higher 24-hr free cortisol consentrations

"Priming"—sensitization

- The primed system hyper-responds to stress (DeBellis, et. al., 2005)
- Sensitized memories trigger flashbacks and rekindle fear neural networks
- Given ↑ R-PFC and ↓ L-PFC fears add to a timelessness—the trauma feels like it is happening now—further kindling.
- Failure to inhibit anxiety ramps it up

Allostasis

- Allostatic adjustments are adaptive over the short term—cortisol helps 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 expenditure against the energy and regulatory gains from rest and recuperation. (McEwen and Wingfield, 2003).

Chronic Cortisol
Ramping up allostatic load

- Hyperactive amygdala
- ↓ PFC and its ability to inhibit amygdala activity
- ↓ working memory (Roozendaal, et. al., 2004)
- Cortisol in PFC augments catecholamines through the blockade of catecholamines reuptake

Cortisol can ↑ the toxic effects of glutamate

- Optimally–repetition of a stimulus ↓ the amount of glutamate necessary to make the next transmission
  - i.e. lowers the threshold & strengthens the connection (LTP) via a glutamate receptor called n-methyl-D-asparate (NMDA)
- Chronic stress *overactivates* NMDA receptors which lets in too much calcium which generates free radicals

Allostatic Load—Stress and Diabetes

- Cells need glucose to fuel cells—Insulin's principal job
- When stressed, the body assumes that more fuel is needed to deal with it
- Stress activates genes in cells to increase glucose uptake
- ↑ adrenaline and cortisol ↑ blood glucose
- ↑ cortisol triggers the breakdown of protein and its conversion in the liver to glucose
- Excessive cortisol results in too much glucose floating around
- ↑ cortisol ↑ risk of insulin resistance –Diabetes II

Allostatic Load

- ↑ cortisol in the evening ↓ sleep
- Sleep deprivation ↑ cortisol and glucose in the evening
- ↓ vagal tone
- R-PFC overactivity ↑ cortisol
- R-PFC overactivity ↓ Natural Killer cell activity

Measures of Allostatic Load

- ↑ BP
- Waist-to-hip ratio
- Blood cholesterol
- Glycosylated hemoglobin (glucose metabolism over a period of days)
- ↑ cortisol and norepinphrine in overnight urine
- All the above can predict cognitive deficits 2 years later (McEwen, 2002)

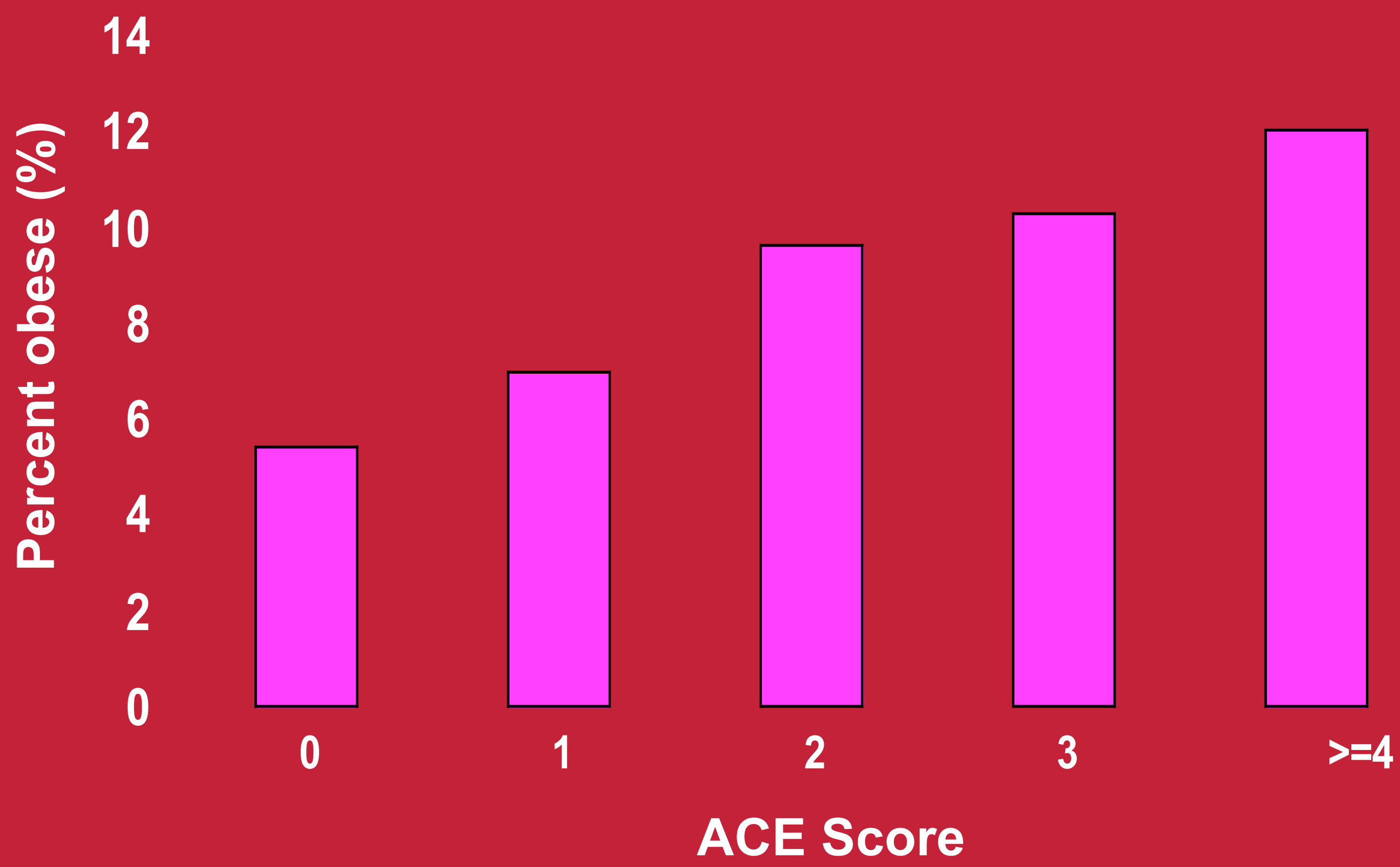
The Good and Bad News

- Enriched environments
  - Neurons sprout more dendrites
  - More synaptic connections are formed
- Deprived environments and trauma
  - Change the brains of abused children
    - Chronically elevated cortisol
    - Smaller left frontal lobes and hippocampal (Bremner et al., 1997)
    - Less integration of left and right hemispheres (Teicher, 2004)
  - Produce more psychopathology, suicides, and medical problems in adults (Felitti)

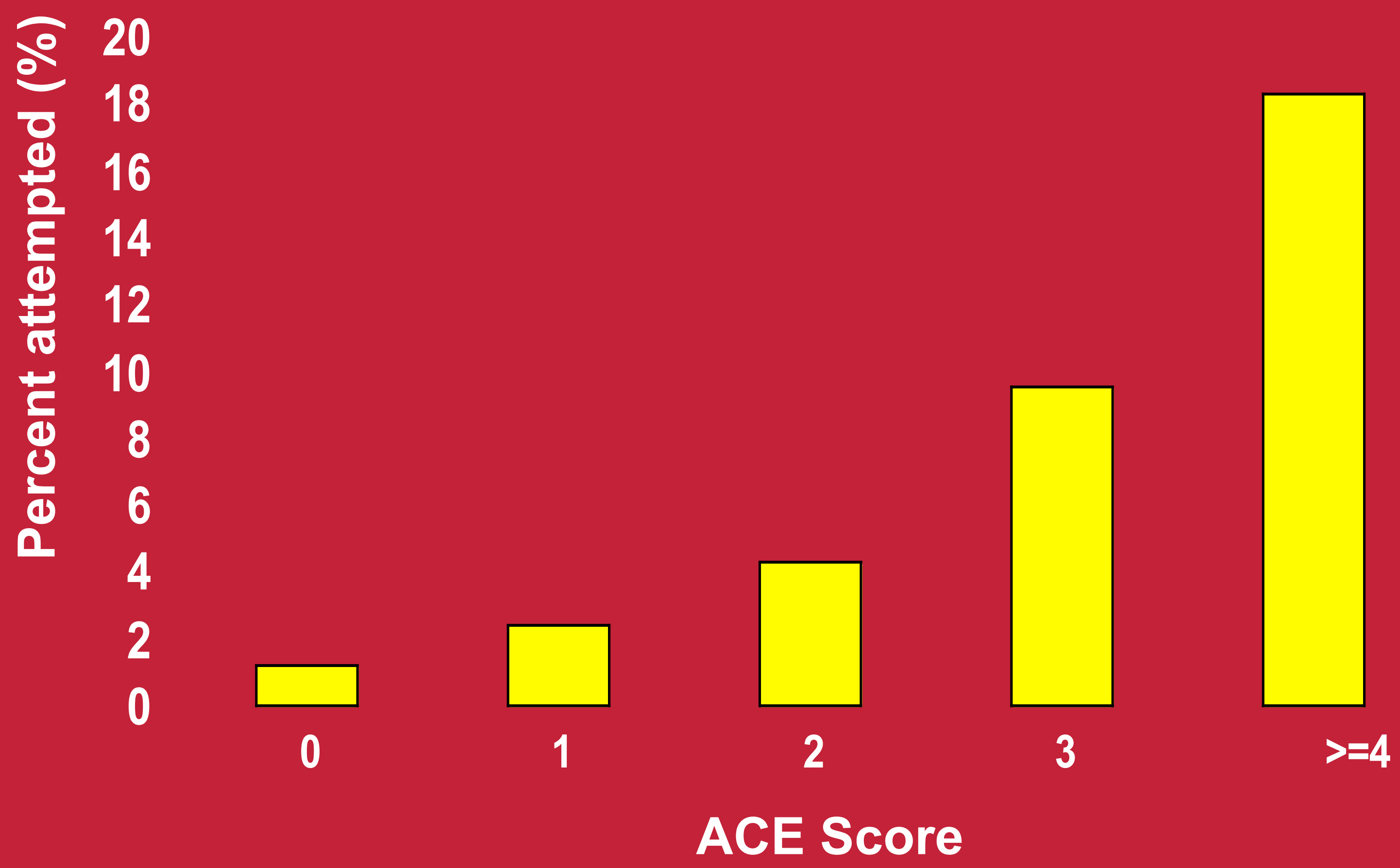
The ACE Study

- Examined the health and social effects of ACE’s throughout the lifespan among 17, 421 members of the Kaiser Health Plan in San Diego county
- What do we mean by Adverse Childhood Experience?
  - Childhood abuse and neglect
  - Growing up with domestic violence, substance abuse or mental illness in the home, parental discord, crime

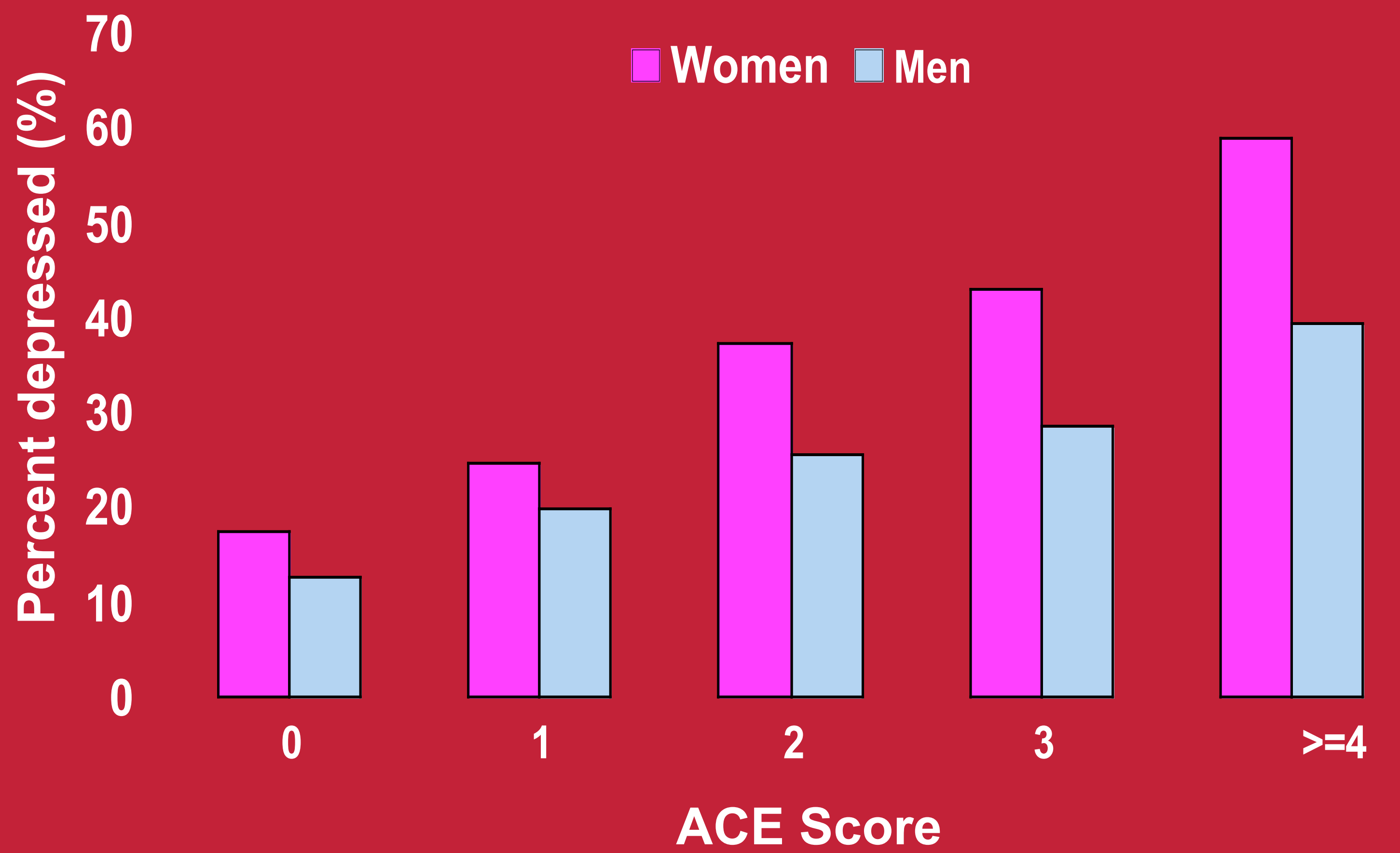
The ACE Score and the Prevalence of Severe Obesity (BMI>35)



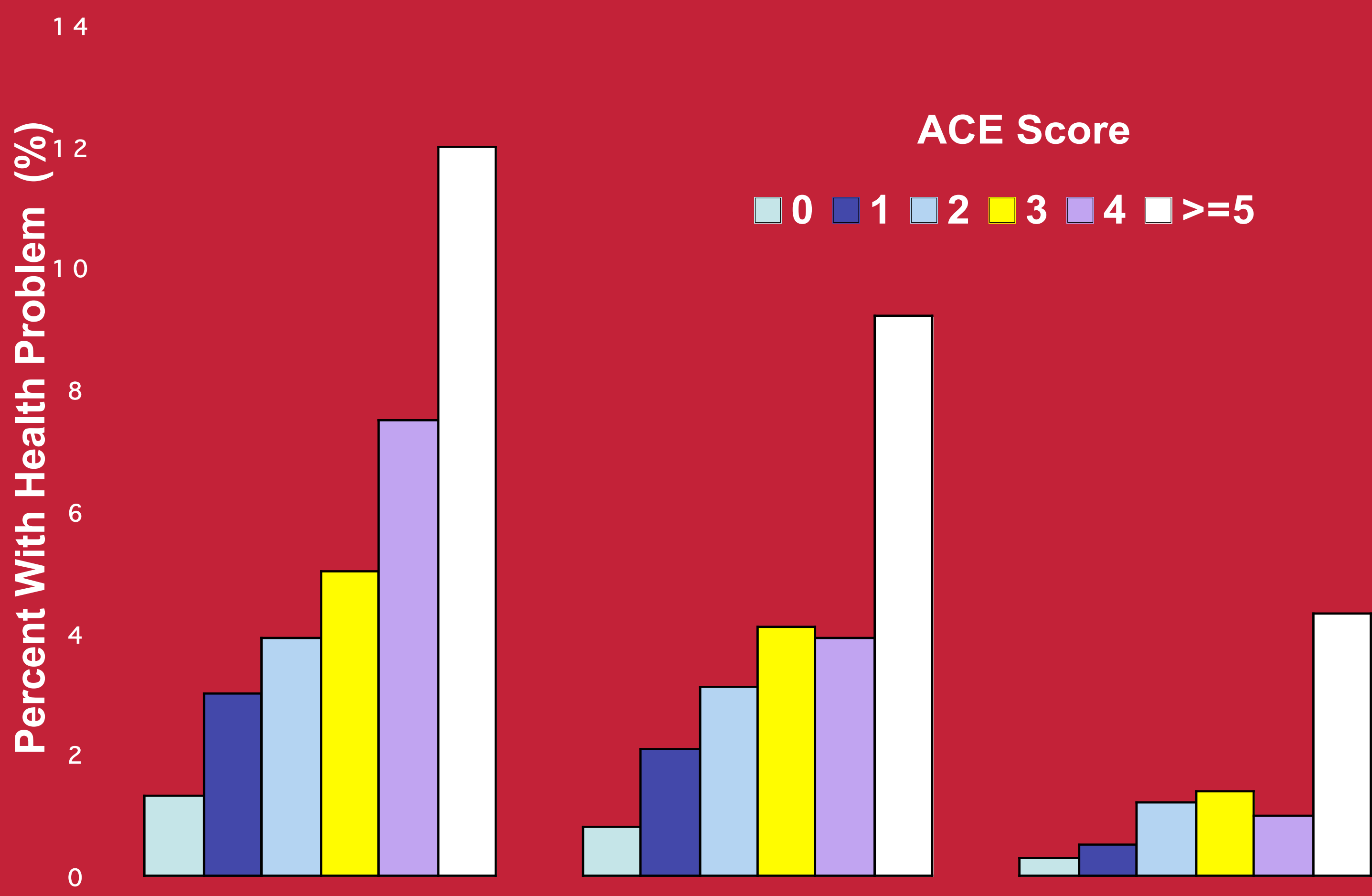
The ACE Score and the Prevalence of Attempted Suicide



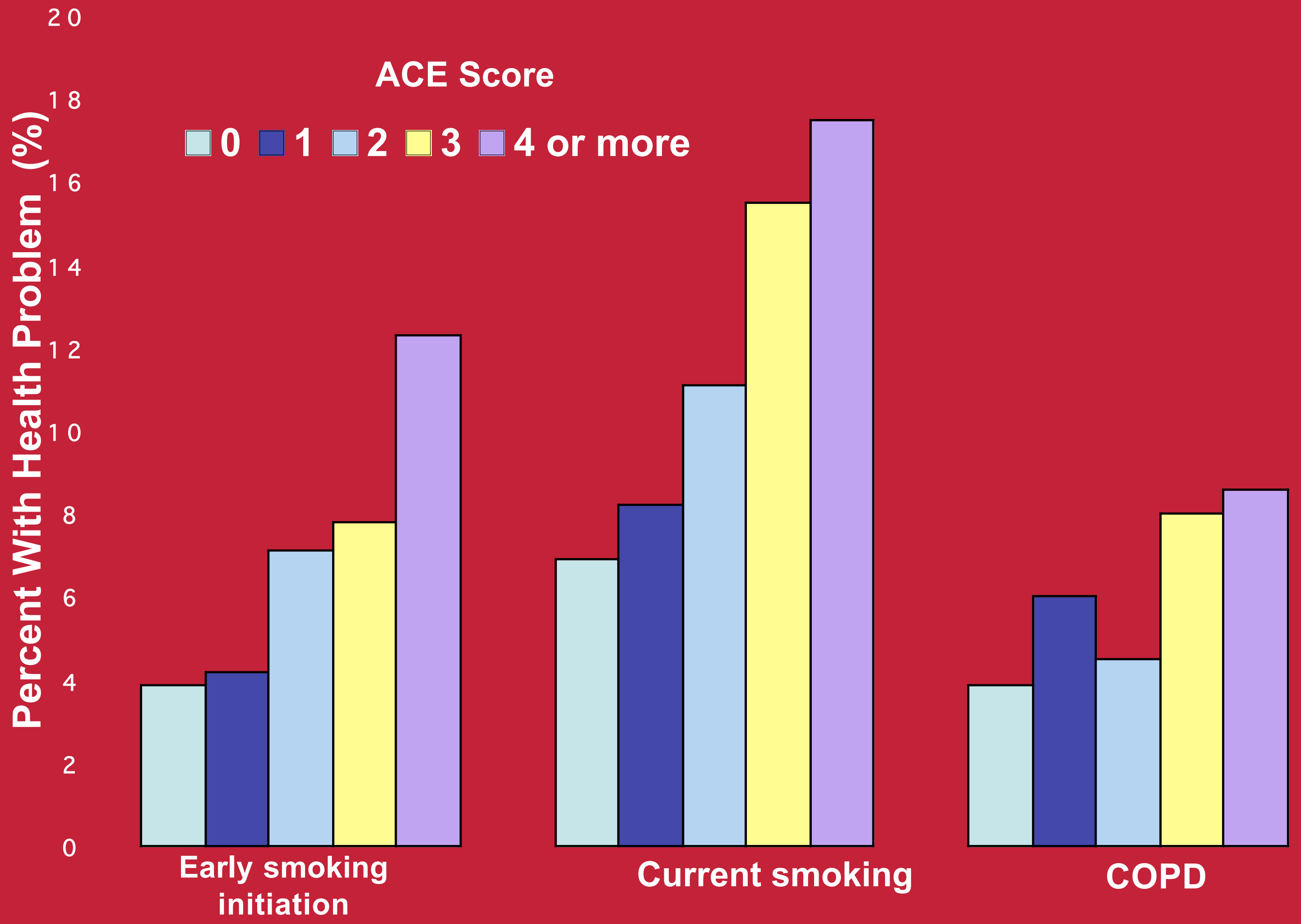
The ACE Score and a History of Lifetime Depression



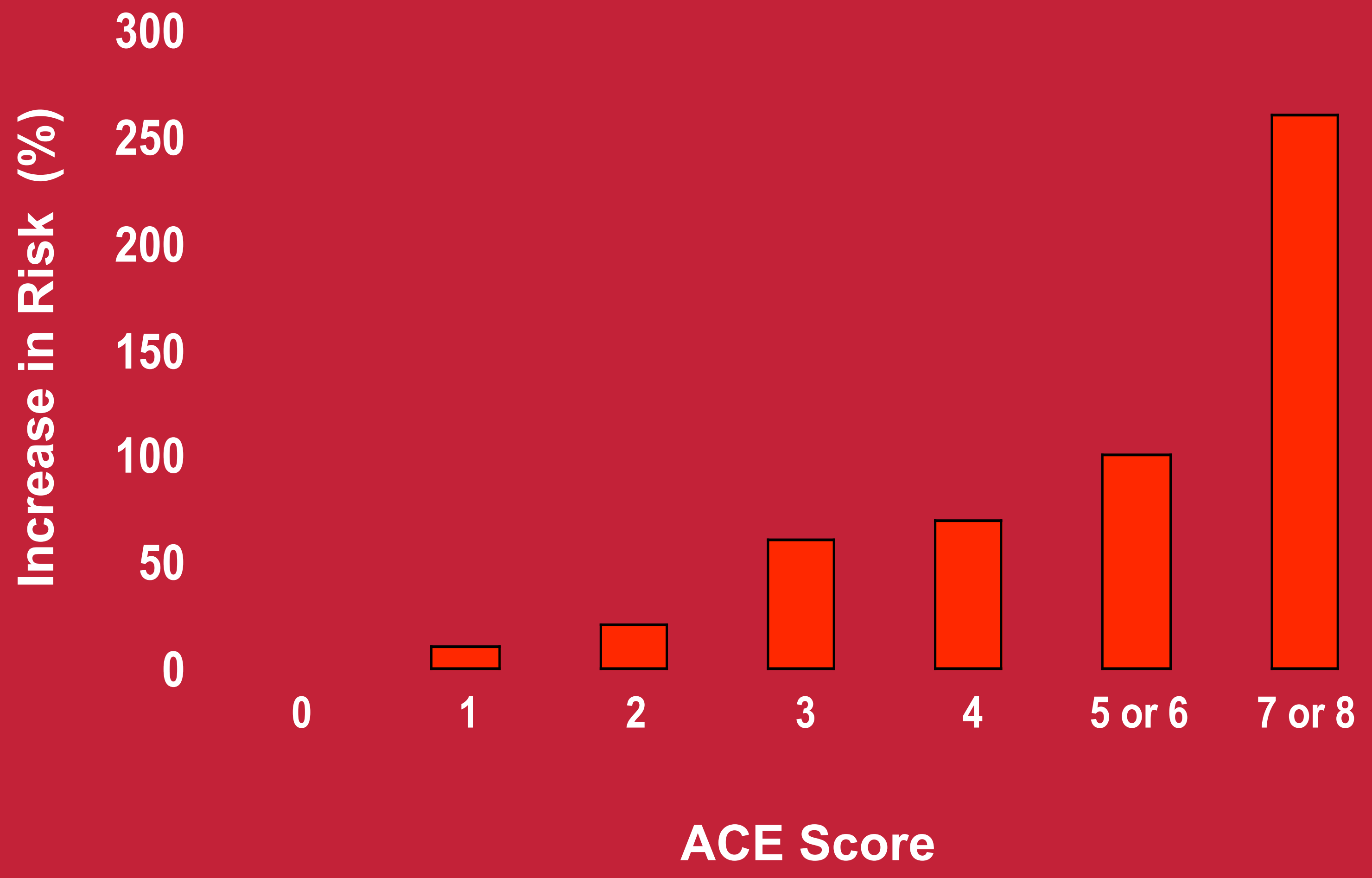
The ACE Score and Drug Addiction



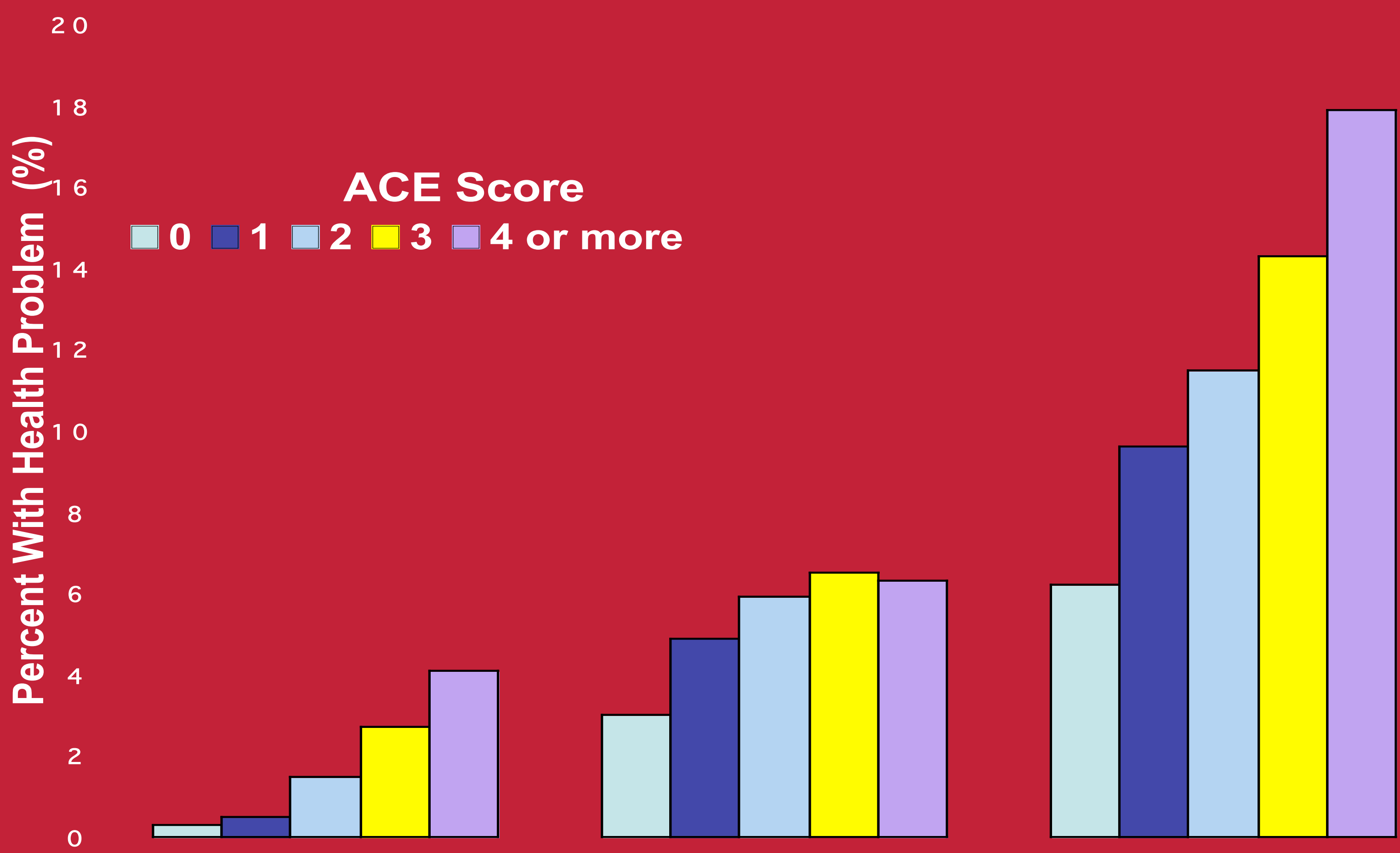
ACE's Smoking and Lung Disease

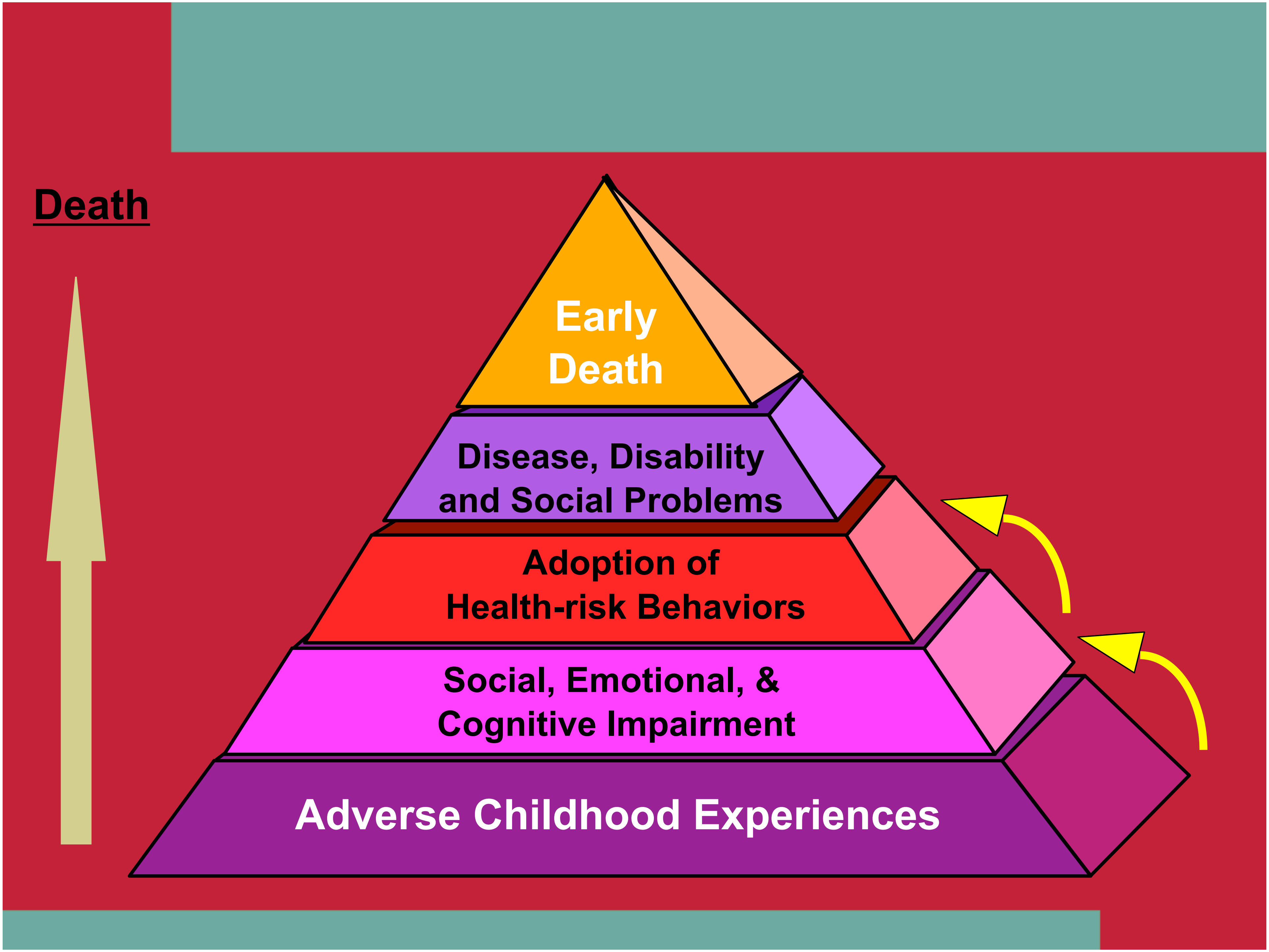


The ACE Score and the Risk of Coronary Heart Disease



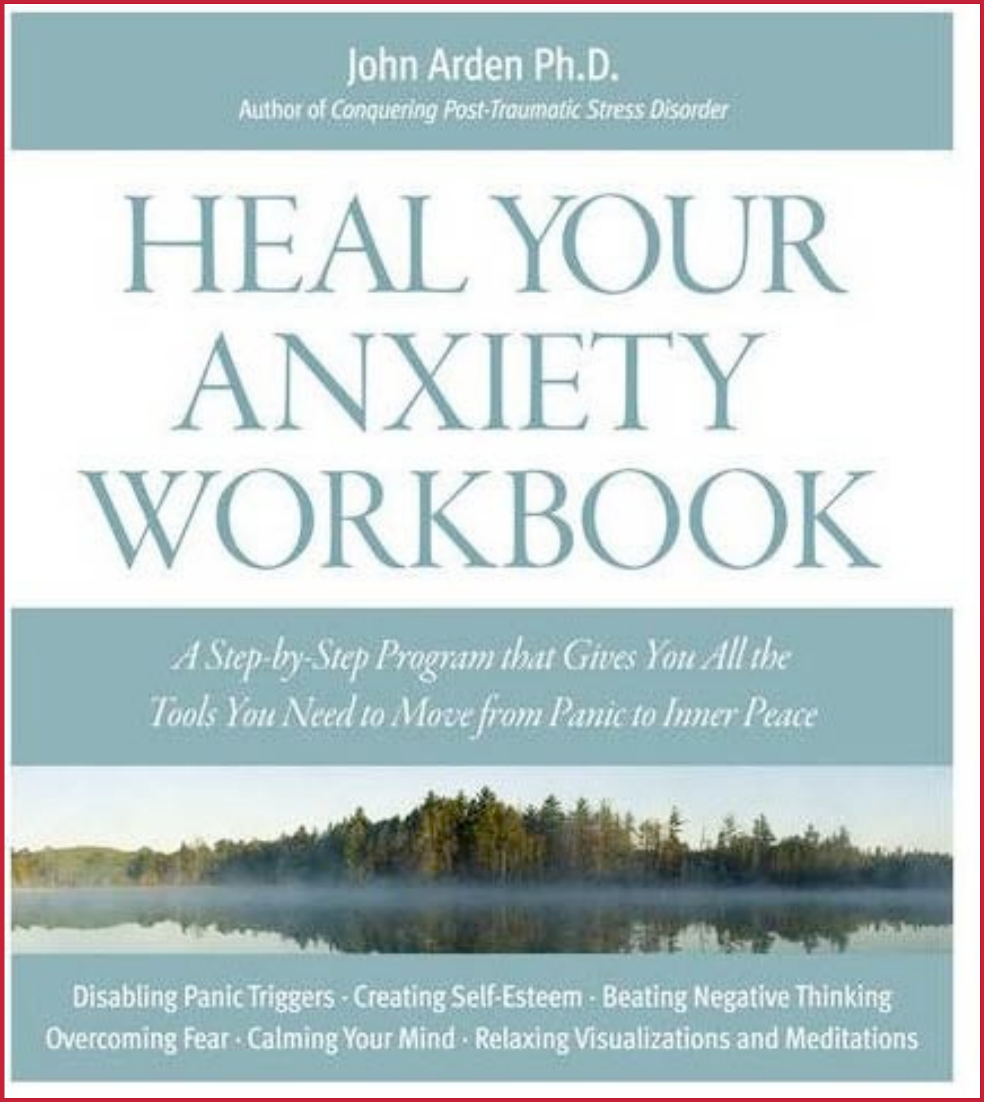
ACE Score and HIV Risks





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

Anxiety


John Arden Ph.D.
Author of Conquering Post-Traumatic Stress Disorder
HEAL YOUR ANXIETY WORKBOOK
A Step-by-Step Program that Gives You All the Tools You Need to Move from Panic to Inner Peace
Disabling Panic Triggers · Creating Self-Esteem · Beating Negative Thinking
Overcoming Fear · Calming Your Mind · Relaxing Visualizations and Meditations

Medical and Drug Related Problems that Mimic Anxiety

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

Neurodynamics of Anxiety

- Amygdala – fear
- Bed Nucleus of the Stria Terminalis (BNST), contributes to a diffuse arousal underlying anxiety (Davis et al., 1997)
- Amygdala maintains projections to the Locus Coeruleus (LC)
  - source of NE which has extensive projections throughout the brain and can trigger the HPA axis (Aston-Jones, et al., 1994).

BNST and GAD

- Bed nucleus of the stria terminalis (BNST) is referred to as the “extended amygdala”
- BNST associated with GAD
- GAD—an intolerance for ambiguity
- GAD—tx. exposure to ambiguity

Factors that impair the PFC

- ↓ 5-HT impairs the OFCs ability to inhibit the amygdala
- ↑ NE through activation of alpha1 –adrenergic receptors
- ↑ cortisol and its interaction with catecholamines

DHEA and exposure

- DHEA is a steroid secreted by the adrenals synchronously with cortisol in response to ACTH
- DHEA positively modulates NMDA receptors and agonize GABAa receptors in the PFC
- ↑ DHEA ↓ PTSD symptoms by enhancing PFC functioning (Rasmusson, et. al., 2004)
- DHEA indirectly effects monoamine release as well as promote FL function through activation of NMDA receptor in the amygdala
- These processes can facilitate extinction through exposure as well as the formation of fear-based memories (Walker & Davis, 2002)

Allopregnanole

- Adrenally derived neuroactive steroid that positively modulate GABAa
- Provides delayed negative feedback inhibition of the HPA axis and anxiolytic effects
- When low it may contribute to prolonged activation of the HPA axis, ↑ amygdala, and ↓PFC activation

Excessive Cortisol

- Thinning of the lining of stomach---↑ gastric ulcers
- Thinning of bones---osteoporosis and bone fractures
- ↓ reproductive systems
- Cardiovascular systems
  - ↑ heart rate
  - Damage to inner surface of the heart
  - Constricting blood vessels
  - Heart beat can decrease in variability--↑ risk of heart attack (i.e. “Soldier's Heart)

Taming the Amygdala

Circumventing the central nucleus by the BNST.

- The central nucleus responsible for the "snowball effect" – linking non-threatening stimuli with legitimately threatening stimuli
- The BNST – the action pathway. By taking action or even thinking about taking action decreases the activation of the central nucleus.
- L-FL vs. R-FL

Neurodynamics of Anxiety

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

Slow Track Features

- Slow track errors—needing rewiring
  - automatic thoughts—fast track impulse
  - Assumptions—worry track
  - core beliefs—state based assessment
- Global/Passive (R-PFC) vs. Detail/Action (L-PFC)

Speeding Up the Slow Track

- Labeling thoughts—”That is an anxiety provoking thought” vs. “This makes me anxious!”
- Externalizing—”What would another person in this situation say and how is s/he right?”
- 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

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

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

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.
- The excessive dissipation of carbon dioxide leads to hypocapnic alkalosis making blood more alkaline and less acidic. This leads to the following:

Over-Breathing and Hypocapnic Alkalosis

- Vascular constriction, resulting in less blood reaching your tissues.
- Oxygen binds tightly to hemoglobin resulting in less oxygen released to the tissues and the extremities. The paradox is that though too much oxygen is inhaled, less is available to your tissues.
- Symptoms: dizziness, light-headedness, and cerebral vasoconstriction, which leads to feelings of unreality, and peripheral vasoconstriction, which leads to tingling in the extremities.
- Abnormally sensitive carbon dioxide receptors in the brainstem may lead to a “false alarm” of suffocation. This dyspnea, the feeling of not getting enough air, can spur a panic attack and more hyperventilation.

Introceptive Exposure +

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

Introceptive Exposure +

- –Swallowing quickly--- to cause a lump in the patient's 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

Exercise and Anxiety

- Provides a distraction
- Reduces muscle tension
- Builds brain resources (neuroplasticity and neurogenesis)
- Increases GABA and serotonin
- Introceptive exposure
- Improves resilience – self-mastery
- Mobilized vs. immobilized feelings – taking action

Pablo’s Bridge

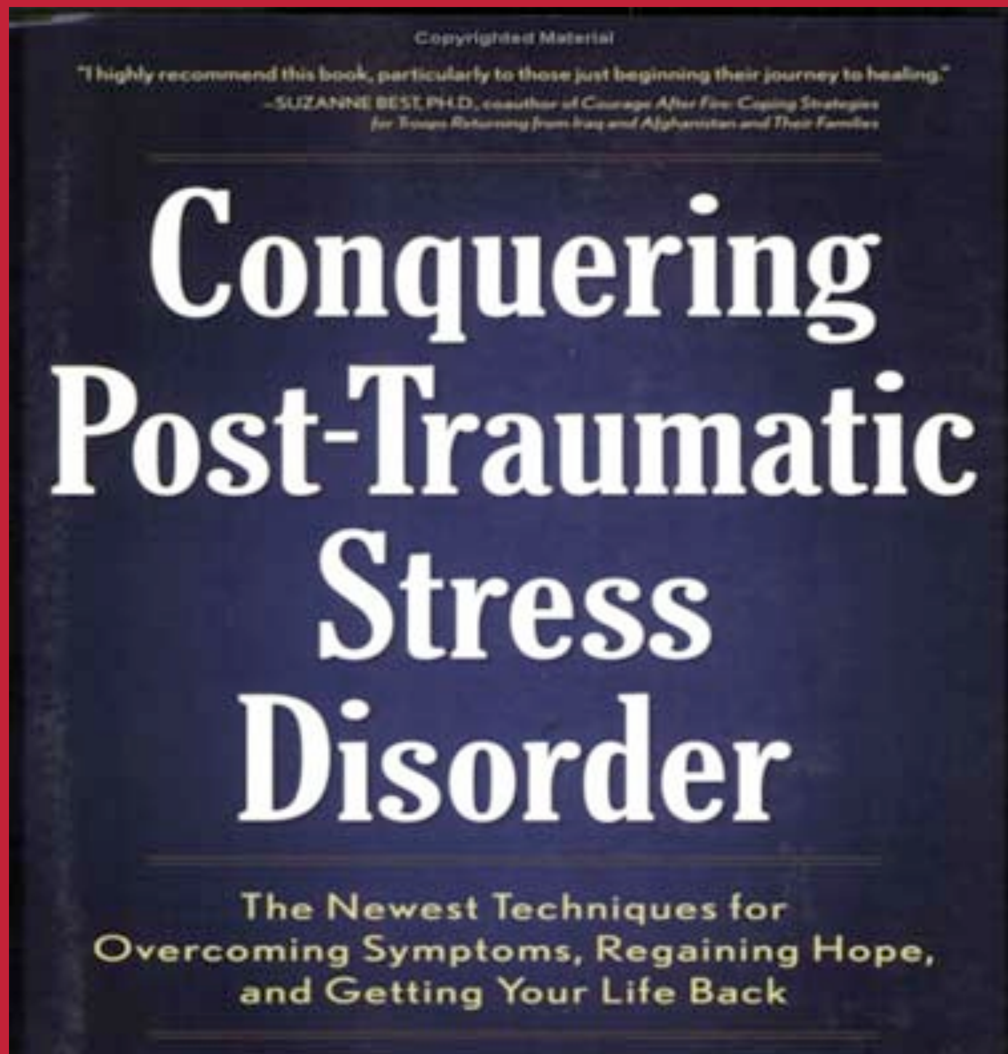
B—Overactive amygdala and R-PFC Swollen throat and diet--Taking action L-PFC

A--Paternal transference

S--Bridge Phobia—panic--anxiety sensitivity

E--New Narratives--Introceptive exposure—swallowing

Post Traumatic Stress Disorder



Long-Term or Traumatic Stress

Cortisol Cascade Hypothesis:

- Stress causes production of cortisol
- Excessive cortisol causes dendrites in the hippocampus to shrivel up (Sapolsky, 1996)
- This feedforward loop leads to heightened reactivity of amygdala
- The hippocampus is essential for turning off HPA axis, damage to it leads to even more cortisol release as time passes
  - PTSD patients with smaller hippocampi (Bremner, 1999)

PTSD Neurodynamic Aspects

- Increased blood flow in the amygdala, reflecting over activity (Pissiota, et al., 2000)
- Reduced grey matter volume in the medial PFC (Carrion, et al., 2001)
- Reductions in hippocampal volume---"gluccocorticoid-cascade hypothesis"
  - for combat related PTSD (Bremner, et al, 1995)
  - childhood physical and sexual abuse related PTSD (Bremner, et al 1997).

PTSD Neurodynamic Aspects

- Monozygotic twin brothers, one who had combat related PTSD and the other who never went to war. Both had smaller hippocampal volumes. – Thus, the vulnerability hypothesis may be viable as a possible *partial* explanation for risk.
- It appears that *both* the "vulnerability hypothesis" and the "cortisol-cascade hypothesis" occur. (Gilbertson, et al, 2002)

PTSD Neurodynamics

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

mPFC and PTSD

- Reduced volumes especially the ACC (Shinn, et. al., 2005)
- N-actyloasparate (NAA)—a measure of neural integrity
  - An MRS study found lower NAA/creatine ratios in the ACC of children and adolescents with PTSD

mPFC and PTSD

- PET studies of rCBF in PFC
  - Found ↓ activation of the PFC
  - ↓ subcallosal cortex
  - Failure to activate the ACC (Bremner, et. al, 1999)
  - As a symptom of PTSD ↑ the rCBF to PFC ↓ and rCBF to the amygdala (Shin, et. al. (2000)

Hippocampal Integrity and PTSD

- 23% reduction of NAA bilaterally in hippocampal region
- 26% $\downarrow$ choline in right hippocampus relative to controls (Schuff, et. al., 2001)
- Reduction in NAA in the absence of hippocampal volume loss in PTSD may reflect metabolic impairments or neuronal loss in the in the presence of glial proliferation
- Overall MRS studies of NAA/creatine

NE and PTSD

- ↑ NE both peripherally and centrally posttrauma (Geraciotti, et. al., 2001)
  - Hyper arousal and re-experiencing (flashbacks) (O'Donald, et. al., 2004; Southwick, et. al., 2004)
  - Contributes to the development and maintenance of intrusive thoughts and nightmares (Cahill, et., al, 1997)
- In PTSD children, NE increases over time

NE and the R-PFC

- ↑ NE ↑ R-PFC
- ↑ NE ↓ L-PFC (van der Kolk, et. al., 1997; Southwich, et. al., 1997)
- ↑ NE involves more global feelings of anxiety and less verbal explanation for them (Kent. Et. al., 2002)

Alpha-2 auto receptors

- Built into the pre-synaptic membrane and provides braking function for NE
- When NE is released by pre-synaptic membrane it contacts both pre and post synaptic membranes, causing:
  - An action potential in the post synaptic neuron
  - Alpha-2 auto receptors slow release of NE

Variations in Alpha-2 auto receptors

- If alpha-2 auto receptors are agonized (blocked) braking action doesn’t occur
- Caffeine and yohombine are alpha-2 agonists
- Hyposensitive alpha-2 auto receptors are insensitive to NE and fail to shut it off—thus ↑ NE

Possible Neurochemical Vulnerability of PTSD

- ↑ NE post trauma may predict PTSD (Yehuda, et. al., 1998)
- ↑ cortisol in the evening not in the morning
- ↑ cytokine 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)

Hypocortisolism

- A meta-analysis of 107 studies on hypocortisolism in the AM found greater concentrations in the PM (Miller, Chen, Zhou, 2007)
- Especially if the person was subjected to pain
  - A flatter diurnal rhythm
  - A higher daily volume of cortisol output

Variations in Cortisol

- More months elapsed since stressor:
  - ↓ Morning cortisol
  - ↓ ACTH
  - ↓ Daily volume
- If chronic stressor is still present:
  - ↑ PM levels
  - ↑ Daily output
- If threat is physical—↑ flat output
- If stress is social (i.e. divorce) ↑ output including AM

PTSD, Hippocampus, and Children

- Many traumatized children without hippocampus shrinkage, why?
  - Though reduction does not appear at the time it becomes smaller with time
- People w/o PTSD have hippocampus symmetry L > R
  - This pattern is not seen in adults who incurred child abuse (Woom & Hedges, 2008)
  - Bilateral hippocampus volume reductions for adults who were abused during childhood

PTSD, Hippocampus, and Children

- Hippocampal volume reductions occurs between childhood and adulthood—associated with PTSD symptom severity
- Lower NAA/creatine ratios in the ACC for children and adolescents with PTSD (De Bellis, et. al., 2000)
- Tx ↑ neurogenesis, cognition, downregulate cortisol and catacholomines which would ↑ NAA

Neurodynamics of Early Trauma

- 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)

Flashbulb Memories

- A particular type, not a special class
- ↑ stress narrows the focus from peripheral aspects to threat focus—i.e. "weapons focus"
- Thus, less accuracy for peripheral stimuli (i.e. color of the car or person's hair) more to the object of threat (gun, knife, etc.)

PTSD and Memory

- People with PTSD typically remember that the traumatic event occurred
- But describe blank periods, gaps, for details
- Recollection for details are often unclear, vague, and disorganized

(Harvey & Byant, 1999)

ERP studies of PTSD

- Event-related potential (ERP)—measured in the context of EEG
- Signal are time-locked to the presentation of a stimulus capturing “event-related cortical activity (Metzger, Gilbertson, & Orr, 2005)
- Time-locked segments are averaged over repeated trials to same or similar event to eliminate “background activity.”

ERP studies of PTSD

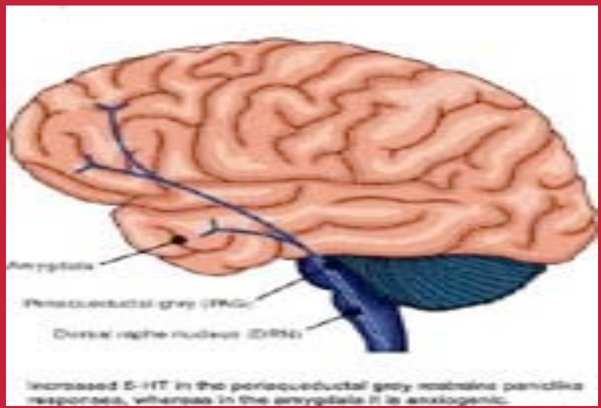
- The resulting average ERP “waveform” consist of positive and negative deflections, referred to as components
- One component, referred to as P3 is considered a general index of cognitive functioning or “efficacy”
- Diminished P36 response amplitude to target stimuli reflecting hypervigilance and attentional impairments due to sensory gating

ERP studies of PTSD

- PTSD patients found with abnormally large P50 ratios indicating:
  - Difficulty attending to any stimuli any stimulus because of problems filtering out irrelevant stimuli
  - Instead they often respond to respond to repetitive or irrelevant stimuli (Arciniegas, et. al., 2003)

↑ Stress

- Enhanced dendritic aborazation in the amygdala (Vyas, et. al., 2002, 2003)
- ↑ NE triggers the periacqductal grey area causing the “freeze” -related to dissociation from psychic and physical stress of trauma (Murburg, 1997; van der Kolk, et. al., 1996)



Continuum of Detachment

- Traumatized people can experience:
  - Mild detachment or absorption: involving a breakdown in the person's ability to notice outside events and extending to an altered sense of self.
  - Moderate detachment: involving an experience of unreality extending to feelings of depersonalization and derealization whereby 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)

Memory and Trauma

- An emotional event-- amygdala links episodic memory to the emotions
  - Over time relevant info about the event is extracted from episodic memory into semantic memory and stored in the cortex
- With PTSD - a breakdown in the extraction process of memory transfer and integration
  - Pts minimize consequences of this failure (i.e. Flashbacks) by avoidance & numbing
- Recovery requires re-establishment of these failed processes in integration

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PTSD and Memory

- Less activation of the left DLPFC cortex which is associated with working memory in patients with PTSD compared to controls (Clark, et al, 2003).

- "Fear networks" --- highly organized and semantic memories periodically activated by environmental cues. (Lang, 1987; Foa, et. al., 1989)

PTSD and Memory

- Foa's "fear network" – 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) unconscious. SAMs are only accessible through cues that activate the unconscious network (Brewin, Dalgleish, and Joseph, 1996).

Possible Neurochemical Vulnerability of PTSD

- ↑ NE post trauma may predict PTSD (Yehuda, et. al., 1998)
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Information Professing in PTSD

- PTSD pts. --difficulty controlling trauma-related thoughts following trauma related cues
- Less support for the concept that PTSD involves increased susceptibility to intentional forgetting or suppressing trauma related material (Constans, 2005)
- Rather, unwanted processing of emotional memories may reflect a cognitive gating deficit – PFC deficit regulating the amygdala

Single Representation Theory and "Fear Networks"

- Consists of networks of thousands of modes with dense set of interconnections between them
- A person, feature, shaped, concept---- interconnections between the nodes
- Frightening experiences create "fear networks" --info about the trauma
  - Meaning
  - Emotion
  - Physiological reactions
- Reactivation of fear network automatically

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Single Representation Theory and “Fear Networks”

- Reactivation of fear network automatically occurs—when encountering a situation that matches a cue or feature of the original fear network
  - Produces the same physiological response
  - Interpretation of being in danger

Emotional Processing Theory (Foa, et. al., 1998)

- Based on single-representation theory
- Fear networks based on:
  - Large numbers of stimulus-danger interconnections between stress nodes
  - Memory networks combine response elements associated with negative self appraisals including -vulnerable or weak
  - Severity of trauma leads to disrupted cognitions and fragmented and disjointed fear structure

Critique of Single Representation Network

- A single level can’t account for how emotionally laddened “hot” way of remembering on one occasion while on another occasion remembered in a “cool” way (Teasdale & Barnard, 1993)
- Extra dimensions are critical in therapy to understand that she <u>feels</u> like a bad person, she can be a good person
- CBT emphasizes language but…

Dual Processing Theory

- Limitations of the "fear network" – doesn't account for implicit memory:
  - Verbally accessible memories (VAMs) on the conscious memory level. VAMs can be accessed in therapy through deliberate recall.
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The VAM system

- Verbally assessable memory (VAM) system—the narrative—autobiographic
  - Can be deliberately retrieved when required (Brewin, 2005)
  - Cortex
  - 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 VAM 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
  - The future—i.e. sadness at the loss of cherished plans or hopeless at the thought of not finding fulfillment
  - Often involve guilt or shame over perceived failure or not preventing the event

SAM system

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

SAM system

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

VAM and SAM interactions

- SAM—implicit memory—amygdala related to the intensity of emotions
- VAM—explicit memory—hippocampus related to context and time
- SAM flashbacks occur via the fast track to the amygdala and override the VAM system
- ↑ cortisol and catecholamines impair the VAM system and kindle the SAM

VAM and SAM interactions

- In therapy deliberately maintaining attention on the content of flashbacks w/o avoidance-- SAM memories can be encoded in the VAM system.
- The timeless qualities of the SAM images and sensations get linked with spatial and temporal context—within the safety of the therapeutic relationship
- “I’m safe now—those things that that happened to me in the past”

VAM and SAM interactions

- The process needs to be repeated for:
  - Neuroplasticity—the inverted “U”
  - Because there is a lot of information in the SAM system
  - To provide easier access to the SAM system
  - So that VAMs can compete with SAMs
  - Dual processing theory acknowledges that SAMs are not altered
    - The new VAM system puts the SAM system in perspective

TBI and PTSD

- TBI dx partially on posttraumatic amnesia (PTA)—length of time pt is unable to store into memory
- Co-existence of ASD and TBI measured in ranges of PTA
  - 5 to 24 hours—mild to moderate PTA -- ASD comparable to non-TBI sample (Harvey & Bryant, 1998)
- But SAMs may be present even though VAMs are not (because hippocampus needs consolidation period) (Joseph & Masterson, 1999)
- Pts with TBI assessed after trauma, then 6 weeks after—no PTSD. But months later-- PTSD evident in both TBI and non TBI groups (Bryant, et. al., 1998)

Converting traumatic memories into narrative memories

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

Converting traumatic memories into narrative memories

- Raw sensory information needs to be interpreted and anchored with personal narrative organization with meaning
- Reactivated through exposure and reconsolidated with more accurate information into a coherent narrative
  - Not “correct” (ie. CBT) but a coherent and acceptable meaning (Constructivist)
- Newly constructed memories compete with original traumatic memory for control over behavioral attention

Research on PTSD Treatments

- Institute of Medicine (IOM) 2007 Review
  – Thorough review of all psychotherapy for PTSD (requested by the VA)
- Few treatments found to have clear empirical support
  – EMDR, group therapy, hypnotherapy, eclectic, CBT alone….all not supported
- One exception: review found efficacy of exposure
  – Prolonged Exposure (PE)
  – Cognitive Processing Therapy (CPT)

PTSD Therapy Goals

- Too early exposure heightens the cascade of stress hormones and neurotransmitters:
  - increases the reactivity of the amygdala when it's already overactive.
  - the hippocampus encodes the traumatic memory
  - you need a healthy hippocampus later to reconstruct a more accurate and durable version of the experience.

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)

Mitchell and Everly (2000)

- Mitchell and Everly (2000), in discussing another approach, emphasize the importance of the following goals:
  - Reducing the person's initial distress
  - Preventing psychological disorders such as PTSD
  - Promoting emotional processing through ventilation and normalization
  - Preparing for future experiences
  - Identifying the need for future treatment
  - Avoiding premature diagnostic labeling
  - Providing education about stress, coping with stress, and opportunities for future treatment

PTSD Therapy Goals

- After memories have been encoded, exposure helps the client emotionally engage and integrate dysregulated memory systems. (Zoellner, Fitzgibbons, and Foa, 2001).
- Organizing the traumatic memory narratives leads to less symptom intensity (Foa, Molna, & Cashman, 1995)
- “Escape Prevention,” helps lessen the contributing effects of avoidance which support the symptoms of PTSD (Cash, 2005).
- “Posttraumatic growth”. Developing a sense of meaning, changes in one’s sense of self, his relationships, and philosophy of life (Tedeschi, 1999).

Sleep and Memory

- Non-REM—strengthening of hippocampal memories
  - Information flow from hippocampus → cortex
  - Reinforcement of old memories
- REM—the strengthening of cortical memories (Plihal & Bora, 1997)
  - Cortex → hippocampus (Buza'Ki, 1996)

Sleep and Memory

  - Dreams—weak associations, unpredictable juxtapositions of barely related objects, locations, and characters in illogical sequences
  - Plotlines float free of anchors in space in time and space
- Blocking of hippocampal outflow during REM helps prevents semantic associations from falling back into predictable, over learned patterns
- Semantic memory activates:
  - Weak associations in REM
  - Strong associations in Non-REM

REM, PTSD, and Neurotransmitters

- Freud’s “Day residue” problem—dream content contains factoids not contextually accurate images and stories from the day
- PTSD is the exception—there is a breakdown of the blockade of hippocampus outflow to the cortex
  - Traumatic memories are replayed in nightmares
- This breakdown prevents the normal integration and the subsequent <u>weakening</u> of episodic memory that leads to PTSD (Strickgold, 2002)

Neurotransmitters and sleep

- REM-- ↑ acetylcholine and ↓ NE and 5-HT (Kametani & Kwamura, 1990)
- Non-REM—5-HT and mild NE (Portas, et. al., 1998)
- Failure to shut down NE with PTSD results in:
  - Fragmented sleep (Mellman, et. al., 1997)
  - ↓ REM (Glaubaum, 1990)
- Instead of weak associations of correlated with negative affect:
  - Replay of traumatic memories and self-perpetuating (Stickgold, 2002)

Orienting Response, REM, and Memory

- Bilateral stimulation of the orienting response (i.e. EMDR, EFT, acupressure etc.) involve alternating attention across the midline
  - 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 involve:
  - The orienting response (Sokolov, 1990)
  - Induces REM like state
- Both facilitate cortical integration of memories (Stickgold, 2002)

Shifting Attention

- Re-orienting of attention and startle response produce shifts in regional brain activation and neuromodulation
  - like REM (Stickgold, 2002)
- Startle response—activates brainstem circuts that initiate REM
  - Pontogeniculoccipital—PGO waves
- Release, shift, and refocusing of attention involves ACC, superior colliculus (activated by the PGO waves) and control eye movements (Nelson, et. al., 1992)
  - Also cholinergic increases and/or noreadrenergic decreases facilitate the release of attention prior to the shift (Clark, et. al., 1987)

Bilateral Re-orienting Response Therapies

- EMDR etc activate re-orienting response
  - ↑ ACC and L-PFC (Levin, et. al., 1999)
  - ↓ galvanic skin response—correlated with ↓ adrenergic drive
- Reorienting therapies facilitate REM-like memory processing (Stickgold, 2002) but with FL input (unlike REM)
  - By holding traumatic image in mind while bilateral shifts attention

Bilateral Re-orienting Response Therapies

  - REM like state facilitates integration of traumatic memories into associative cortical networks w/o interference from hippocampal mediated episodic recall
  - The integrated corticohippocampal circuts induce a weakening of the traumatic episodic memory with its associated affect
  - Allows pt to see the significance and meaning of the traumatic event from an entire life perspective and lessen the emotionally charged impairment that the trauma caused
- Modulating NE though the therapeutic “safe emergency” maximize neuroplasticity.

Shifts in attention and asymmetry

- EMDR has morphed from eye movements to knee slapping and special lights—all bilateral
- Why activate the RH when it is already overactive? Why not tap the right hand and/or foot? Interaction between RH and LH still occurs
- The right limb tapping method still includes:
  - reorientation response
  - attentional shift
  - grounding
- This method is portable—the client can practice on his own (neuroplasticity)
- L-PFC activation facilitates inhibiting of the amygdala

PTSD and Memory

- Normally when an emotional event occurs the amygdala links the episodic memory to these emotions
- Over time relevant info about an event is extracted from the episodic memory into semantic memory and stored in the cortex
- PTSD involves a breakdown in the extraction process of memory transfer and integration

PTSD and Memory

- If the episodic memory is a traumatic one the consequence is PTSD
- The pt can minimize the consequence of this failure to integrate by avoiding stimuli that reactivates the memories or by blocking emotional responses (numbing)
- Recovery requires the re-establishment of these failed processes of cortical memory consolidation and integration

Memory Reconsolidation

- Every time a memory is retrieved the underlying memory trace becomes once again fragile
- The memory trace goes through another period of consolidation
- Beta-adrenergic antagonists (i.e. propranolol) blocks reconsolidation of implicit fear-based memories by indirectly influencing protein synthesis in the amygdala (Debiec & LeDoux, 2004)

Transgenerational PTSD

- Pregnant women with PTSD ↑ HPA axis (i.e. 9-11) had babies with ↑ bedtime cortisol
  - Thus, fetal programming of HPA axis
- Mother’s psychological response to stress also correlated with vulnerability of PTSD

NE and the R-PFC

- ↑ NE ↑ R-PFC
- ↑ NE ↓ L-PFC (van der Kolk, et. al., 1997; Southwich, et. al., 1997)
- ↑ NE involves more global feelings of anxiety and less verbal explanation for them (Kent. Et. al., 2002)

Alpha-2 auto receptors

- Built into the pre-synaptic membrane and provides braking function for NE
- When NE is released by pre-synaptic membrane it contacts both pre and post synaptic membranes, causing:
  - An action potential in the post synaptic neuron
  - Alpha-2 auto receptors slow release of NE

Variations in Alpha-2 auto receptors

- If alpha-2 auto receptors are agonized (blocked) braking action doesn’t occur
- Caffeine and yohombine are alpha-2 agonists
- Hyposensitive alpha-2 auto receptors are insensitive to NE and fail to shut it off—thus ↑ NE

CRH-NE interactions

- ↑ CRH targets the LC to ↑ NE
  - Which further activates the amygdala
- Some pts': Pituitary shuts down—too much CRH
  - Adaptive down-regulation of CRH receptors in anterior pituitary so that not too much cortisol floating around (Bremier, et. al., 1997)
- Pituitary volumes higher in pubertal/post pubertal PTSD pts (Thomas & DeBellis, 2004)

D-cycloserine (DCS)

- Antibiotic drug used in higher doses to tx TB—(binds NMDA receptors)
- Promotes and speeds ups exposure effects via neuroplasticity within the amygdala via NMDA receptors (Myers & Davis, 2003)
- Efficacious prior to exposure or immediately following (Legerwood, et. al., 2003)
- Applied successively in social phobia with fewer number of sessions (Davis, et. al., 2006)

Seven Principles of Growth After Trauma

- Growth occurs when one's psychological schemas are changed by traumatic events. Old schemas are destroyed and replaced by new schemas. "I almost died! Why?"
- Some assumptions are resistant to disconformation. These assumptions buffer us from initial distress from the trauma but reduce the possibilities for schema change and growth.

Seven Principles of Growth After Trauma

- Certain personality characteristics are related to the possibility for growth. For example, hardiness, optimism, and self-efficacy allow one to see growth within those perspectives.
- Growth occurs when the trauma serves as a central pivotal change in one's life. It allows one to shift perspective to a new era.
  - *Wisdom results from growth. One sees what's possible and what is not. Like the Serenity prayer* (Tedeschi and Calhoun, 1995)

Bret's BASE

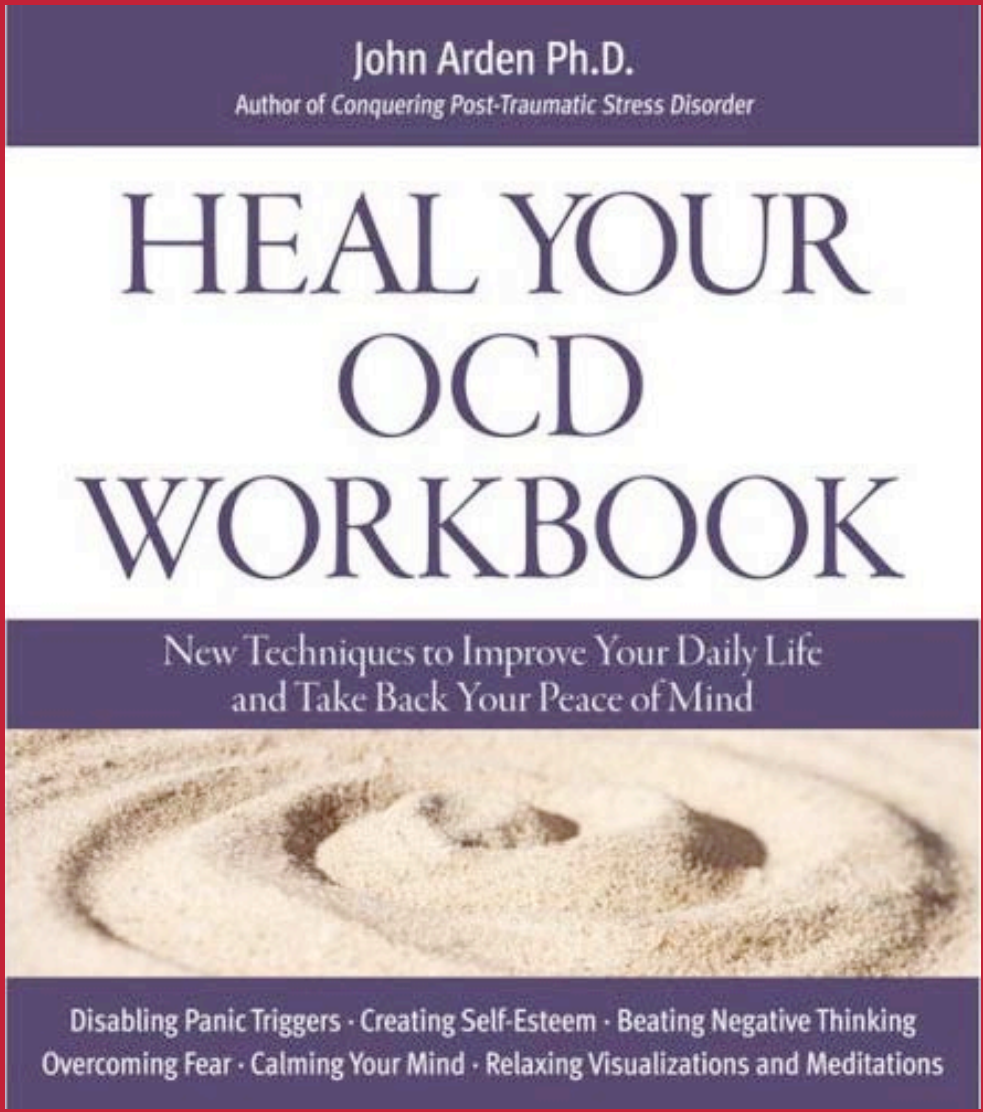
B--Increased amygdala and dampened hippocampus—Substance abuse

A--Buddy connection

S--Numbing, re-experiencing (barbecue) and avoidance

E--New Narratives—Exposure at McJack Jr's—Posttraumatic Growth

OCD


John Arden Ph.D.
Author of Conquering Post-Traumatic Stress Disorder
HEAL YOUR OCD WORKBOOK
New Techniques to Improve Your Daily Life and Take Back Your Peace of Mind
Disabling Panic Triggers · Creating Self-Esteem · Beating Negative Thinking
Overcoming Fear · Calming Your Mind · Relaxing Visualizations and Meditations

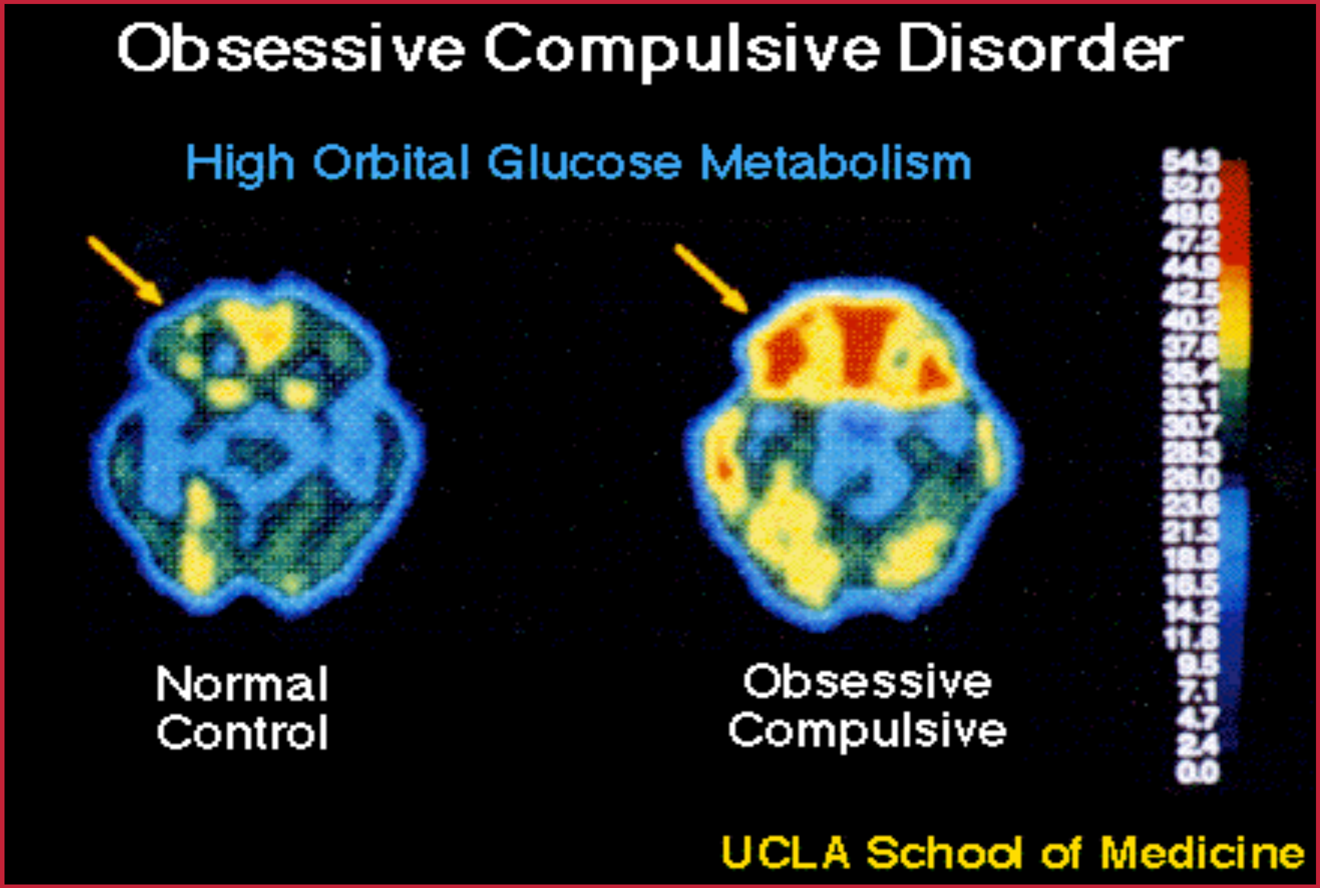
OCD Neurodynamics

- MRI studies show the OFC, ACC, and caudate activity (Baxter, et. al., 1987; Swedo, et. al., 1992)
- Compulsions recruit inefficient striatum (caudate nucleus) in order to achieve thalamic gating to neutralize obsession and anxiety

Structures with Roles in OCD

- Striatum-- gate is left open
  - caudate part serves as a gate for thoughts and emotions
  - putamen part serves as the gate movement
- Amygdala-- activates the fear circuit
  - fight-or-flight response (HPA axis)
  - hijacks the OFC
- Orbital frontal cortex-- gets flooded with information
  - generate error messages: “This is wrong!” Then you engage in compulsive behaviors to “make it right.”

Flooded OFC in OCD



OCD and the OFC

- OFC flooded with nuance information 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”
- To pull out use the L-PFC
  - Self talk
  - acceptance

Pulling Out of the OCD Circuit

- Prefrontal Cortex (DLPFC and OFC)
  - DLPFC—Decides "time to do something new"
  - OFC can learn to inhibit the amygdala and the fear network
- Hippocampus-- provides context and what is worthy of fear
  - Remembers that you engaged in a compulsive behavior that never seems to solve the problem.

Real OCD ORDER

- O—Observe-- Observing the OCD thoughts and behaviors for what they are: obsessions and compulsions.
  - PFC (DLPFC the OFC) activation.
  - Attention key first step for neuroplasticity.
- R—Remind--By reminding yourself that you are obsessing you call it a symptom of your brain's OCD habit and nothing more to be concerned about. “This is just OCD. Nothing bad ever happens.”

Real OCD Order

- D—Doing--By doing something different than the usual OCD compulsive behaviors establishes a new habit. The new behavior draws attention and interest.
  - L-Frontal activation
- E—Exposure--To the situation or place that is intolerable. Exposure allows habituation. This is the “E” of ERP.
  - Taming of the amygdala

Real OCD Order

- R—Response Prevention--Refraining from compulsive behaviors that contribute to momentarily "feeling better." This is the "R" and "P" in ERP.
  - –Strengthening all inhibitory circuits

Penelope’s BASE

B—Stratum's open gate –OFC gets flooded (DLPFC activation to start neuroplasticity)

A—Forming an alliance based on a common enemy to fight against OCD

S—Conceptualizing the need to strengthen inhibitory circuits

E—Exposure Response Prevention and using the ORDER system

Penelope’s Kitchen ORDER

O—Observing (DLPFC activation to start neuroplasticity)—B

R—Reminding (“Oh that just my OCD—L-PFC)—B

D—Doing something different (“I think I’ll bake a pie”)—A & S

E—Exposure (Leaving the kitchen dishes)—E

R—Response Prevention (strengthening inhibitory circuits—reframing

5. Depression

"5 of 9"

- Depressed mood
- Psychomotor agitation or retardation
- Anhedonia
- Social withdrawal
- Feelings of worthlessness
- Weight gain or loss
- Disturbed sleep
- Fatigue
- Thoughts of death

Illness and Depression

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

Inflammatory Thoughts and Moods

- Short term inflammation (i.e. Post surgery) dulls memory and moods (7 to 26% of pts.)
- Diabetes 2 and rheumatoid arthritis increase an enzyme called IDO which is associated with inflammatory proteins called cytokines.
  - Drugs that block IDO have revealed the connection between inflammation and sour moods

Cytokines

- Protein molecules that act as cellular messengers
- Healthy people optimally regulate cytokine at moderate levels.
- Too little activity -- immunodeficiency, severe infection, and even death.
- Hyperarousal can also in death, or in illness, tissue damage, or shock (Granger, et al, 2006).

Cytokines

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

Systems of Depression

- Mood changes (dysphoria, hopelessness, suicality, anhedonia, anxiety)
- Circadian dysregulation (low drive, energy, appetite, sleep, libido)
- Motor deficits (slow movement, restlessness, agitation)
- Cognitive impairment (poor attention, working memory, executive function, ruminations)

Risk Factors for Depression

- Prior episodes
- Family history
- Prior suicide attempts
- Female gender
- Postpartum phase (10-15%)
- Medical comorbidity
- Lack of social support
- Stressful life events
- Current substance abuse
- Intimate partner abuse

Gender Differences and Depression

- **2:1 women > men**
- **Male symptoms –anger, irritability, recklessness**
- **Female symptoms—sadness**
- **4:1—men for suicide “Women seek help, men die**

Gender and Depression

- Only Post pubescence 2:1 women
- One possible factor – genetics
- Some women have a mutation in a gene called CREB-1 associated with depression
  - CREB-1 has a switch turned on by estrogen
- Serotonin transporter gene (5-HTT)—associated with women and depression
  - Switched on by threats and stress

Gender differences and depression

- **Premenopausal Women respond best to SSRI** (Kornstein, 2008)
- **SSRIs work best in the presence of estrogen**
- **Men respond best to Wellbutrin and Tofranil –targets DA and NE**
- **Postmenopausal women respond best to non 5-HT meds**
- **Male brains make 5-HT faster and generally have move available**

Postpartum Depression

- Mothers who receive little emotional support during pregnancy are more likely to develop postpartum depression (Nielsen, et, 2000)
- They have been observed to touch their infants less at the second day after delivery (Ferber, 2004)
- Tx with: Omega 3, iron, calcium, B Vitamins

Gender differences and depression

- **Estrogen inhibits GABA**
- **Testosterone stimulates GABA**
- **Testosterone boosts BDNF**

Cultivating Depression

- Pessimism
- Self-critical
- Irritability
- Apathy
- Inactivity
- Poor diet
- Alcohol/drugs

Intergenerational Transmission

Infants of depressed mothers have

- Over-active right frontal lobes
- Under-active left frontal lobes
- Lower levels of dopamine and serotonin
- Higher levels of stress hormones

(Field et al., 1998)

QuickTime™ and a decompressor are needed to see this picture.

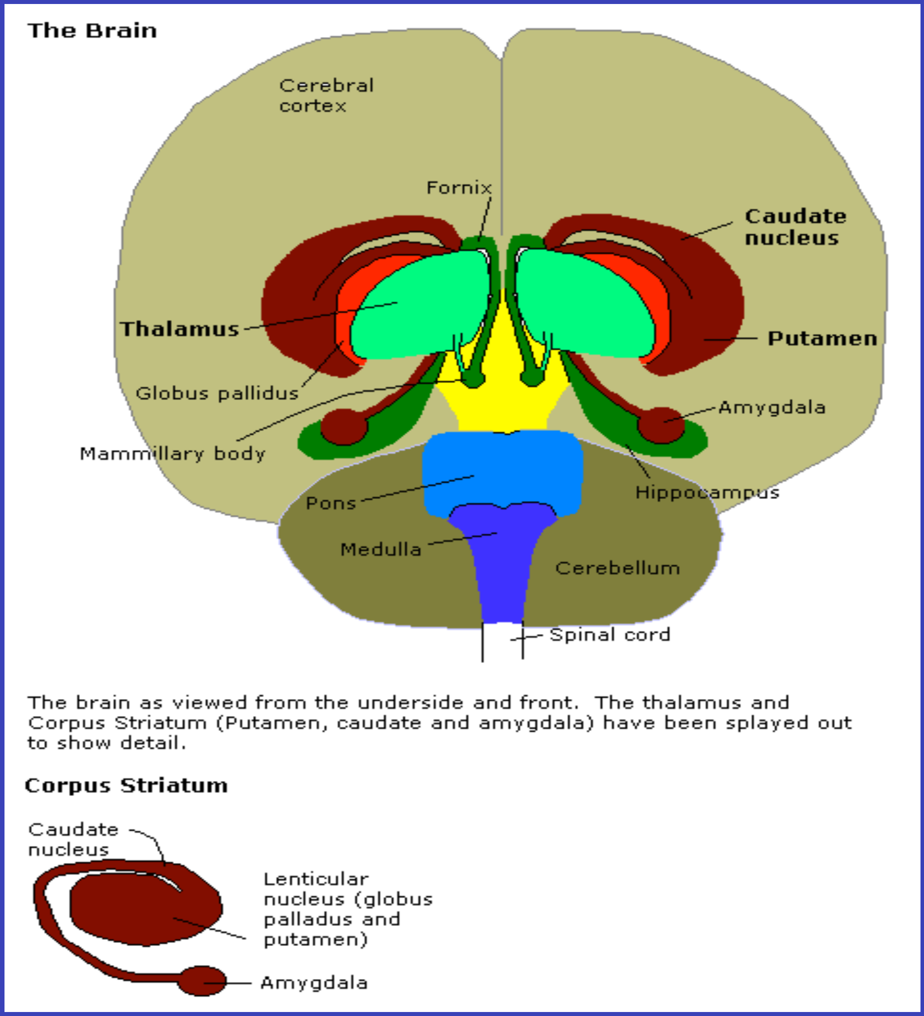
Treating the mother's depression can contribute to the child's improvement

Insecurity

Lasting effects of parental insecurity

- **Dismissing**
  - Client doesn‘t know much about emotional life, has problems with intimacy
  - Over-reliance on avoidance and autonomy
- **Preoccupied**
  - Hyper-awareness of loss
  - Increased susceptibility to feeling unloveable
  - Hyper-cathexis of attachment system makes independence challenging

Stress and Depression



- **Stress and depression are closely linked**
- **Where there is comorbid anxiety disorder, *treat that first***
  - **Amygdala *turns* up the HPA and the sympathetic NS**
  - **Hippocampus *turns down* the HPA but may get overwhelmed**

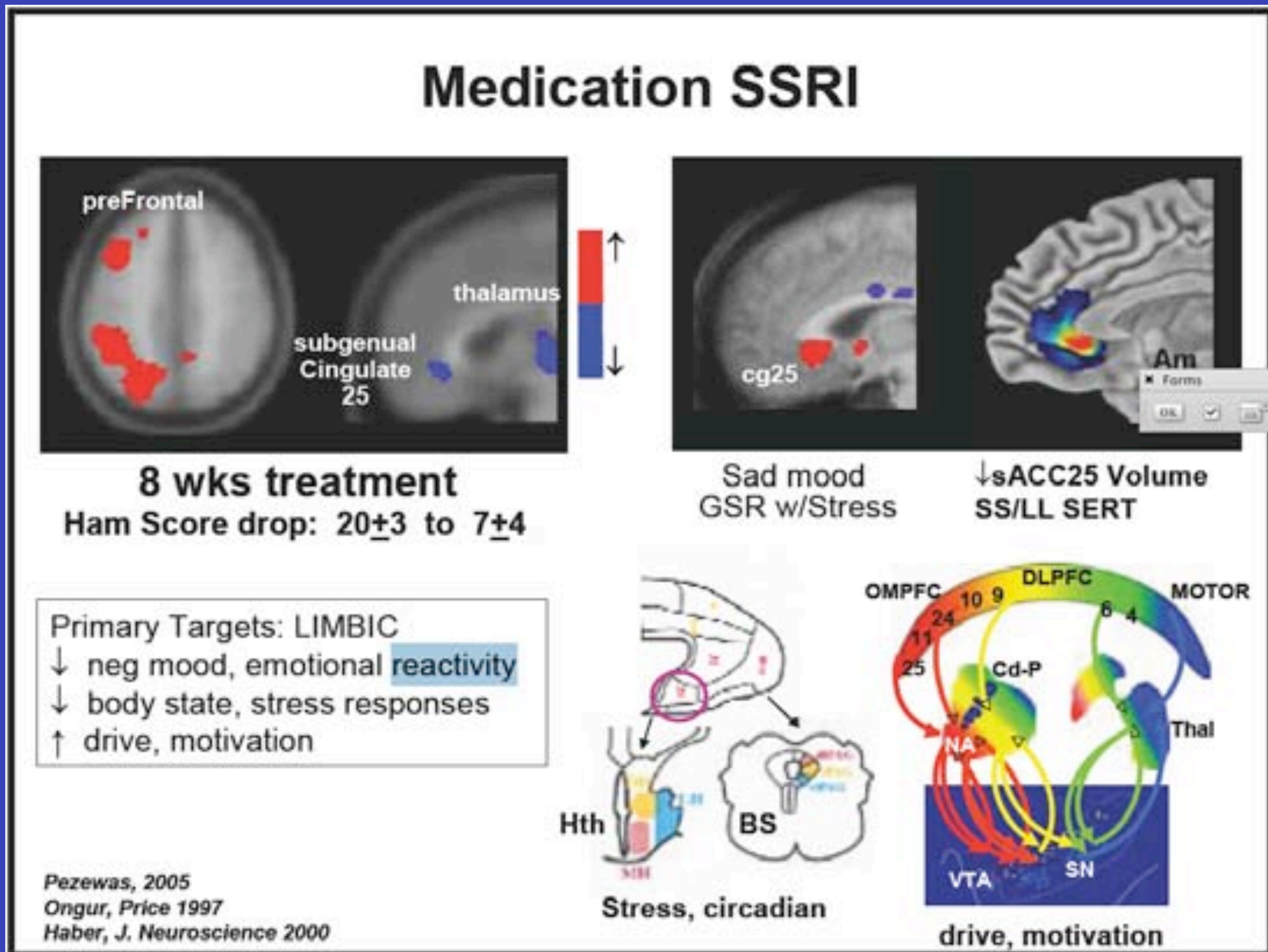
Depression and Stress

- Chronic depression associated with increased levels of cortisol
- Heightened sensitivity of the amygdala to cortisol may make anxiety more likely during depression
- Increased amygdalar volume and anxiety (Sheline, et al., 1998)
- NE and CRH dysregulation reduces 5-HT and + risk of depression

Stress Induced Depression

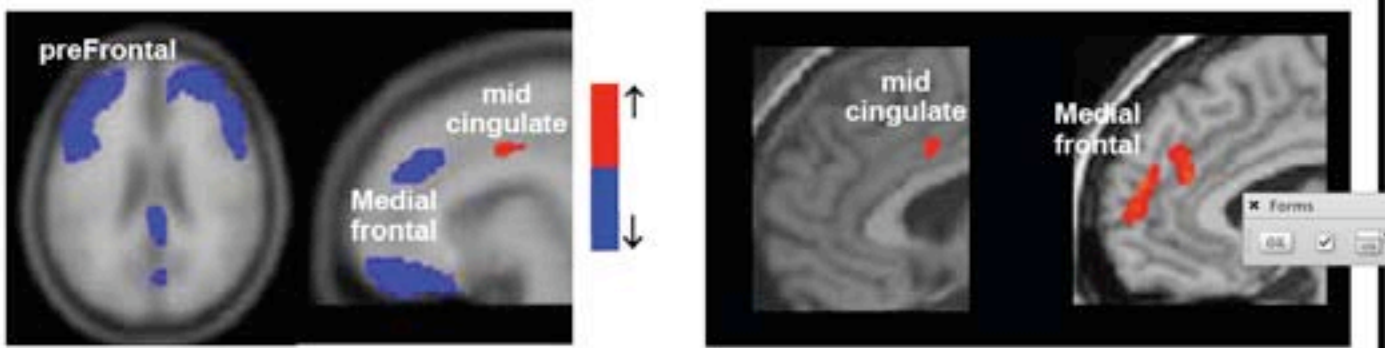
- ↓DA, NE, and 5-HT as soon as 90 minutes post stress (Irwin, 2000)
- ↓DA is associated with psychomotor retardation
- Psychomotor retardation is associated with ↓blood flow to the L-DLPFC
- L-PFC can inhibit negative affect (Davidson & Sutton, 1995)
- Greater L-PFC activation ↓amygdala activation

Medication SSRI



Cognitive Behavior Therapy

Cognitive Behavior Therapy



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

Reappraise emotion
Body-state awareness

Emotional
Self-relevance

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

TOP-DOWN

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

Estrogen and 5-HT

- ↓ estrogen results in less responsive estrogen which are less responsive to 5-HT
- When progesterone is low relative to estrogen ↑ anxiety (Northrup, 2001; Leibenluft, 1999)

Mixed Depression and Anxiety

- Chronic depression has been associated with increased levels of cortisol
- The heightened sensitivity of the amygdala to cortisol may make anxiety more likely during depression
- Increased amygdalar volume and anxiety (Sheline, et al., 1998)

Anxiety and Depression

- The interaction of NE and CRH results in dysregulation of 5-HT and the risk of depression
- Pt's anxiety (ie. PTSD) are at risk for depression (Breslau, et. al., 2000)

Depression and the Amygdala

- Increased activation of the amygdala with some depressed people (Davidson, et al. 2003)
- Enlarged amygdala has been associated with bipolar disorder (Altshuler, et al, 1998; Strakowski, et al, et 1999)
- Amygdala activation increases the chances that memories will be encoded or anxiety or depressive stimuli will be remembered.

Depression and Hippocampus

- Some previously depressed people show hippocampal shringage in the range of 8 to 19%
- Causes?:
  - –Corisol (Sapolsky, 2001)
  - –Excitotoxicity (Margarines, et al, 1999)
  - –Blocked neurogenesis (Jacobs, et al, 2000)

Hippocampus and Over-generalizing

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

Neurodynamics of Depression

- Exercise reduces depression, boosts BDNF, increases serotonin, norepinephrine, and dopamine
- Fatty acids also play a part in making us depression-proof by limiting the devastating effects of cortisol on neurogenesis

DBS and the Depression Switch

- Complexity in Action
  - Area 25 of the anterior cingulate cortex implicated in chronic depression (Mayberg)
  - ACC associated with error detection and social monitoring
  - Area 25 activates when people look at sad pictures
  - It is smaller but more active in depressed people and re-regulates after remission

Deep Brain Stimulation

- Complexity in Action
  - ACC wired into both top-down and bottom-up modules
  - Plays an important role in modulating fear, memory, error recognition, motivation, sleep
  - Electrodes implanted to *inhibit* area 25
  - Dramatic results
  - Consistent with other research that shows that reduced activity may mean *more efficiency*
  - Improved Executive Functions

Hemispheric Asymmetry

- **Evidence from neurology—strokes**
  - Left side stroke—*catastrophic* effect and become very depressed
  - Right side stroke— *laissez-faire* effect and demonstrate more acceptance and much less depression
- **Relative inhibition of the left PFC and relative activation of the right PFC** (Davidson, 2000).
- **Left PFC associated with positive emotions and is action oriented**
- **Right PFC associated with negative emotions and is passive--withdrawal oriented**

Hemispheric Asymmetry

- Language, making interpretive sense of events, and generating positive, optimistic emotions are all products of robust left hemispheric functioning
- Instead of putting details into context, depressed patients are overwhelmed by a global negative perspective. Right hemisphere favors global thinking
- Behavioral activation (left PFC) is one of the principal therapies for depression

Effort-Driven Reward Circuit (Lambert, 2008)

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

Effort-Driven Reward Circuit (Lambert, 2008)

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

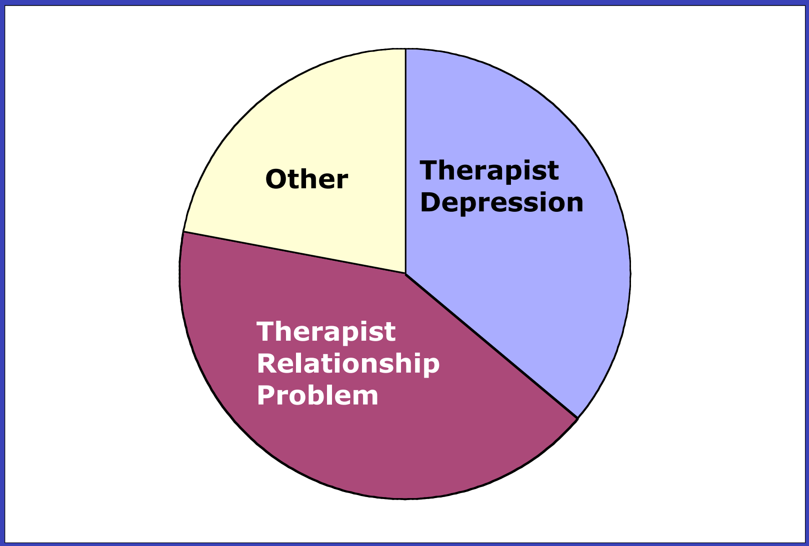
Effort-Driven Reward Circuit (Lambert, 2008)

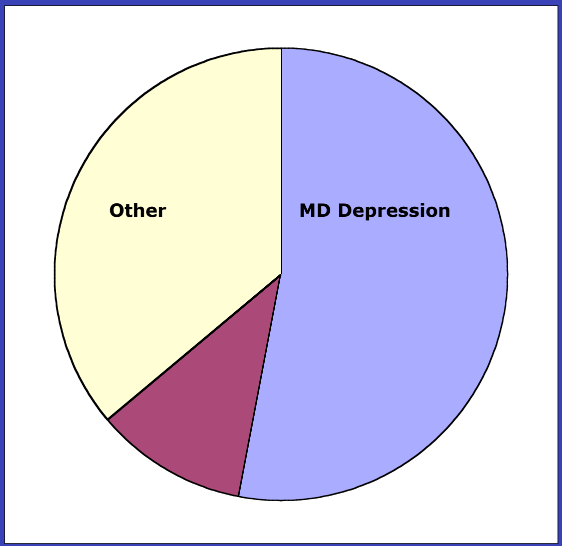
- PFC activates when you plan an activity
- Striatum activates as you do it
- Accumbens activates when you feel the pleasure of doing it
- All the above increases the sense of self control

22

Therapist vs Psychiatrists in Dx

53 11 36



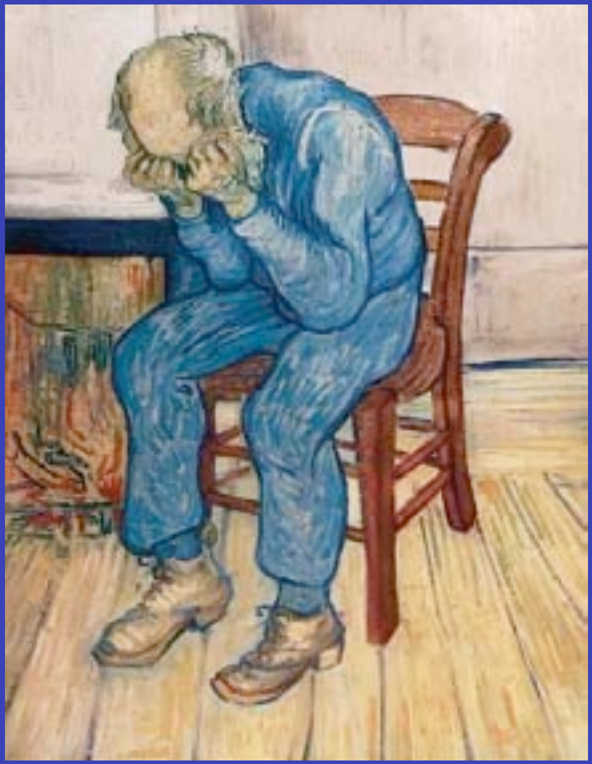


Therapists were three times as likely as MDs to see the issue as a relationship problem

Psychiatrists dxed depression and made scant mention of relationships

Loneliness

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



The Cost of Loneliness

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

WAIS (not WAIS IV)
subtests for Teresa

- Information: 8
- Digit Span: 12
- Vocabulary: 9
- Arithmetic: 6 **
- Comprehension: 9
- Similarities: 12

- Picture completion: 11
- Picture arrangement: 9
- Block Design: 9
- Object Assembly: 8
- Digit Symbol: 5 **

Teresa’s BASE

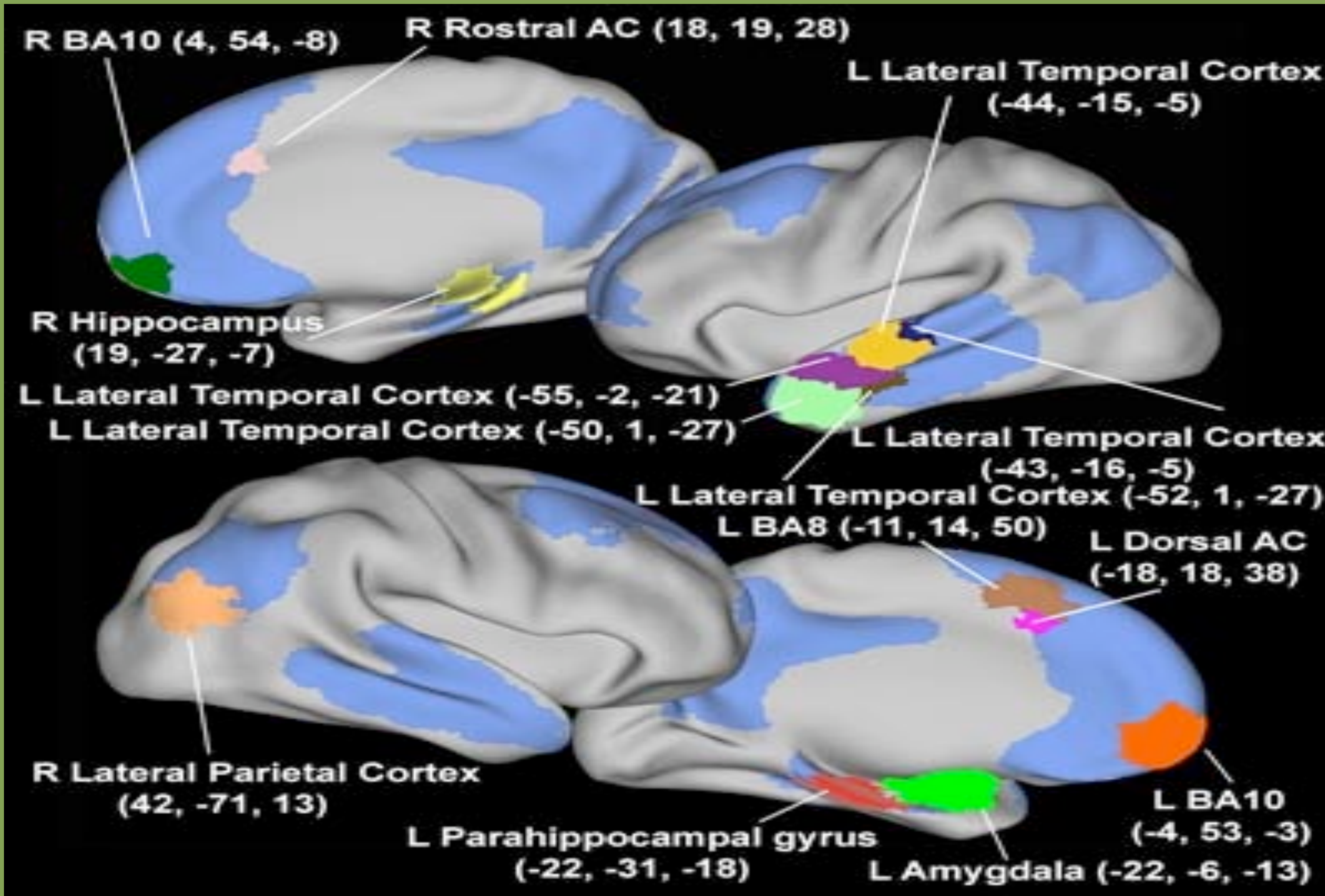
B –Diet (laying of the sugar and transfats)—Aerobic boosting—BDNF—memory

A—Attunement--- Trust and alliance with a man

S---System---positive frame vs. learned helplessness

E--- Narrative (“I’m a survivor--Wiring positive thinking)--- Behavioral activation-L-PFC

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



DMN and Depression

- Increases when DLPFC is not engaged:
  - Stressed, bored, no novelty, or tired
  - Obsessive ruminations over negative experiences
  - Ruminations fade with:
    - Exercise
    - Social activities
    - mindfulness

Principles of Depression Therapy

- Psychodynamics/ITP - Alliance enhancing the CBT (activating L-PFC)
  - Cognitive restructuring
  - New narratives
  - Behavioral activation
  - Affect regulation
  - Social brain networks--relationships

Brain-Based Therapy

Up regulate

- **The Social Brain**
  - Individual psychotherapy
  - Groups
  - Antidepressants
- **Activity Reward Circuit**
- **Hippocampus**
  - Behavior activation
  - Exercise and sleep hygiene
- **Frontal lobes**
  - Mindfulness
  - Psychotherapy

Brain-Based Therapy

Down regulate

- **Right hemi bias**
  - Talk therapy/ labeling moods/ attachment
  - Active behavior
  - Challenging generalizations

- **The amygdala and the HPA axis**
  - Mindfulness
  - Exercise
  - Attuned psychotherapy relationship

- **The ACC**
  - Challenging self-criticism

AAI and Outcomes

- Depression is associated with insecure attachment styles
- The psychotherapeutic alliance can change circuits mediating relatedness, mentalization and flexibility of attention
- The AAI and Outcomes Management are aids to enhancing the alliance

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 (Ratey, 2008)

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

Mindfulness: General Concepts

Decentering – thoughts and feelings are events—not realities

Intentionality – breaking out of automatic thoughts and behaviors

Reducing Avoidance -- turning toward difficulties

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

Jim's Goat

B- Behavioral activation- L-PFC

Diet (laying of the sugar and transfats) Aerobic boosting—BDNF Light chemistry (open the curtains)

A- Trust with a kindred spirit

Social medicine

S- Depressive spiral with no meaning

E- Narrative ("I'm cultivating new meaning")
Wiring positive thinking – Labeling emotions

Brain-Based Therapy

Interventions that bolster under-active areas of the brain

- **Activity Reward Circuit**
- **Hippocampus**
  - **Counter mood-congruent bias with inquiry—CBT**
  - **Exercise**
  - **Sleep hygiene**
- **Rebalance right hemi bias**
  - **Details**
  - **Active**
  - **Labeling moods**
- **Mindfulness**
  - **Quieting ruminations—via observation**

Brain-Based Therapy

6. Summing up

BBT

- **Put distress in the context of brain functioning and development**
  - Stress, neuroplasticity, neurogenesis
- **A different way of handling resistance**
  - Putting distress in a biological context typically reduces the shame
  - Expect and relish ruptures
  - Repairs are a vital part of change

BBT

- Talk about the brain!
- Educate clients about the mind-brain connection
  - Discuss stress and fast and slow route to the amygdala
  - Discuss right vs left hemisphere affective processing
  - Discuss how behavior changes the brain
- Don’t forget to plant SEEDS

Brain.Based.Therapy@gmail.com
www.drjohnarden.com

Biopsychosocial Meaning

- Meaning comes from the compatibility of biological, psychological, and social systems
- These states co-exist in varying degrees over the flow of time
- "Do I think, feel (physically and emotionally) in synch with others in the space we create together

5 Healthy Habits

Planting SEEDS

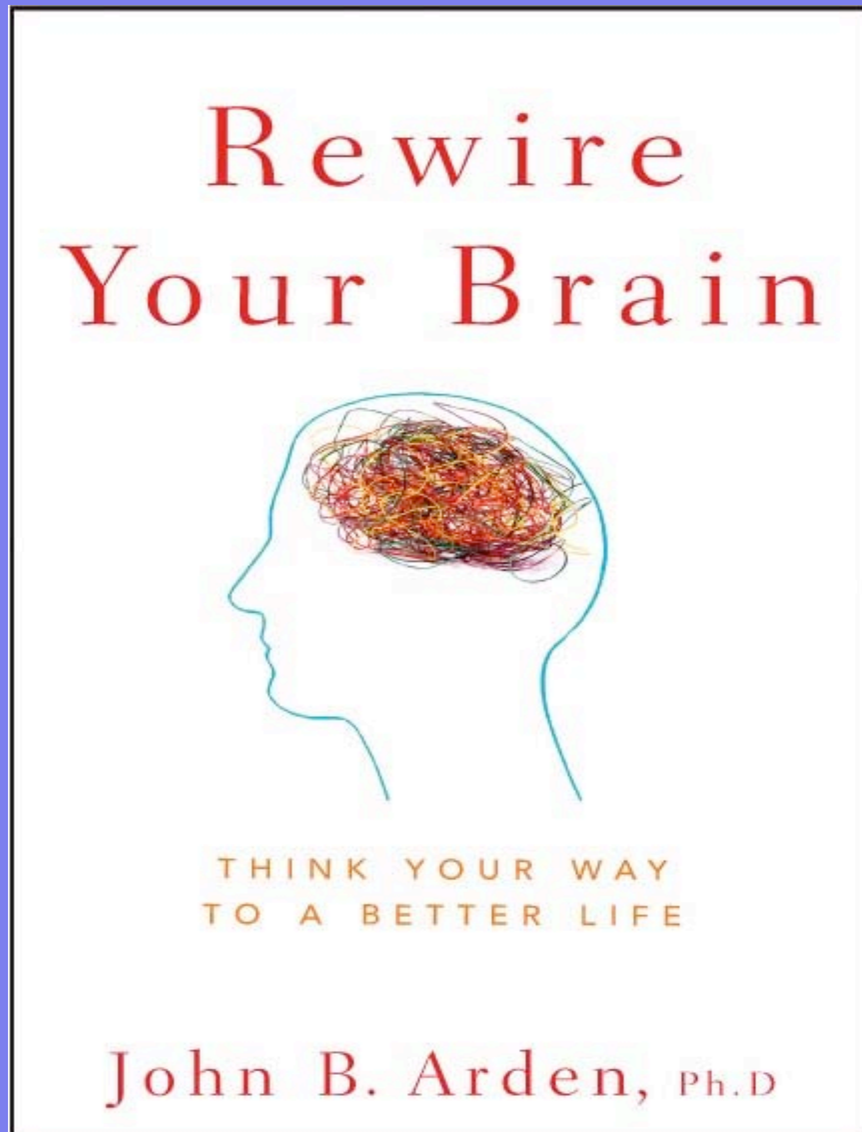
S—Social Medicine

E—Exercise

E—Education

D—Diet

S—Sleep Hygiene


Rewire
Your Brain
THINK YOUR WAY
TO A BETTER LIFE
John B. Arden, Ph.D

7 Principles of Relaxation

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—By shifting attention on the here and now you can transform each experience into a rich and calm experience in the present. This activates your PFC to inhibit the over-reactivity of your amygdala.

7 Principles of Relaxation

- 3) A quiet environment—This will give you an opportunity to learn how relax without distractions.
- 4) An accepting and a nonjudgmental attitude—By shifting away from rigid expectations and to an accepting attitude you'll appreciate reality as it is, rather than what you fear it could be.
- 5) A relaxed posture—This can include sitting in a relaxed posture or stretching (e.g. hybrid yoga)

7 Principles of Relaxation

– 6) Observation—This allows you to detach from anxiety by not denying its existence.
  - As you observe whatever experience nonjudgmentally you can simply note what is occurring at any one time.
– 7) Labeling what you experience accesses your left frontal lobe and its positive emotions.

Mindfulness and the Brain

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

Mindfulness and Open Focus

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

Mindfulness for Various Groups

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

Mindfulness and Anxiety Reduction

1) The process of labeling your emotions reduces anxiety.
2) Strong relationship between high mindfulness and L-PFC regions which tame the amygdala.
3) These positive effects seem also to correlate with enhancements in these neural emotional regulation pathways.

The Importance of Sleep for the Brain

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

Medications and Insomnia

- Decongestants
- Corticosteriods
- Diuretics
- Heart medications
- Parkinson’s medications
- Asthma medications
- Appetite suppressants
- Kidney medications

Medical Conditions - Insomnia

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

“Learned” Insomnia

- “I’m not going to get to sleep tonight.”
- Bed becomes an enemy—a negative cue.
- Sleep later on the weekends to compensate.
- Next night you feel as you are losing sleep.
- You try too hard to get to sleep.
- Thoughts about sleep add to daytime stress.

Negative Sleep Thoughts (NSTs)

- I have to get the same number of hours of sleep every night.
- There is something wrong with me.
- I will never get to sleep.
- I will be ruined tomorrow.
- I can’t get my mind to turn off.

Defusing NSTs

- This isn't great but at least I've got my core sleep.
- If I don't get a good night sleep tonight I will tomorrow night.
- I may get back to sleep, I may not. Either way it is not the end of the world.

Sleep Hygiene

- Cut your caffeine intake and don’t drink caffeine on an empty stomach
- Force yourself 3 meals a day
- Avoid sugar

Sleep Hygiene

- Don't "try too hard" to go to sleep.
  - You'll frustrate yourself, leading to a paradoxical effect, and work yourself into an anxious state of mind.
- Tell yourself "it's okay if I get just a few hours sleep tonight. I will catch up the next night."
  - This change in expectation will free you up to be able to relax. The harder you try to go to sleep the harder it will be to induce sleep.

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 Hygiene

- Avoid drinking large quantities of liquid at night.
  - This will lower the sleep threshold and cause you to wake up to urinate.
- Avoid bright light at least a few hours before going to sleep.
  - Don’t work on the computer into the late evening.

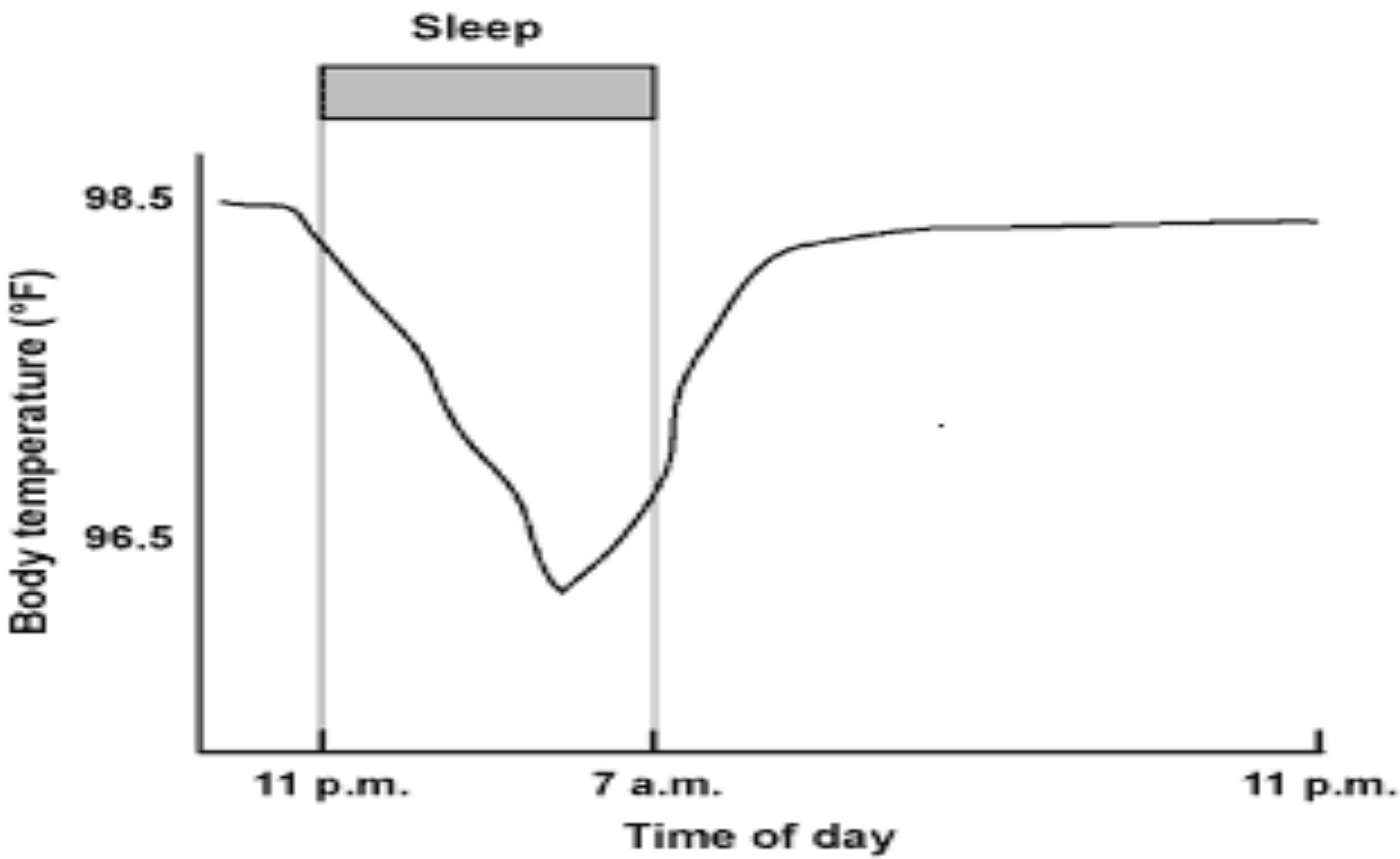
Sleep Hygiene

- Do all planning for the next day before you get into bed.
  - If you think of something you need to remember get up and write it down.
  - Tell yourself that you will postpone thinking or worrying about anything until the next day.
- Avoid all daytime naps.
  - Think of naps as a way to steal sleep from the night time.

Sleep Hygiene

- Try eating a light snack with complex carbohydrates before bed.
  - Foods rich with L-Tryptophan are advisable. Don't eat anything with sugar or salt before bed.
- Avoid protein snacks at night because protein blocks the synthesis of serotonin and as a result promotes alertness.

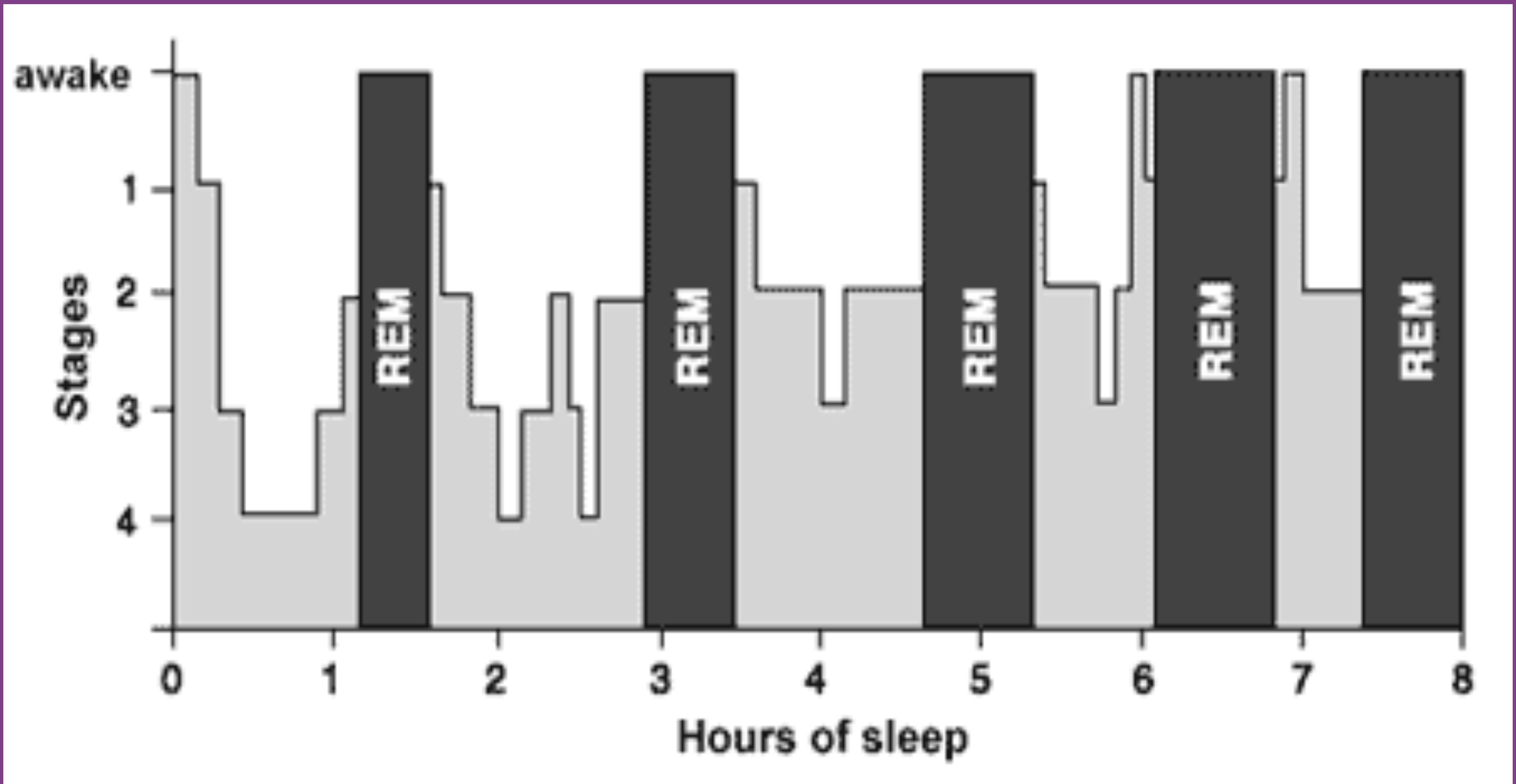
Body Temp and Sleep

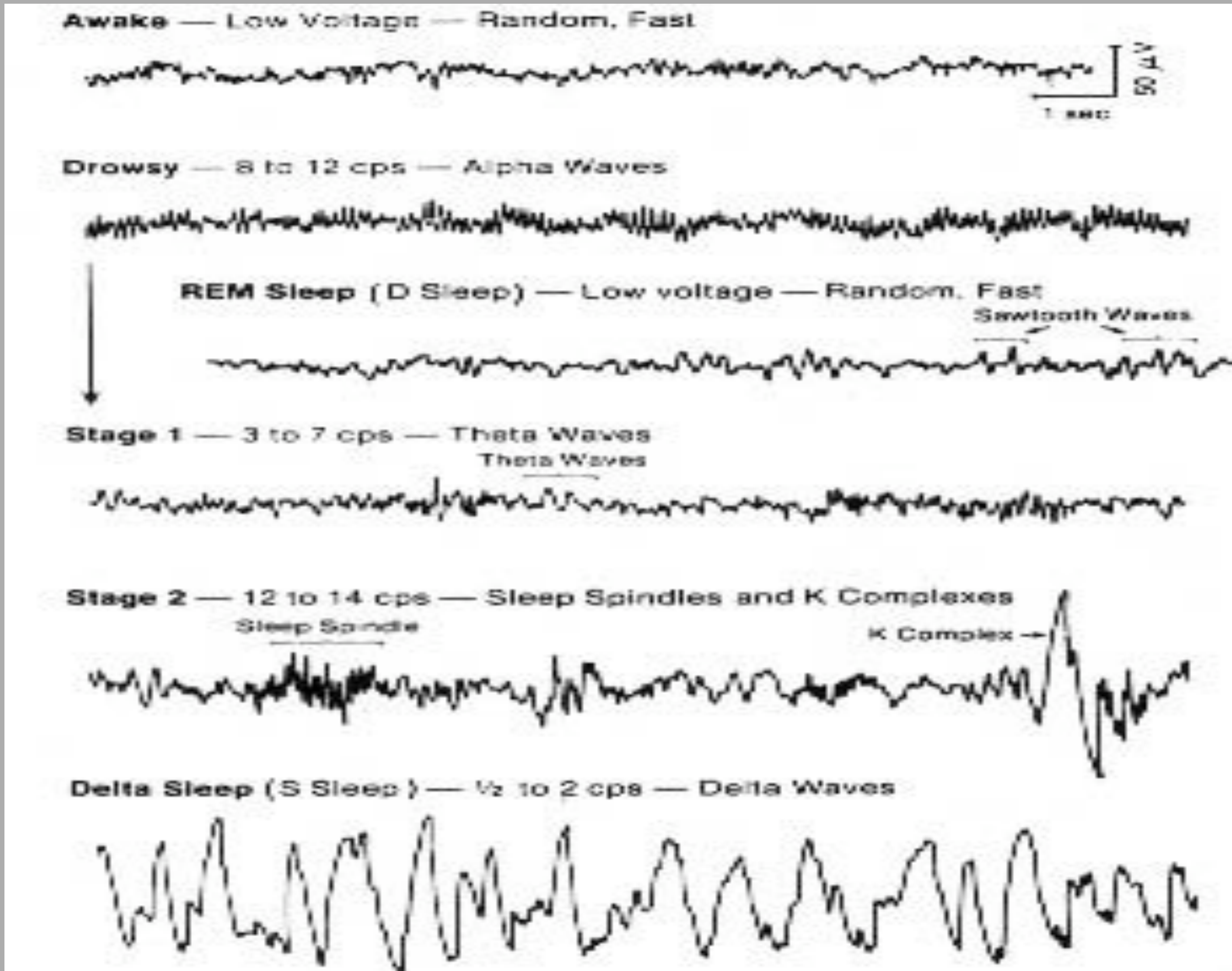


Medications and Insomnia

- Decongestants
- Corticosteriods
- Diuretics
- Heart medications
- Parkinson’s medications
- Asthma medications
- Appetite suppressants
- Kidney medications

Stages of Sleep




Awake — Low Voltage — Random, Fast
50 µV
1 sec
Drowsy — 8 to 12 cps — Alpha Waves
REM Sleep (D Sleep) — Low voltage — Random, Fast
Sawtooth Waves
Stage 1 — 3 to 7 cps — Theta Waves
Theta Waves
Stage 2 — 12 to 14 cps — Sleep Spindles and K Complexes
Sleep Spindle
K Complex
Delta Sleep (S Sleep) — ½ to 2 cps — Delta Waves

Emotions and Sleep

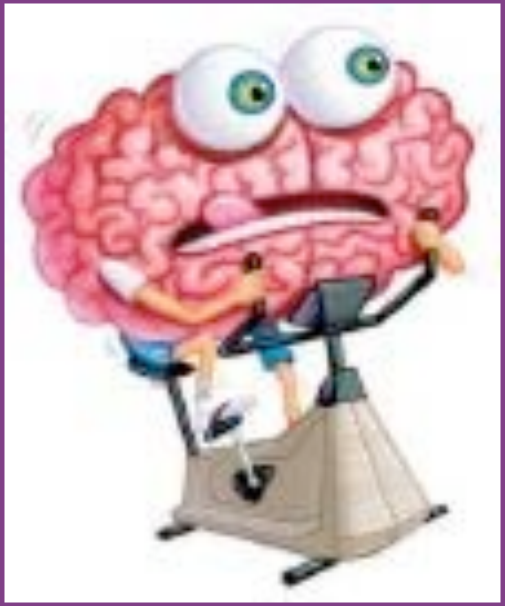
- "Never go to sleep angry" makes sense
- Sleep selectively enhances:
  - episodic memory that are emotionally salient
  - Emotional memories creating a long-lasting and potentially traumatic representation of distressing experiences

Sleep Hygiene

- Exercise 3 to 6 hours before you go to bed. A brisk walk before or after dinner time is perfect.
- Avoid alcohol
- Sleep scheduling technique.
- Try the relaxation exercises. These help you go to sleep or go back to sleep if you wake up during the night.

Exercise Optimizes

- Mood
  - ↑ neurotransmitters
    - »Serotonin
    - »Dopamine
    - »norepinephrine
  - –physical health



Exercise Optimizes

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

Exercise Optimizes

- Neurogenesis
  - new neurons in the hippocampus
- Neuroplasticity
  - ↑ BDNF

Exercise and Repair Processes

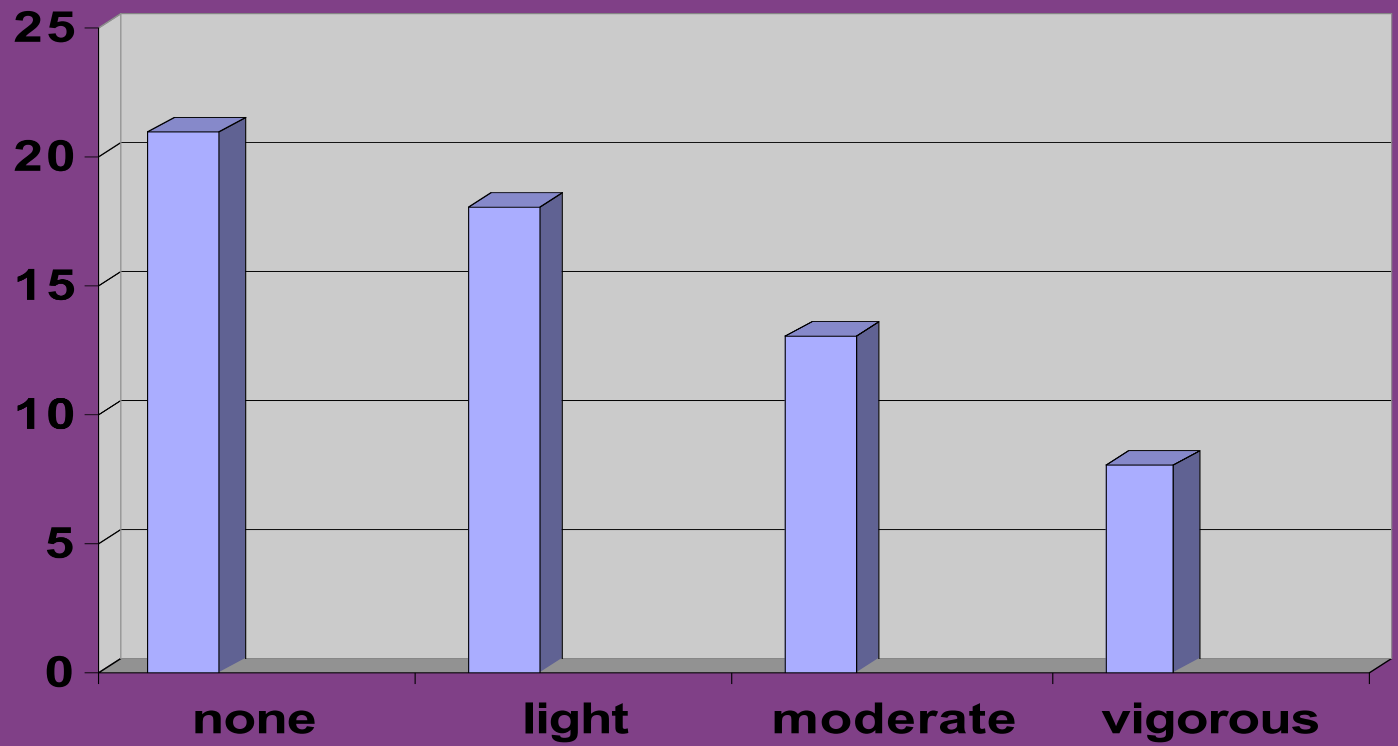
- Insulin-like Growth Factor (IGF-1)
- Vascular Endotheclial Growth Factor (VEGF)
- Fibroblast Growth Facto (FGF-2)
- Brain Derived Neurotrophic Factor (BDNF)

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 (Neeper, et al, 1996)
Vascular Endothelial Growth factor (VEGF)	Enhanced Neurogenesis (Fabel, et al, 2003)

Effect of 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)**

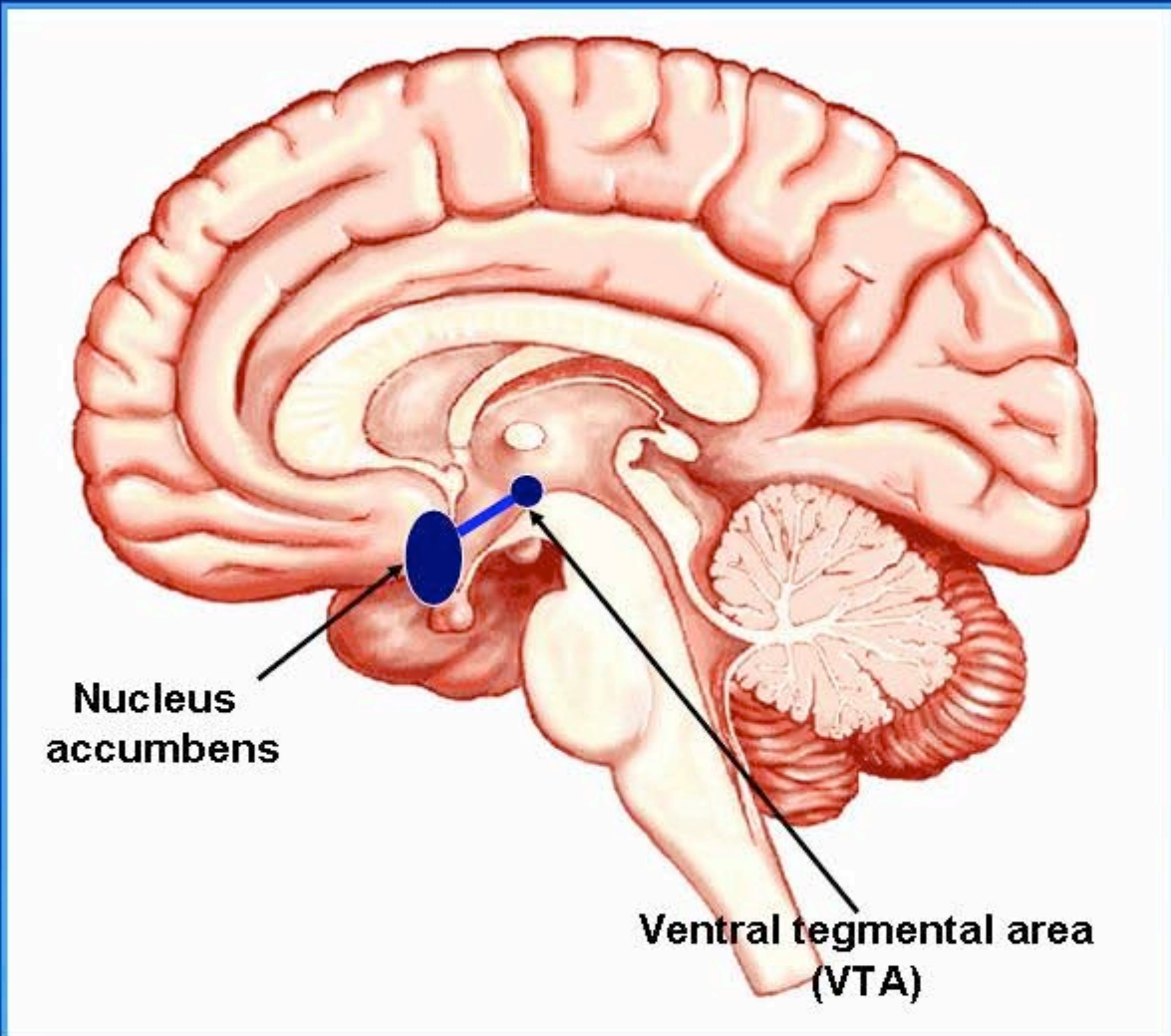


Defining the "Standard Drink"

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

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

Brain Reward Pathways



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

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

Effects of Acute Alcohol on Other Neural Circuits

GABA and Glutamate Systems

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

GABA = gamma-aminobutyric acid.

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

Effects of Alcohol on Neural Circuits

Glutamate System

Administration of Alcohol

Acute Alcohol Effect

- Inhibits NMDA receptors
- **Effect:** ↓ anxiety, ↑ sedation

Chronic Alcohol Use

Alcohol Free

CNS Equilibrium

Adaptation

- ↑ # and/or function of NMDA receptors on neurons
- Balances acute alcohol effect
- **Effect:** tolerance, dependence

Withdrawal

- Increased glutamatergic activity
- **Effect:** - *Acute:* dysphoria, hallucinations
  - *Post-acute:* sleep/mood disturbances

Removal of Alcohol

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

Differences in Alcohol Metabolism Between Men and Women

- Women are smaller than men
- Women have lower total body water content (49%) than men (58%) of comparable size
- Gastric ADH lower in women
- Fluctuations in gonadal hormone levels during the menstrual cycle may affect the rate of alcohol metabolism

Alcohol Alerts #10 & #46 - NIAAA

Alcohol

- Alcohol can have a destructive effect on your fatty acid pathways. It can:
  - Block enzymes needed to form DNA
  - Block the enzymes needed to form prostaglandin E1 (PGE1)
  - Dissolve fatty acids within the brain's membranes and replaces them with a poor substitute docosapentaenoic acid (DPA)

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

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

Marijuana

- 2 endogenous cannabinoid (CB) receptors:
  - Anadamide (Sanskrit for bliss)
  - 2-archidonyl-glycerol (2-AG)
- Anadamide inhibits the release of glutamate and acetycholine within the cortex and the hippocampus
  - Impairing the formation of memory
- The CB receptors enhance the release of DA
- Stimulation of the CB receptors in the hypothalamus underlies the “munchies”

The BASE of BBT