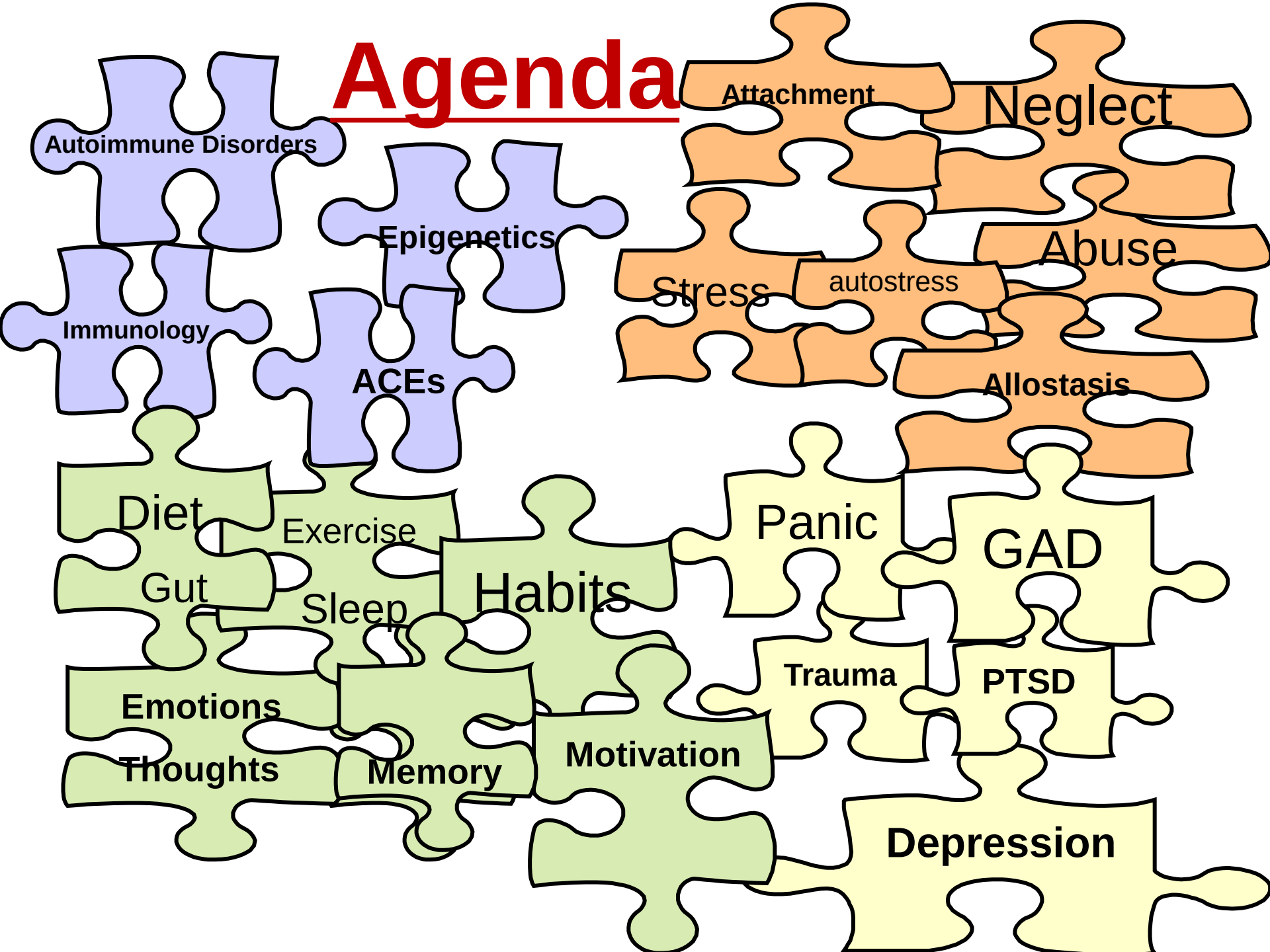
Mind-Brain-Gene:

Psychotherapy Integration

John B. Arden, PhD, ABPP


Agenda
Attachment
Neglect
Autoimmune Disorders
Epigenetics
Abuse
Stress
autostress
Immunology
ACEs
Allostasis
Diet
Exercise
Panic
GAD
Gut
Sleep
Habits
Trauma
PTSD
Emotions
Motivation
Thoughts
Memory
Depression

Therapy might have been different

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

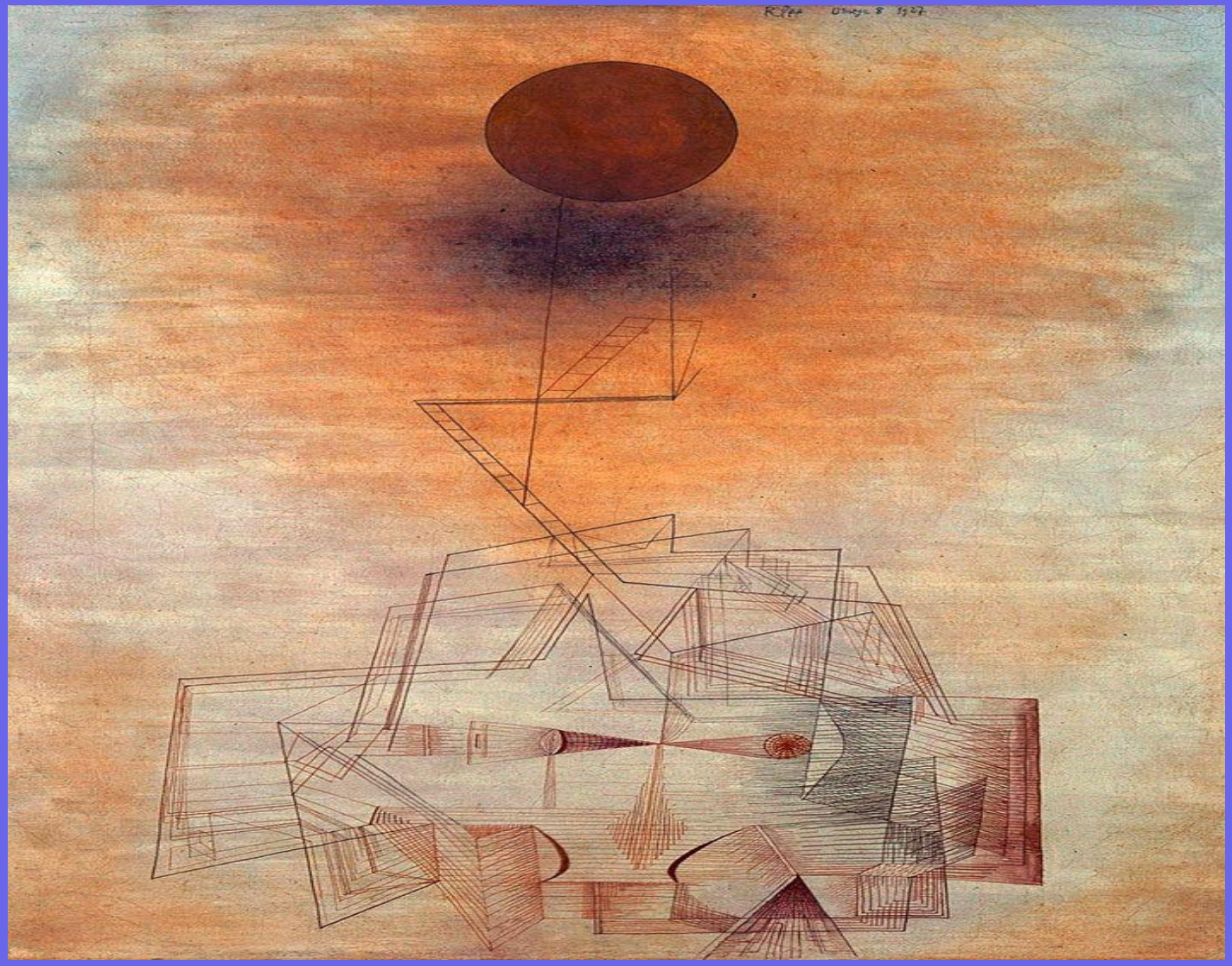
--Sigmund Freud

"The act of will activates neural circuits"

--William James

But……

Limits of Understanding (Klee)



The Cartesian Blizzard

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

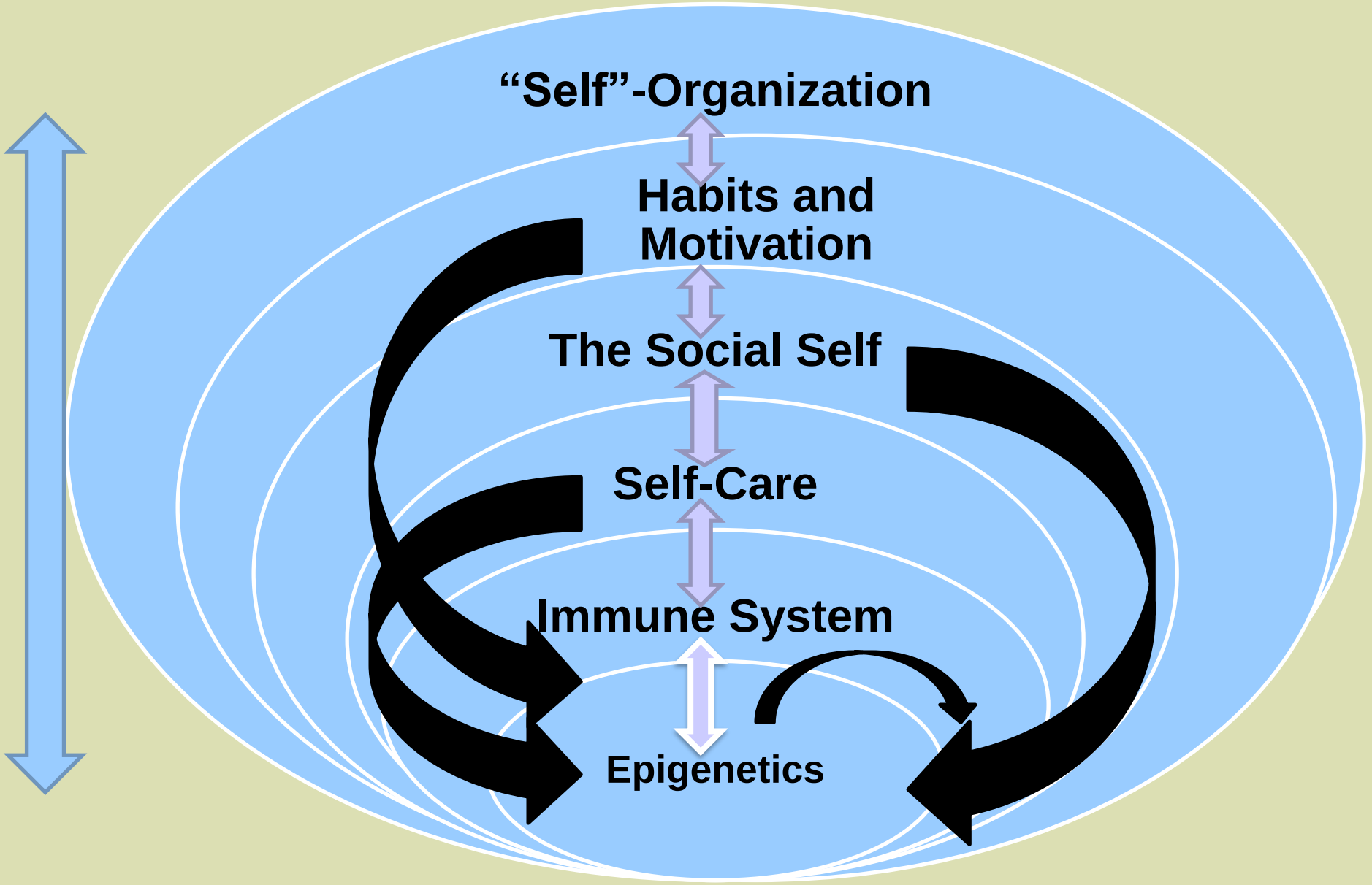
The Science has Changed

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

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

Mind-Brain-Gene Feedback Loops

Mind-Brain-Gene Feedback Loops

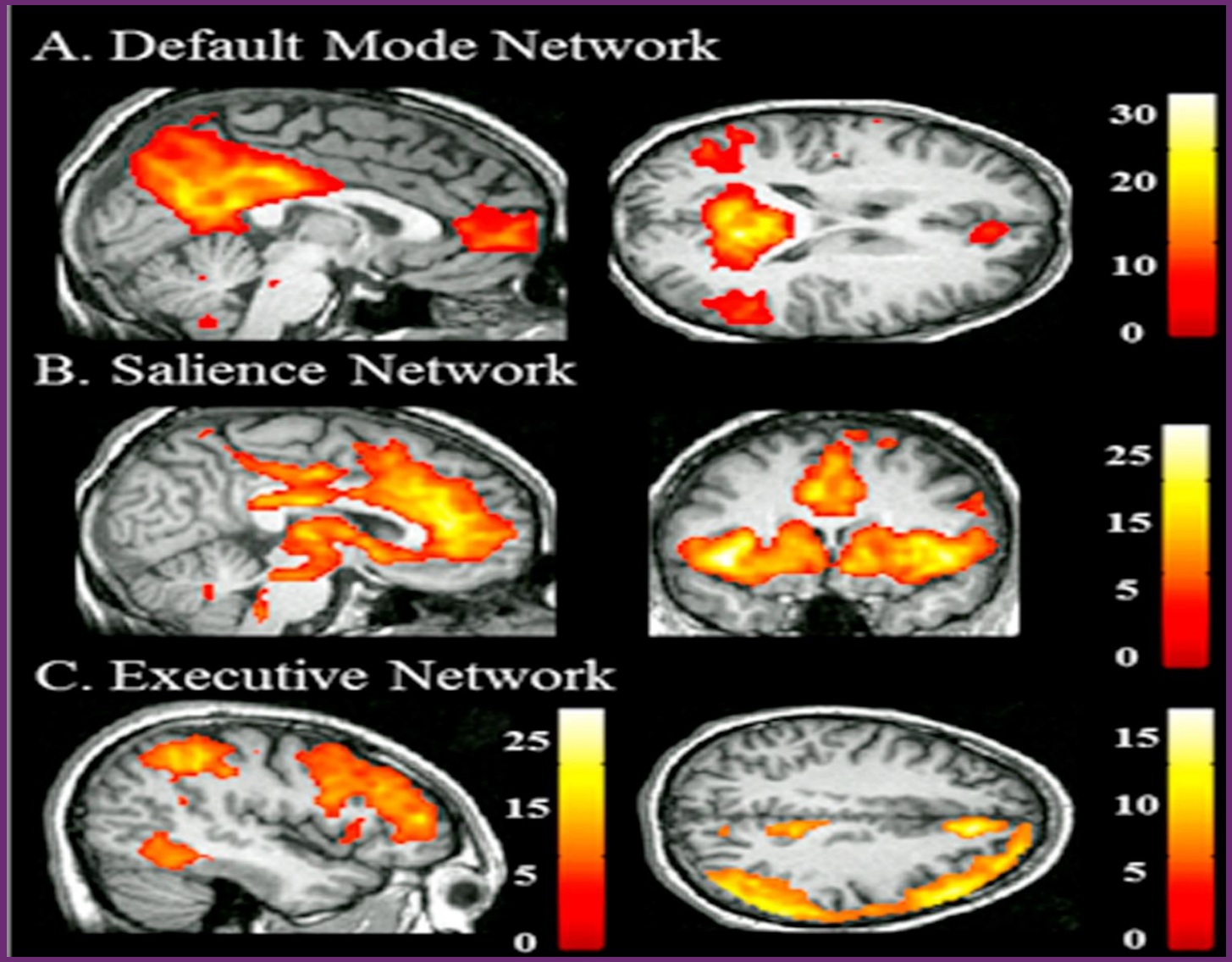


Mind-Brain-Gene Feedback Loops

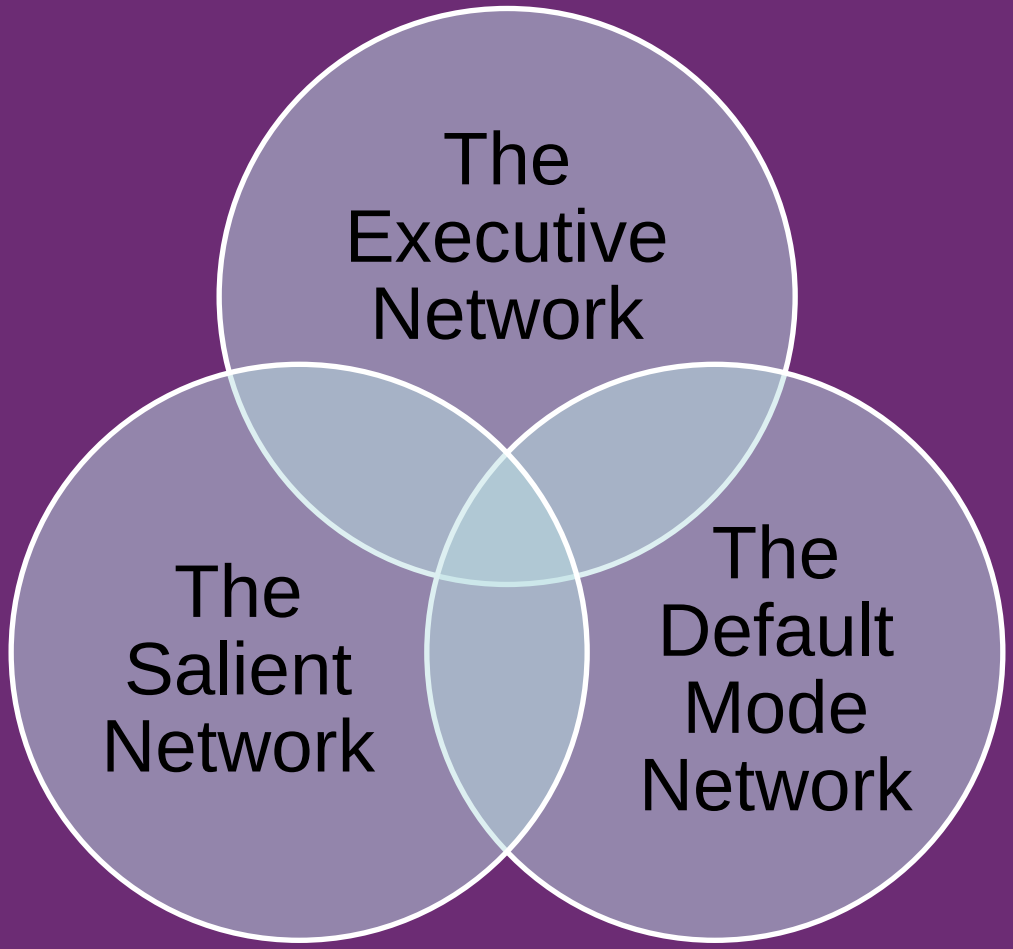
The Mind's Operating Networks:

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

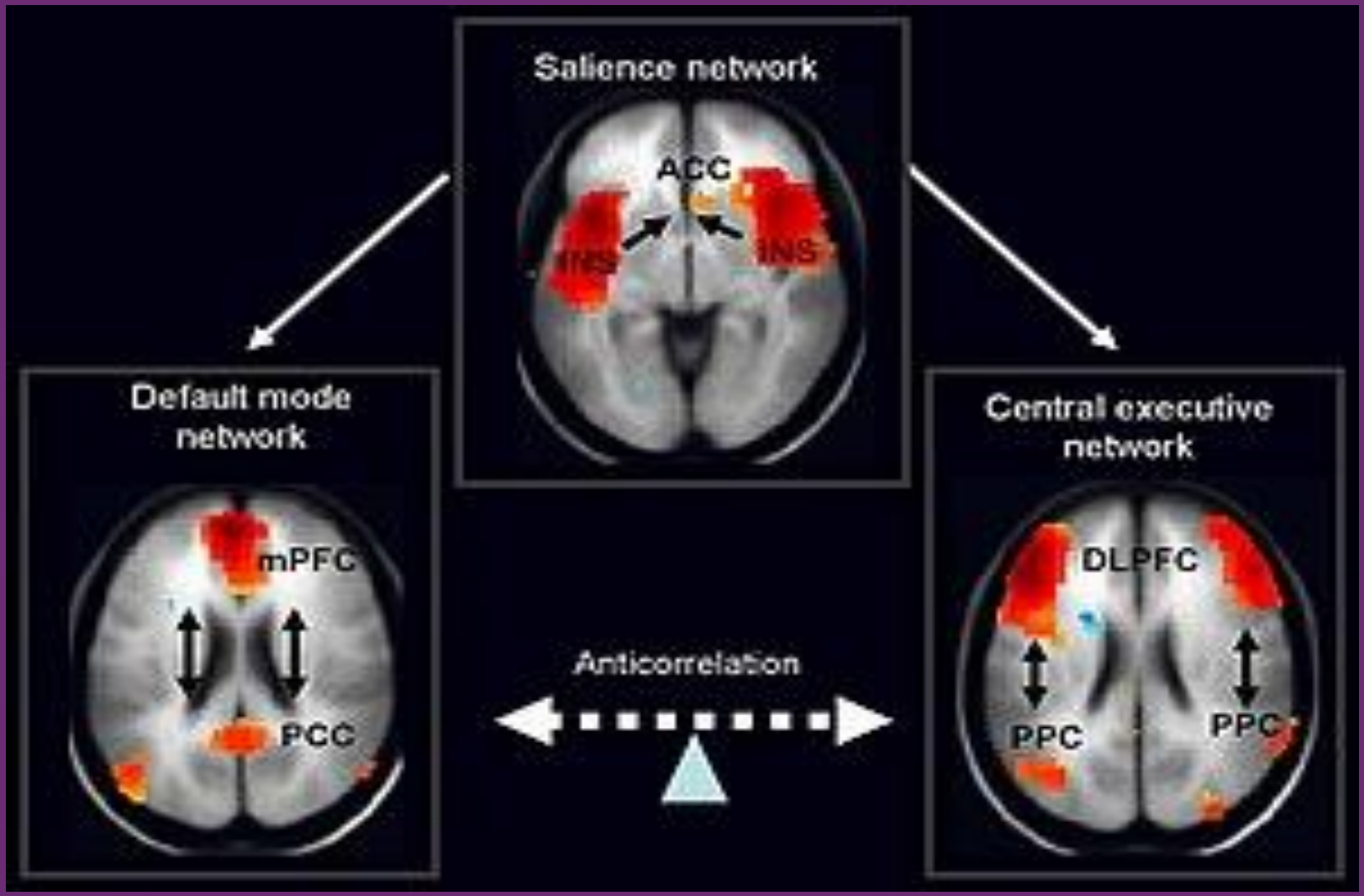
The Mental Networks



Balancing the Mental Networks



The Mental Neworks

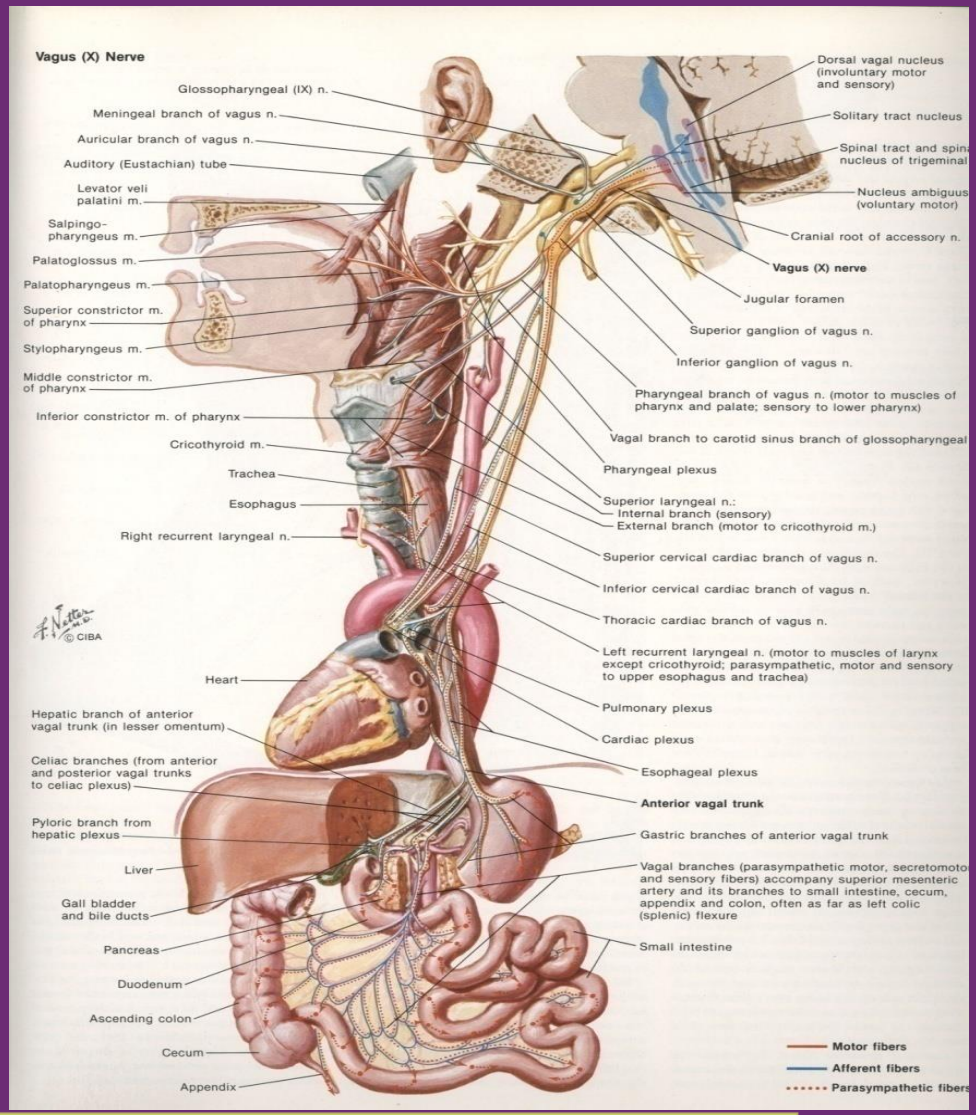


Salience Network:

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

The Vagus Nerve System

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

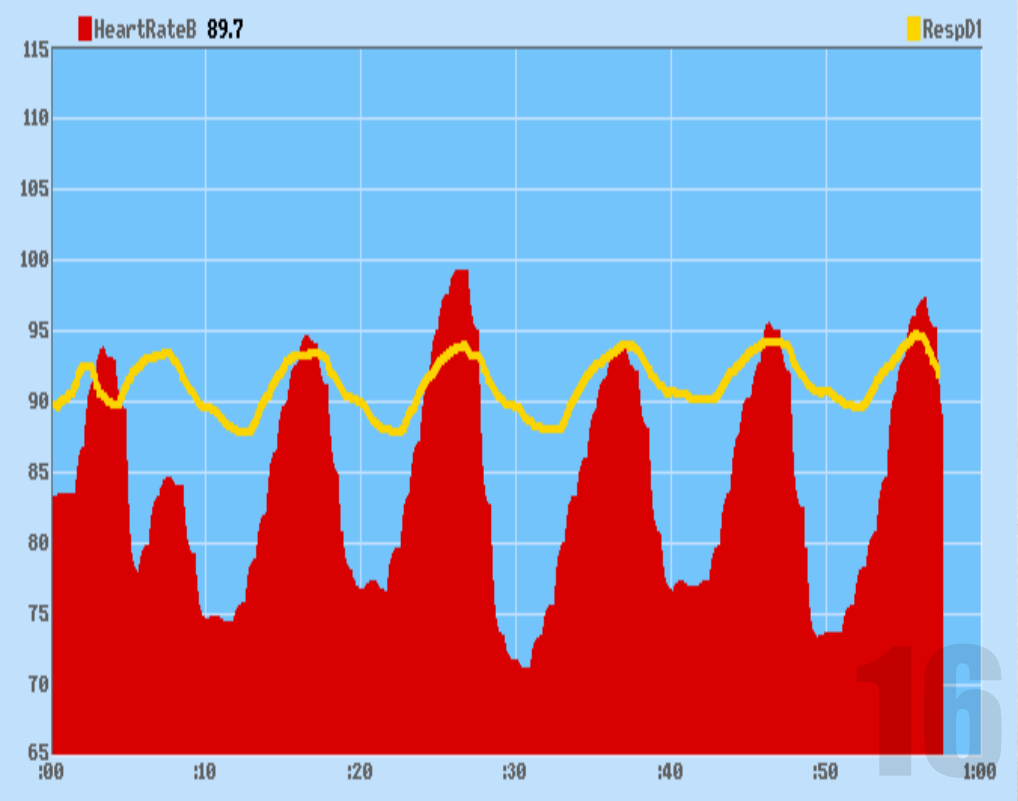


Variability is good

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

Heart rate increases with inhale.

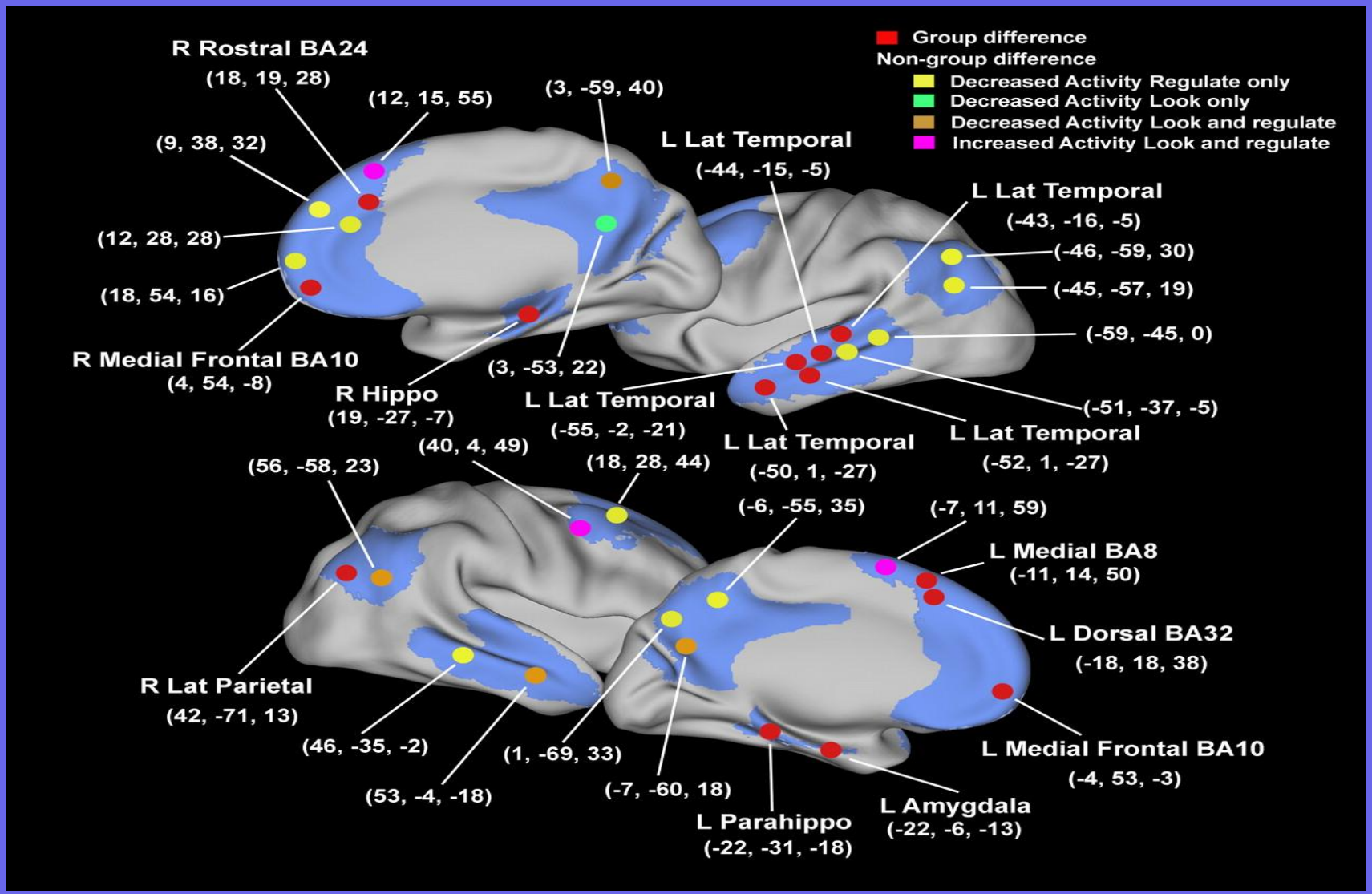
Heart rate decreases with exhale. This pattern shows high vagal tone (high PSNS activity) and a high amount of heart rate variability.



Default Mode Network:

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

Activity in the default mode network



Sheline Y I et al. (2009)

DMN Variations

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

“Where is the Anxiety?” bumping the DMN

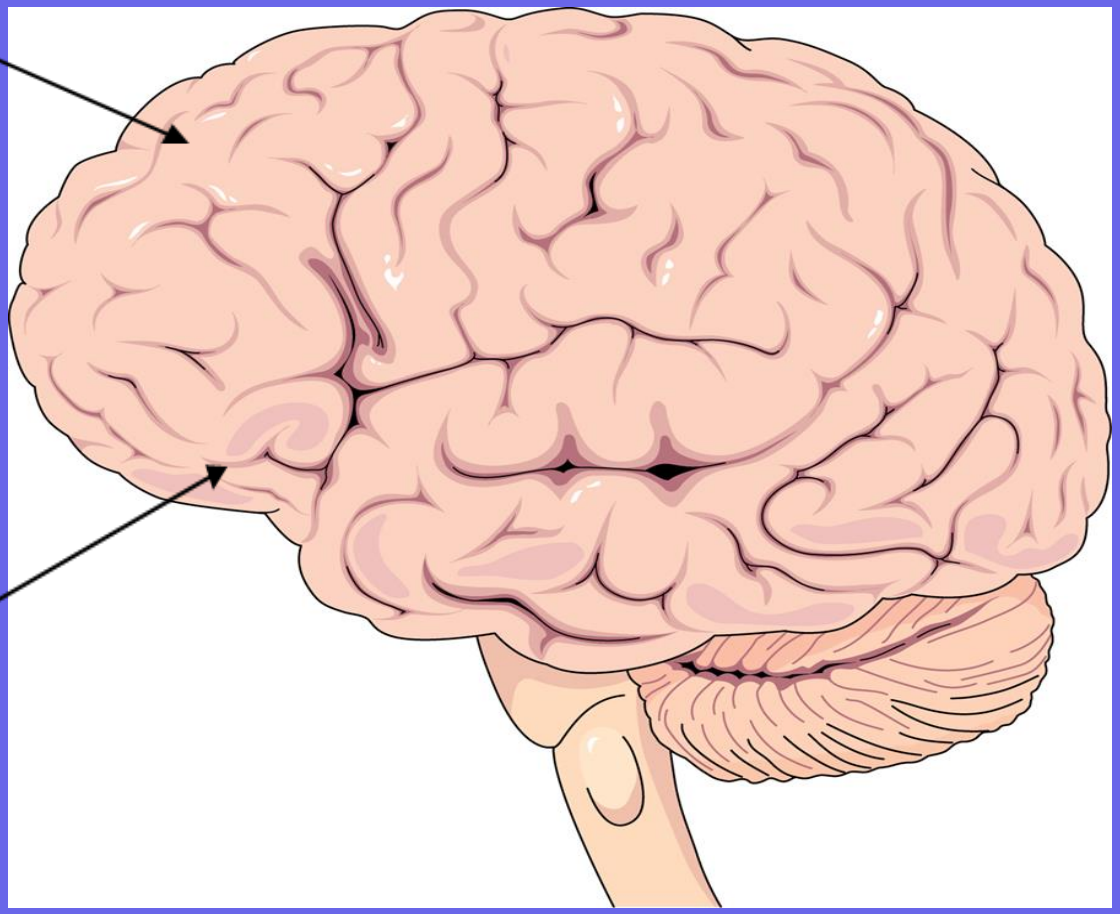
Central Executive Network:

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

DLPFC and the OFC

Dorsolateral Prefrontal Cortex

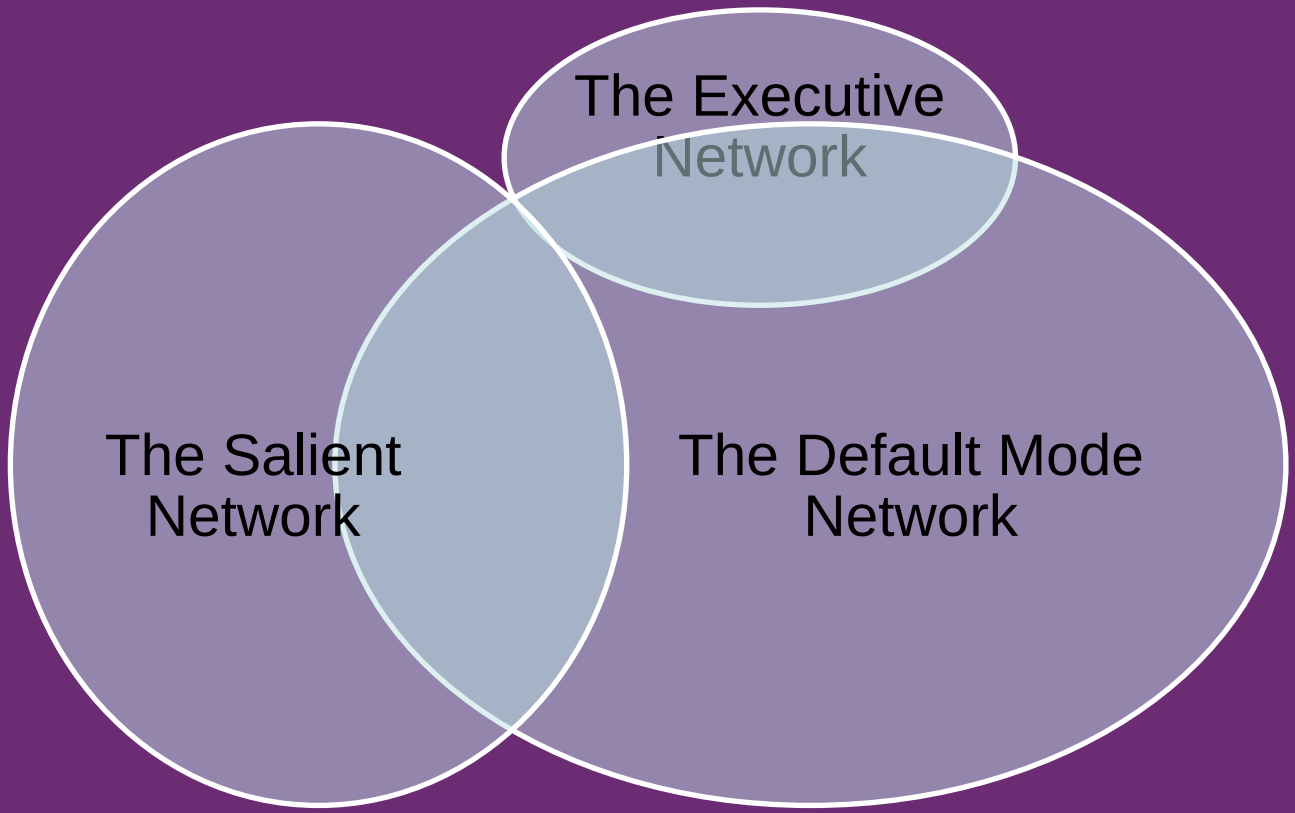
Orbital Prefrontal Cortex



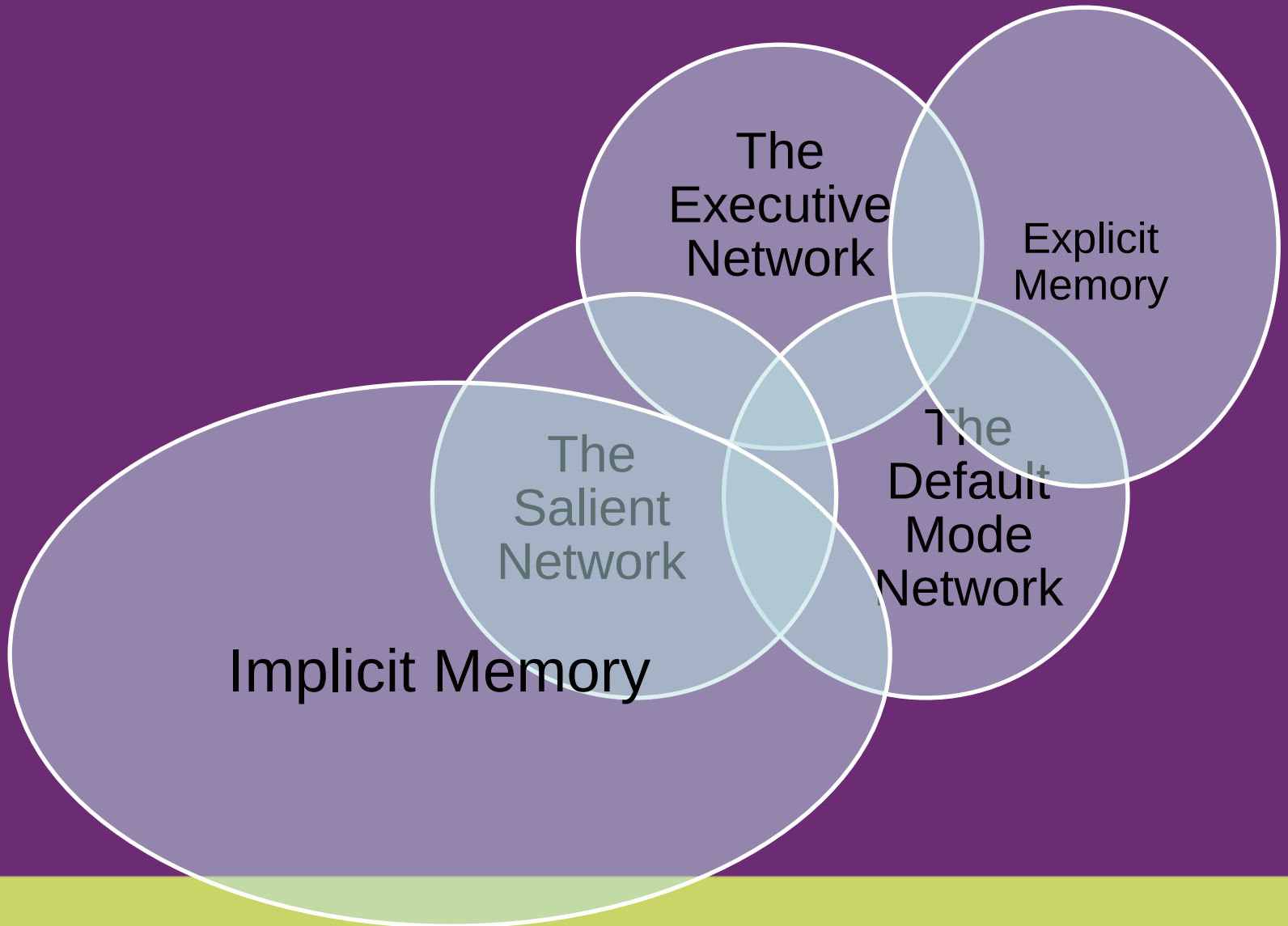
Pre-Frontal Cortex

- 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

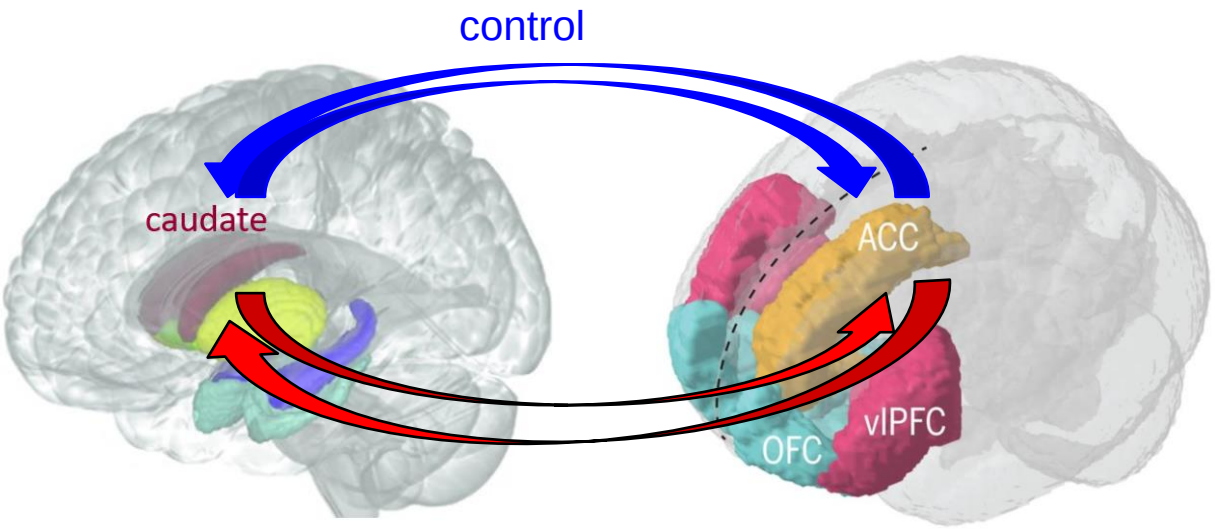
Imbalanced Mental Networks



The Mental Neworks & the Long-Term Memory Systems



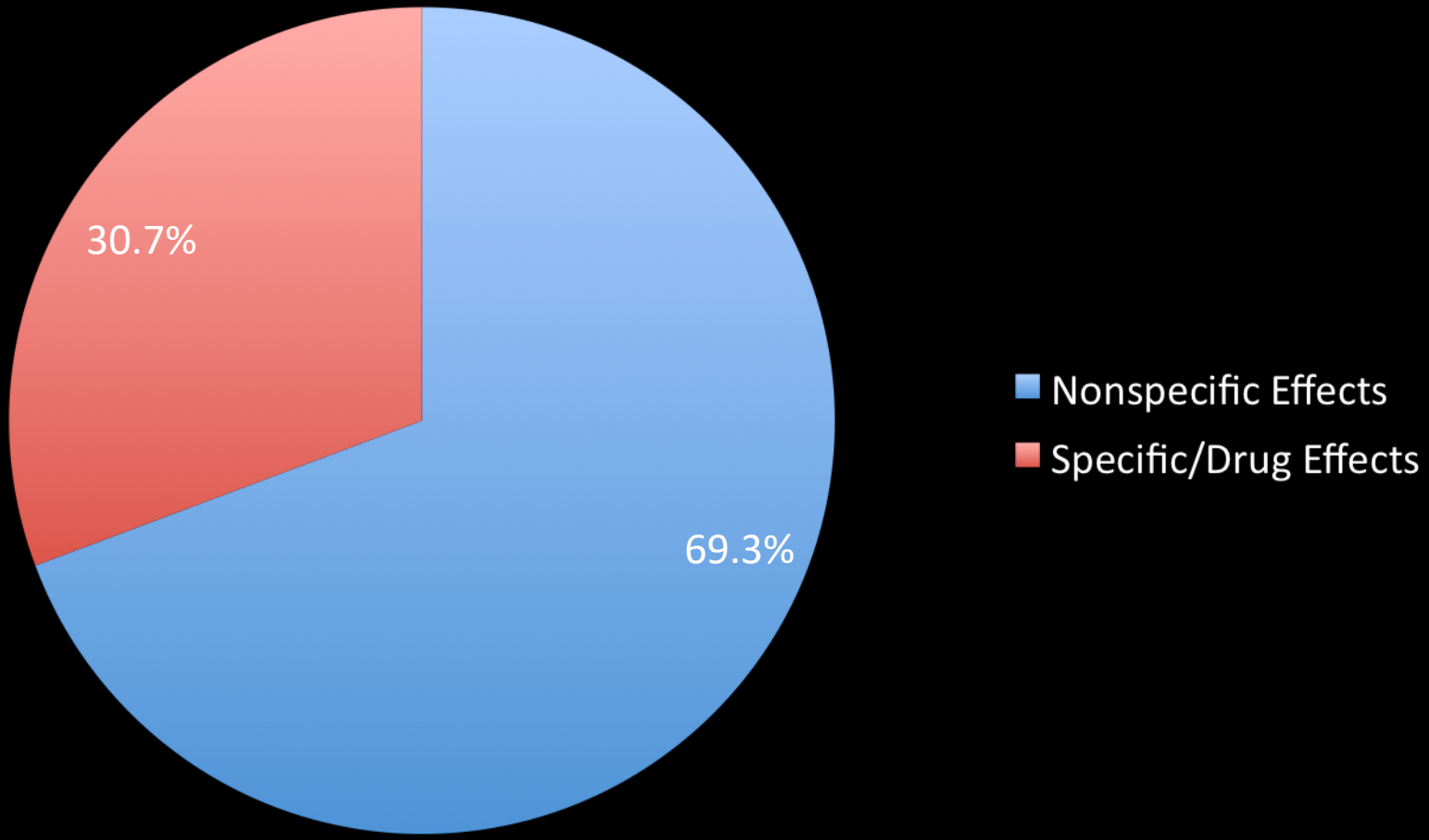
Subcortical-Cortical Connectivity



ADHD/CD

Shannon, Sauder, Beauchaine et al., 2009

Placebo

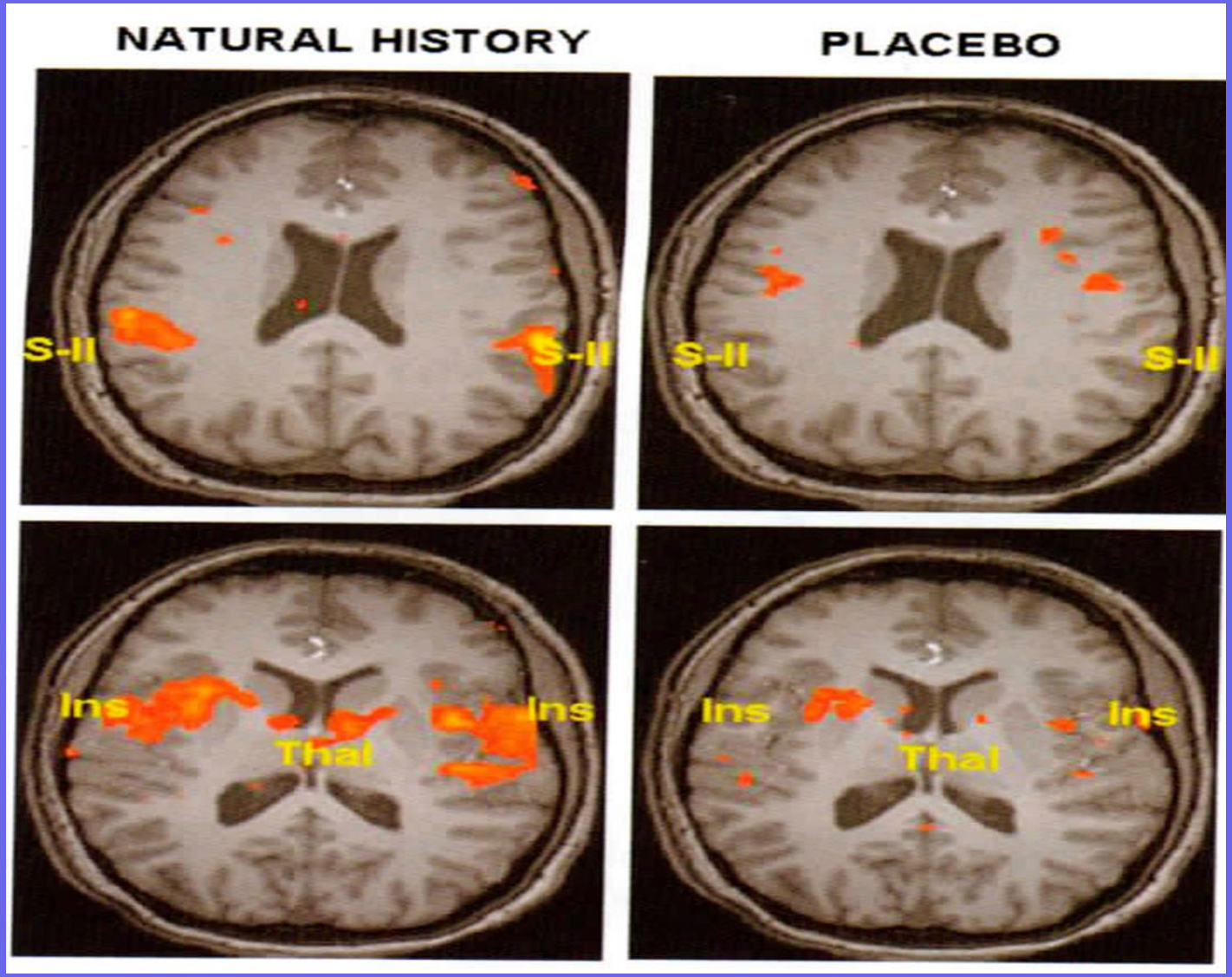


*Derived from pooled response rates for drug and placebo of 53.8% and 37.3%
Papakostas, *Eur Psychopharmacol*, 2009

Incidence of Placebo Response

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

IBS and Pain vs. Placebo



Mind-Brain-Gene Feedback Loops

Hunter-gatherer Adaptation Boosted the Social Brain

Hungry Social Networks

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

(Kolb & Gibb, 2001)

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

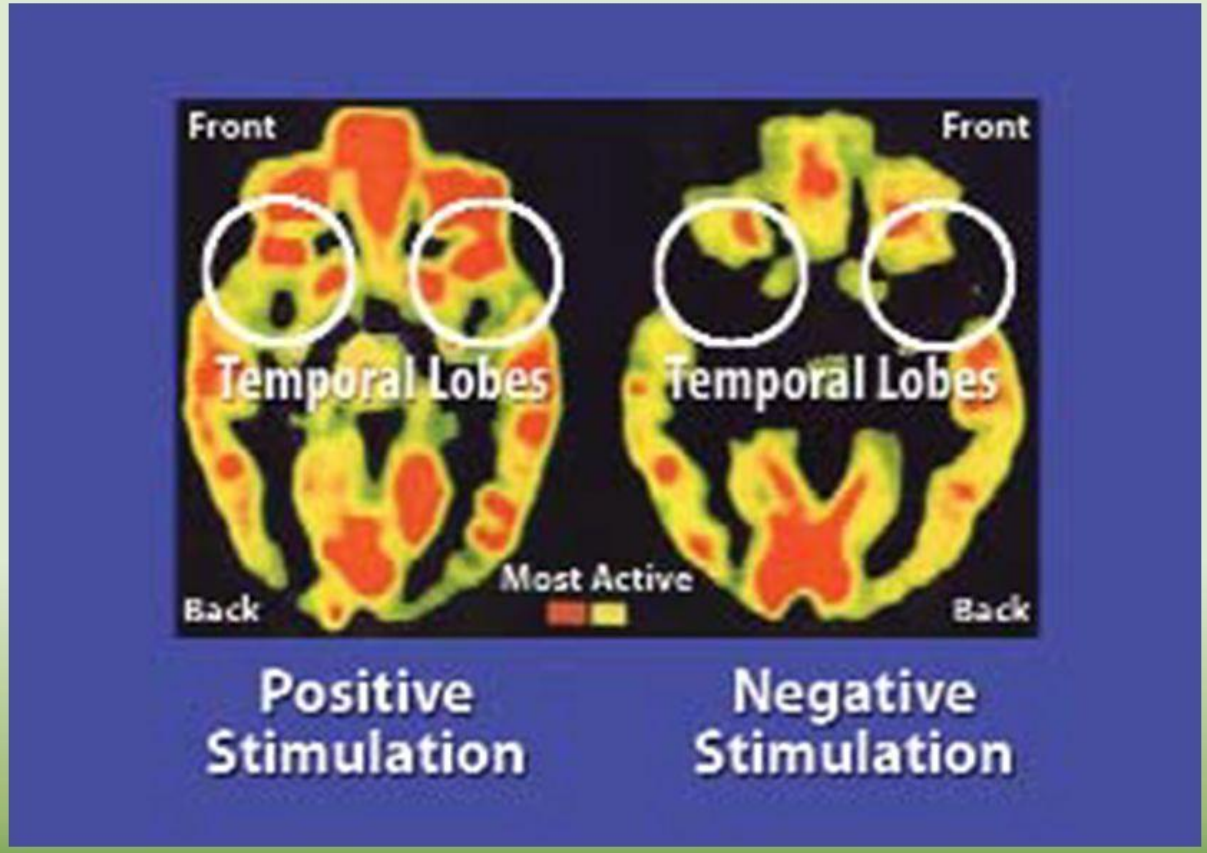
Deprived Social Brain Networks

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

Sustained impairment if over one year

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

“Normal” vs Romanian Brains

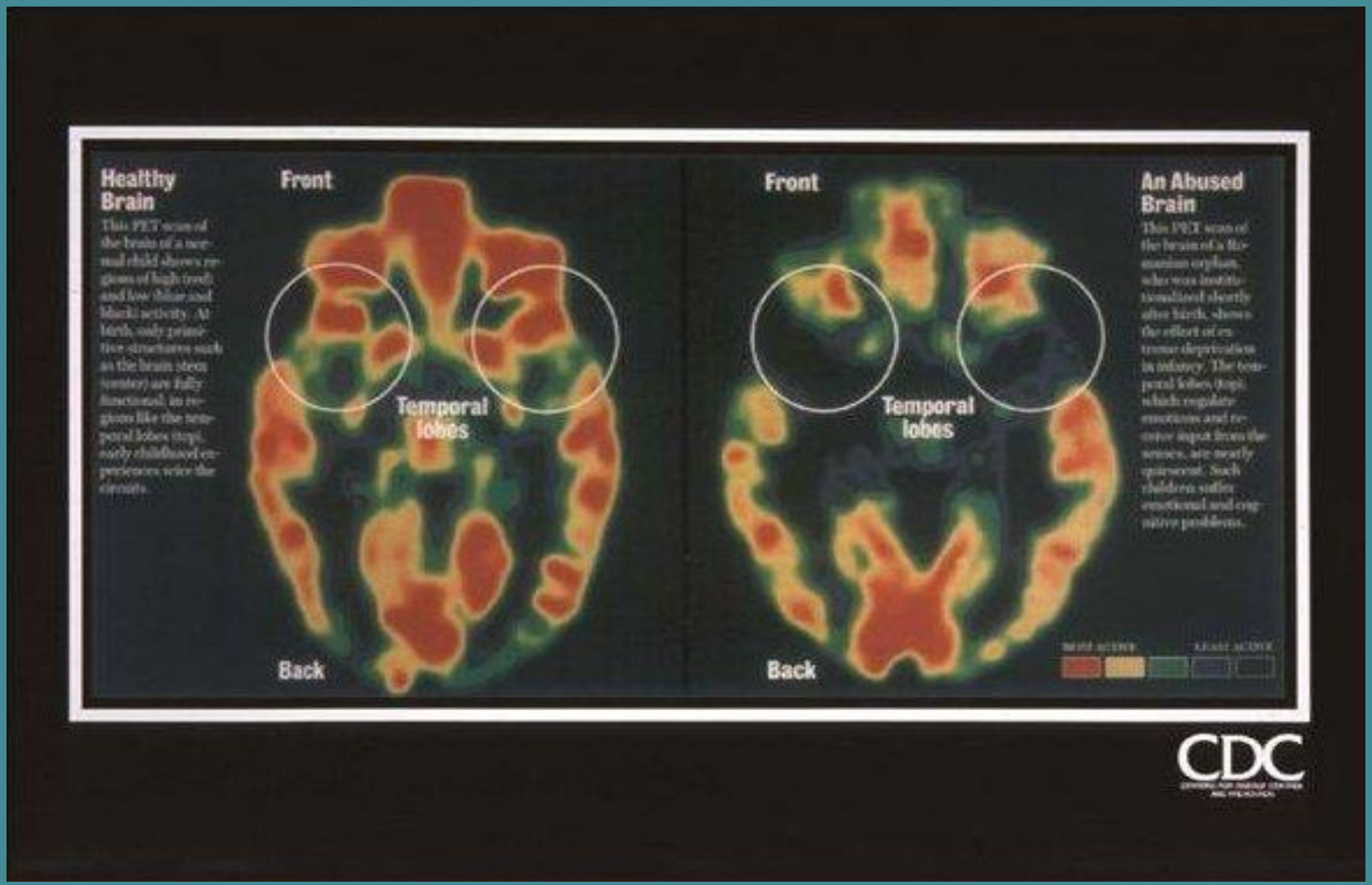


Brain activity of a normal five-year-old child (left)
and a five-year-old institutionalized orphan neglected in infancy (right).

Child Abuse and Neuropathology

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

“Normal” vs Abused Brains



The Neuroscience of Attachment

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

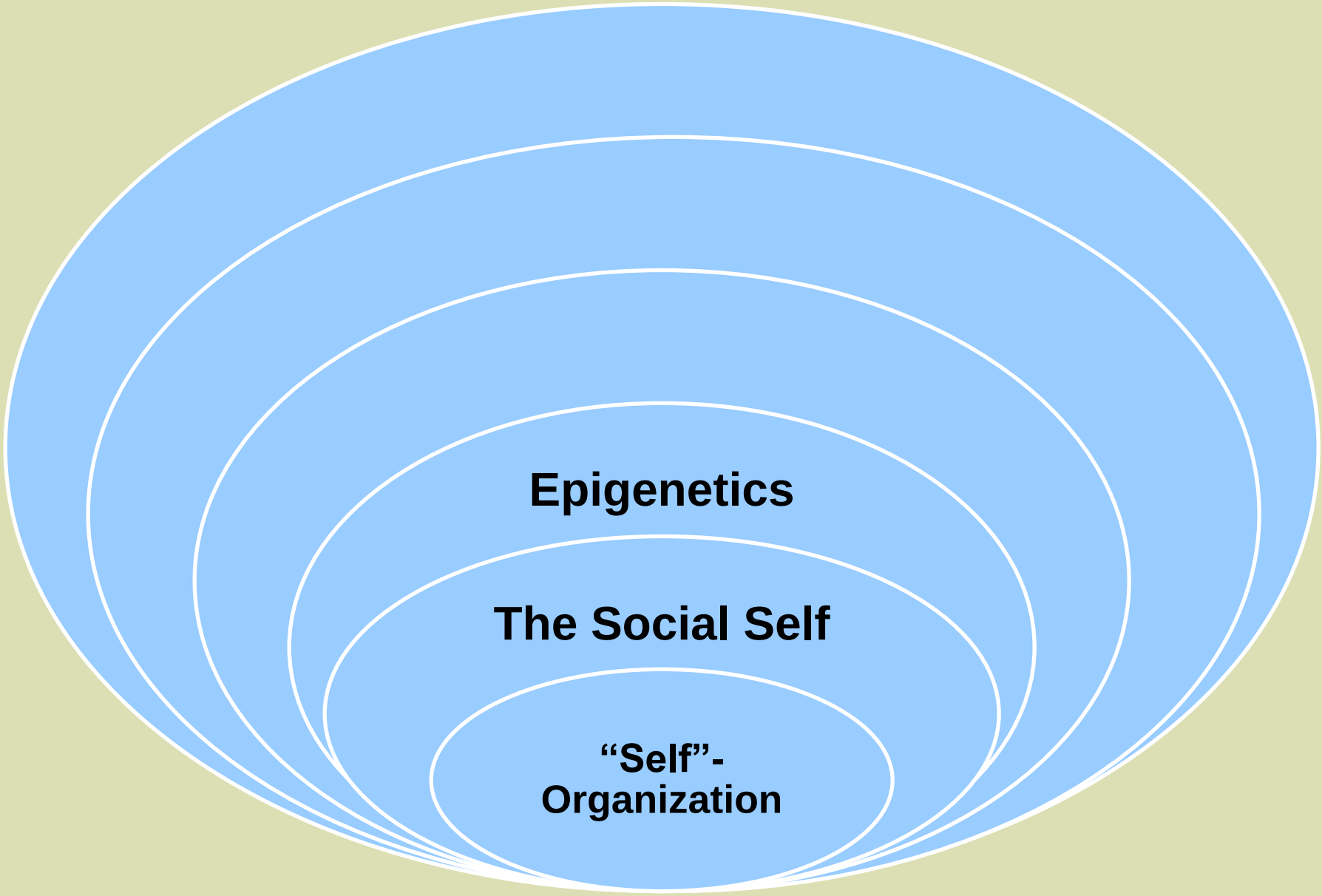
Good-enough parenting and frustration tolerance

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

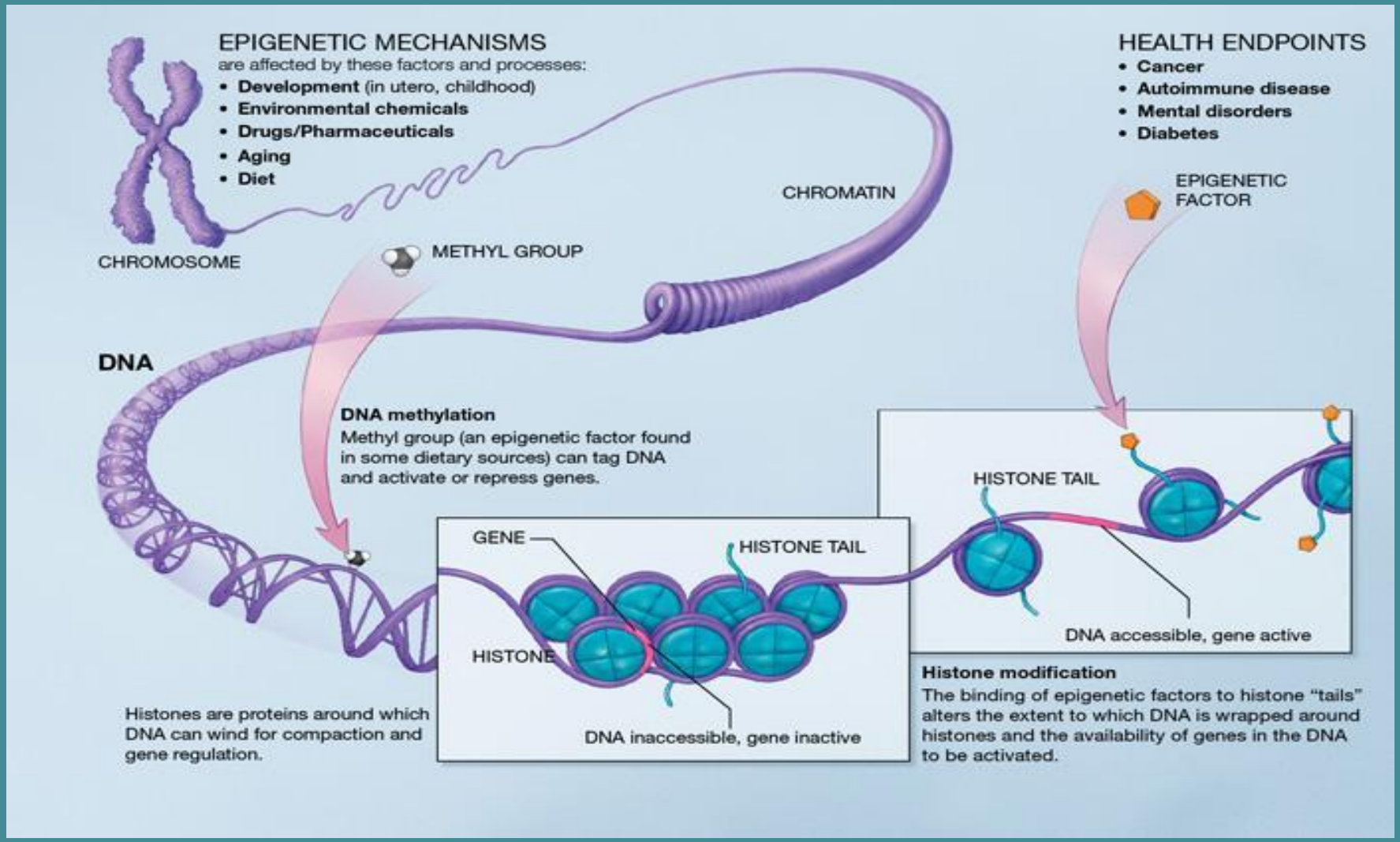
Hyperatunement

Family Time?

Mind-Brain-Gene Feedback Loops



Epigenetics



Someone Needs to Play (behave)

Epigentics and parenting

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

Cortisol level

Loneliness and Epigenetics

- Pro-inflammatory genes are overexpressed
- Anti-inflammatory genes are under-expressed
- Elevated herpesvirus antibody titers reflect poor cellular immune system control over the latent virus.

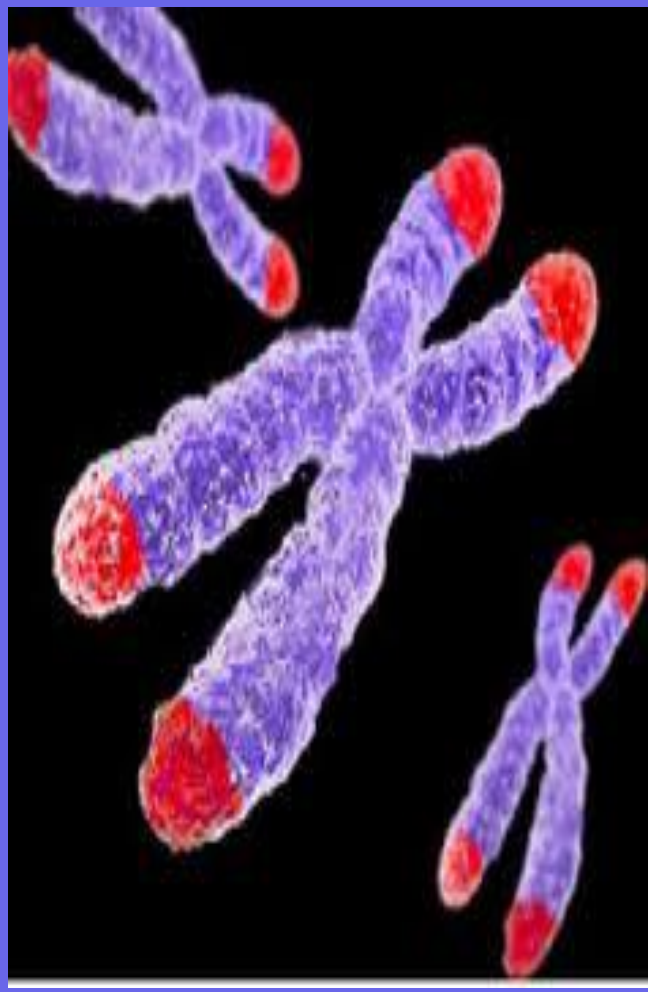
Lisa M. Jaremka et al: 2012, 2013

Factors that Impair DNA and Cells

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

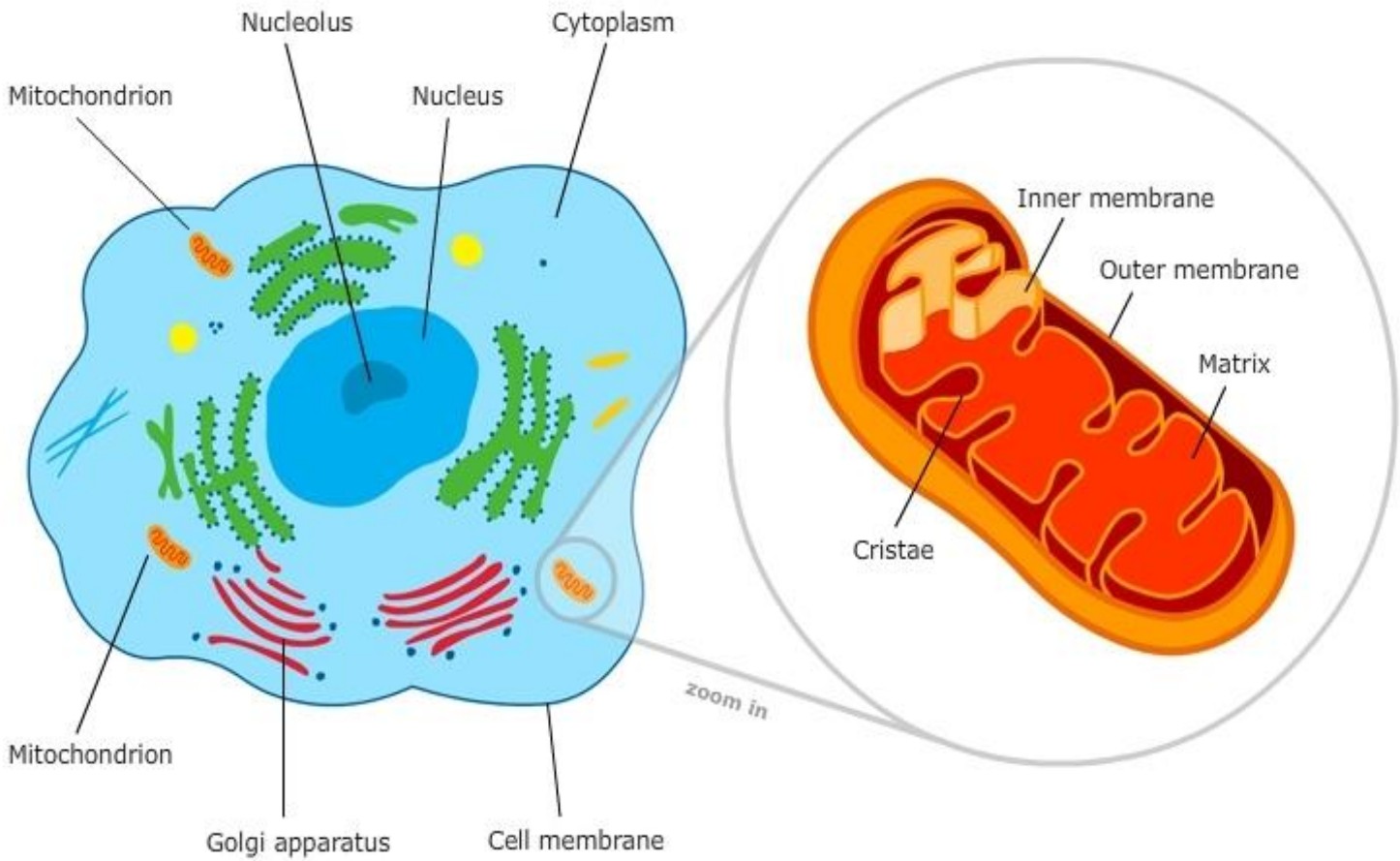
Factors that Shorten Telemeres

- Smoking
- Obesity (more than smoking!)
- Type 2 Diabetes
- Social isolation
- Poor diet
- No exercise
- Poor sleep
- Alcohol and other drugs



- **All rendering DNA vulnerable to damage**

Cells and Their Energy Factories



Mitochondrial Dysfunction

- Energy deficiency to astrocytes—which supply lactate to rapidly firing neurons
- Less also to oligodendrocytes where lactate is used for myelin synthesis
- Lactate uptake glucose from blood, stored as glycogen, conversion to lactate
- Since neural activity triggers the astrocytes to uptake glucose from blood and breakdown stored glycogen into glucose
  - Both get metabolized into lactate—which shuttles to neurons
  - Neurons take the lactate into the TCA cycle to produce ATP

Free Radicals

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

Free Radicals

- Generally we produce antioxidant enzymes and DNA repair mechanisms
- But when damage accumulates faster than repairs, damage to the mitochondria themselves occur, especially to the mDNA
- As cells lose their ability to produce energy, they die.
- The organs of those cells falter, including the brain.

Use up cell's energy or suffer

- When energy demand is high, electrons flow down the ETC rapidly, the protons are pumped swiftly (the proton reservoir fills up)
  - The greater the reservoir the greater the pressure to form ATP
- However if there is no demand for ATP (but plenty of calories)
  - Proton gradient is too high (reservoir overfills)
  - The ETC backs up and electrons escape and form superoxide free radicals
  - Oxidize lipids and mitochondrial membranes, DNA damage
  - Necrotic cell death (necrosis)—cells swell and rupture
  - Organelles disintegrate and inflammation occurs

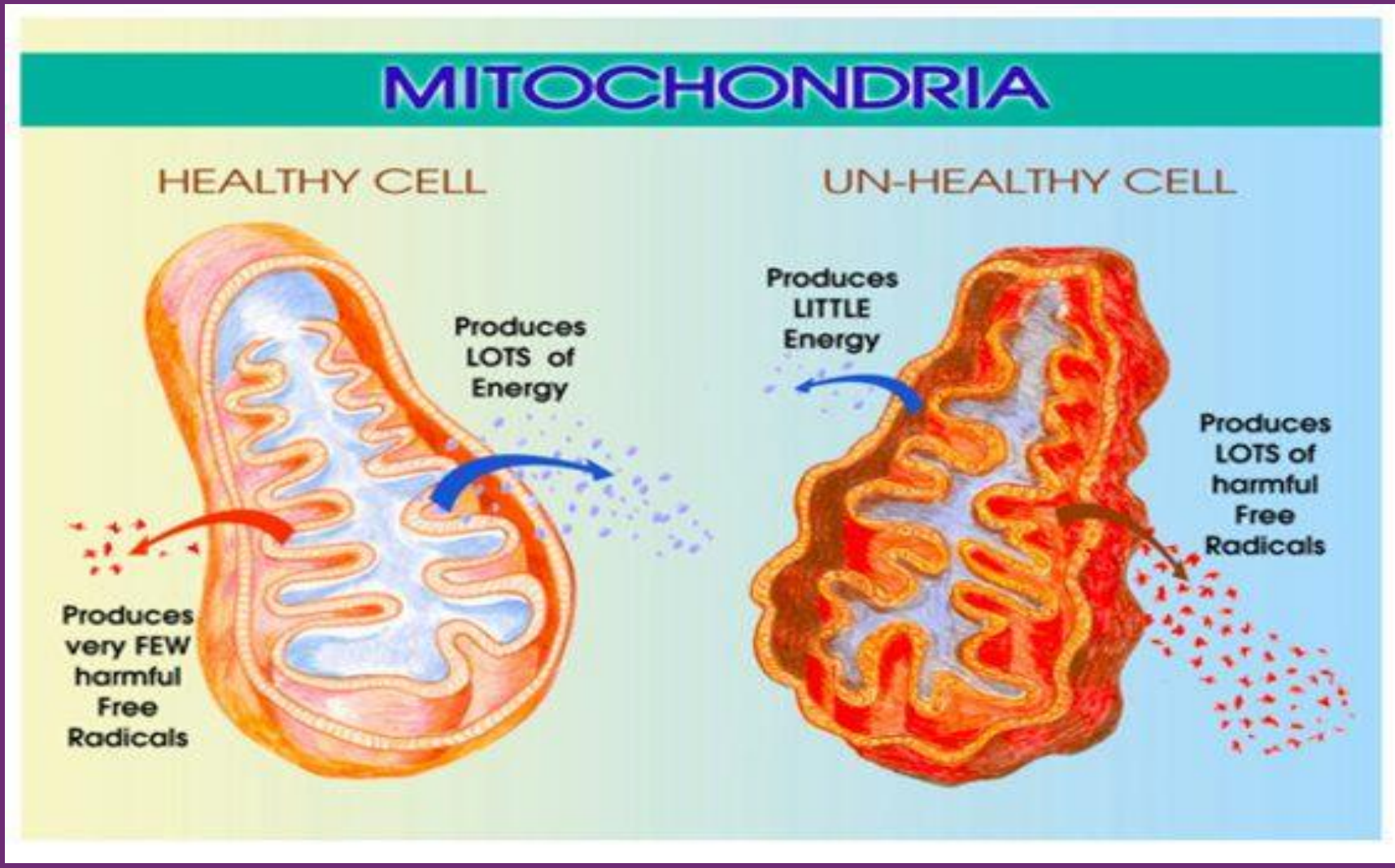
Consuming 2100—6000 calories per day **doubles risk for MCI**

Hyperglycemia

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

  Eating 2100-6000 calories a day doubles the risk of MCI

Free Radicals



Mind-Brain-Gene Feedback Loops

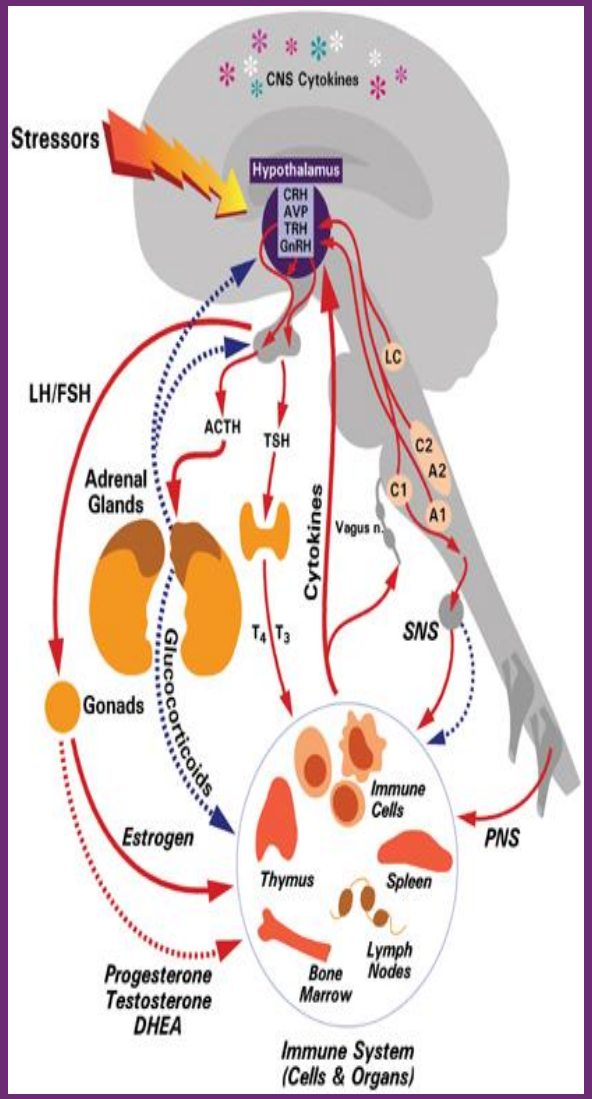
The Brain Controls the Stress Pathways

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

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

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

The hypothalamus also controls HPA stress response system



Stress

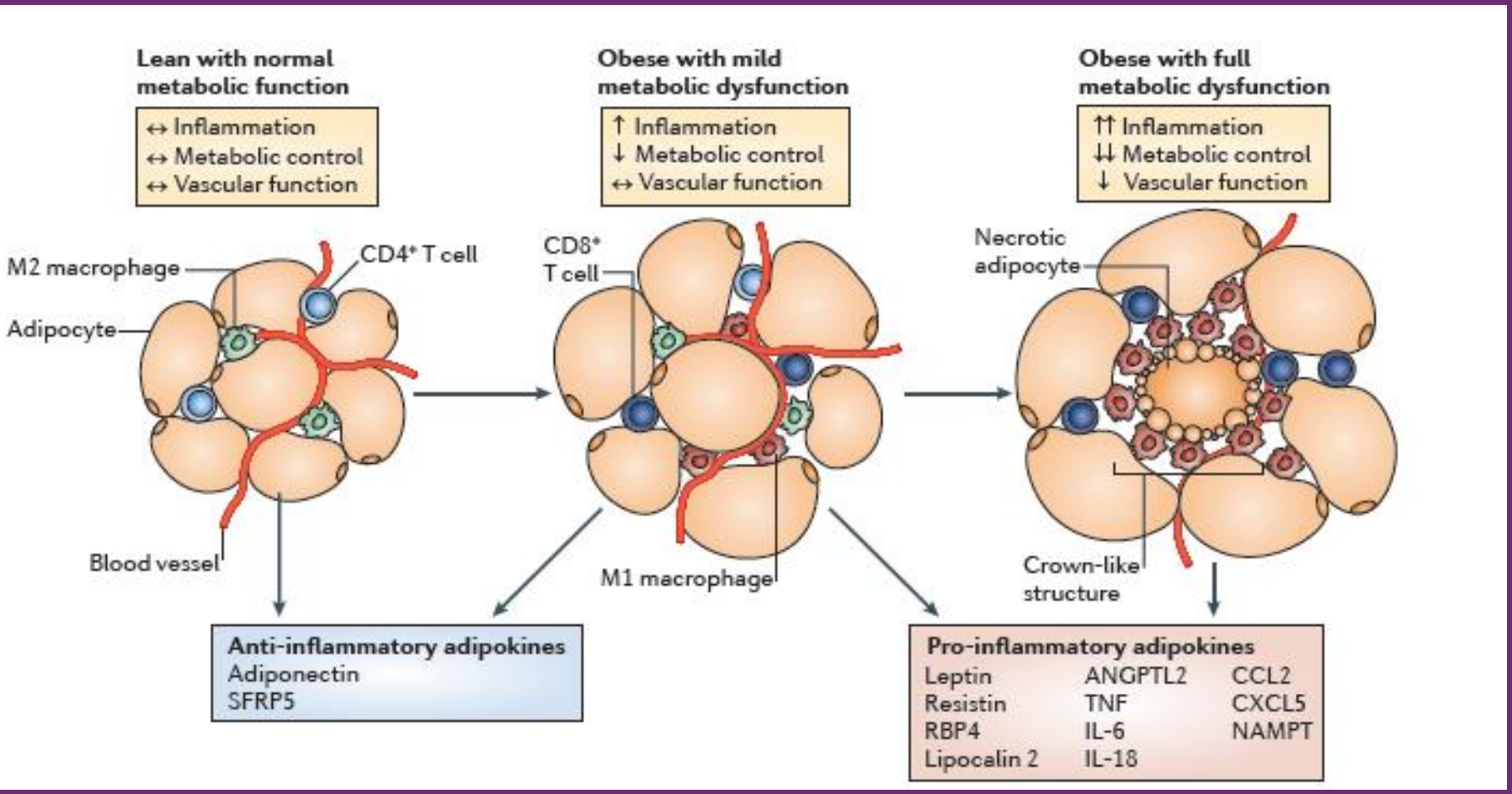
Activation of corticotropin releasing hormone (CRH):

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

Pro-inflammatory Cytokines

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

Obesity-Associated Adipose Tissue Inflammation

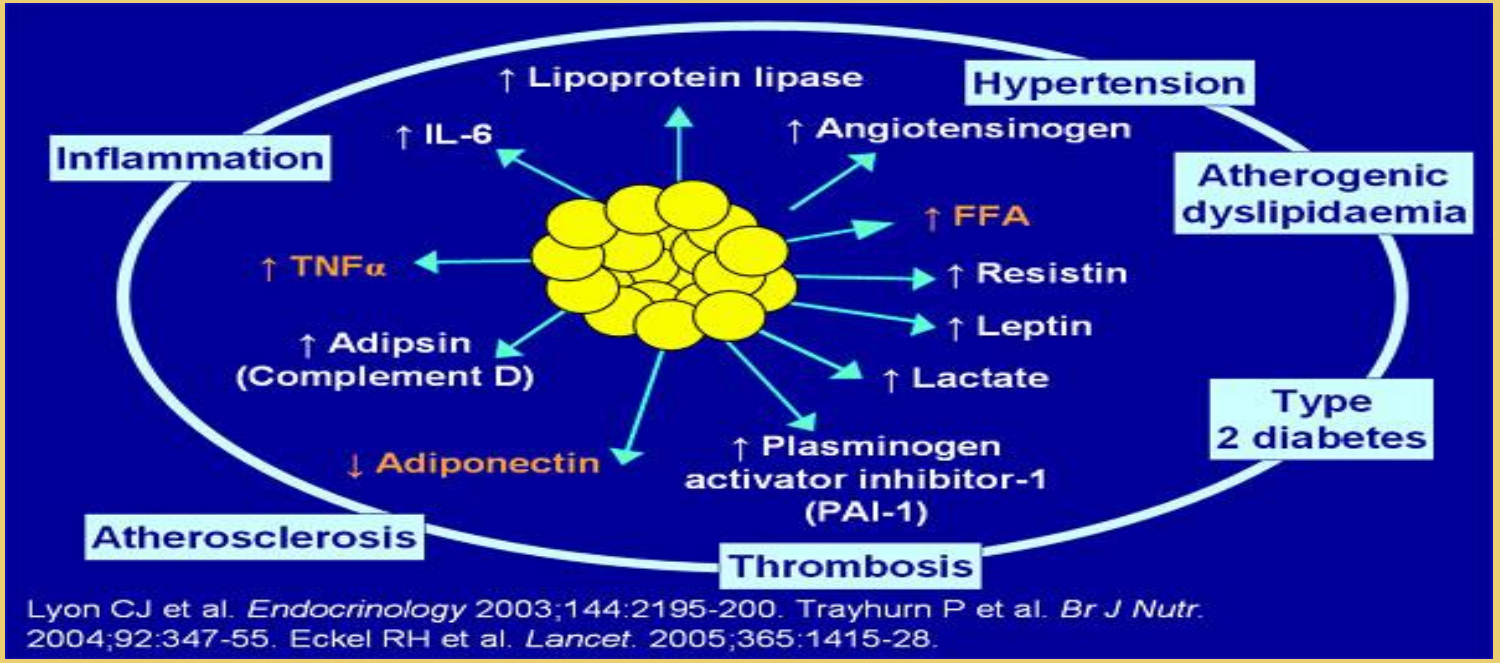


INFLAMMATION

Obesity, Inflammation, and Diabetes

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

Higher IL-6 may predict diabetes type 2

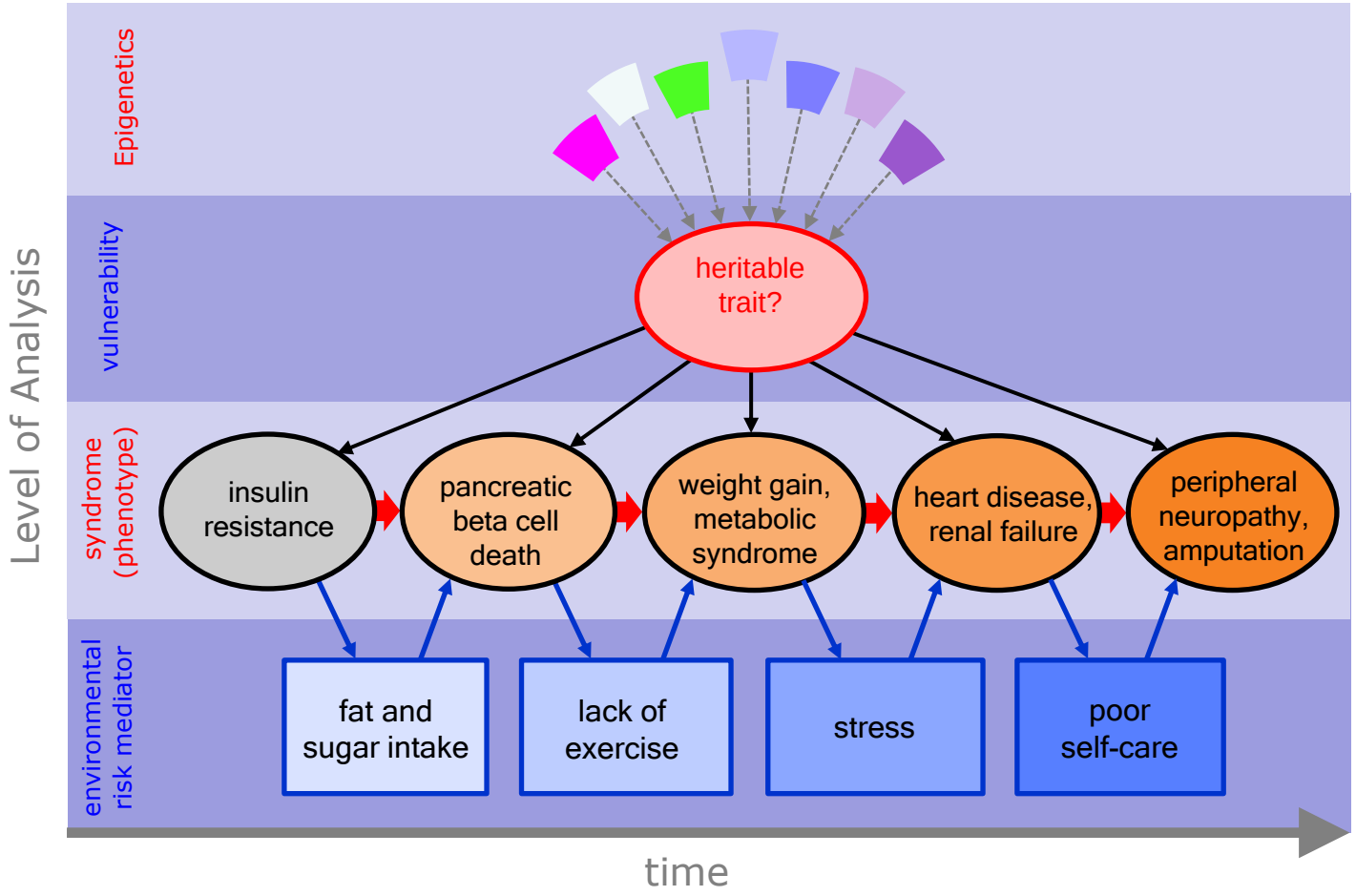


Lyon CJ et al. *Endocrinology* 2003;144:2195-200. Trayhurn P et al. *Br J Nutr.* 2004;92:347-55. Eckel RH et al. *Lancet*. 2005;365:1415-28.

Diabetes and Psychological Disorders

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

Ontogenesis of Type II Diabetes

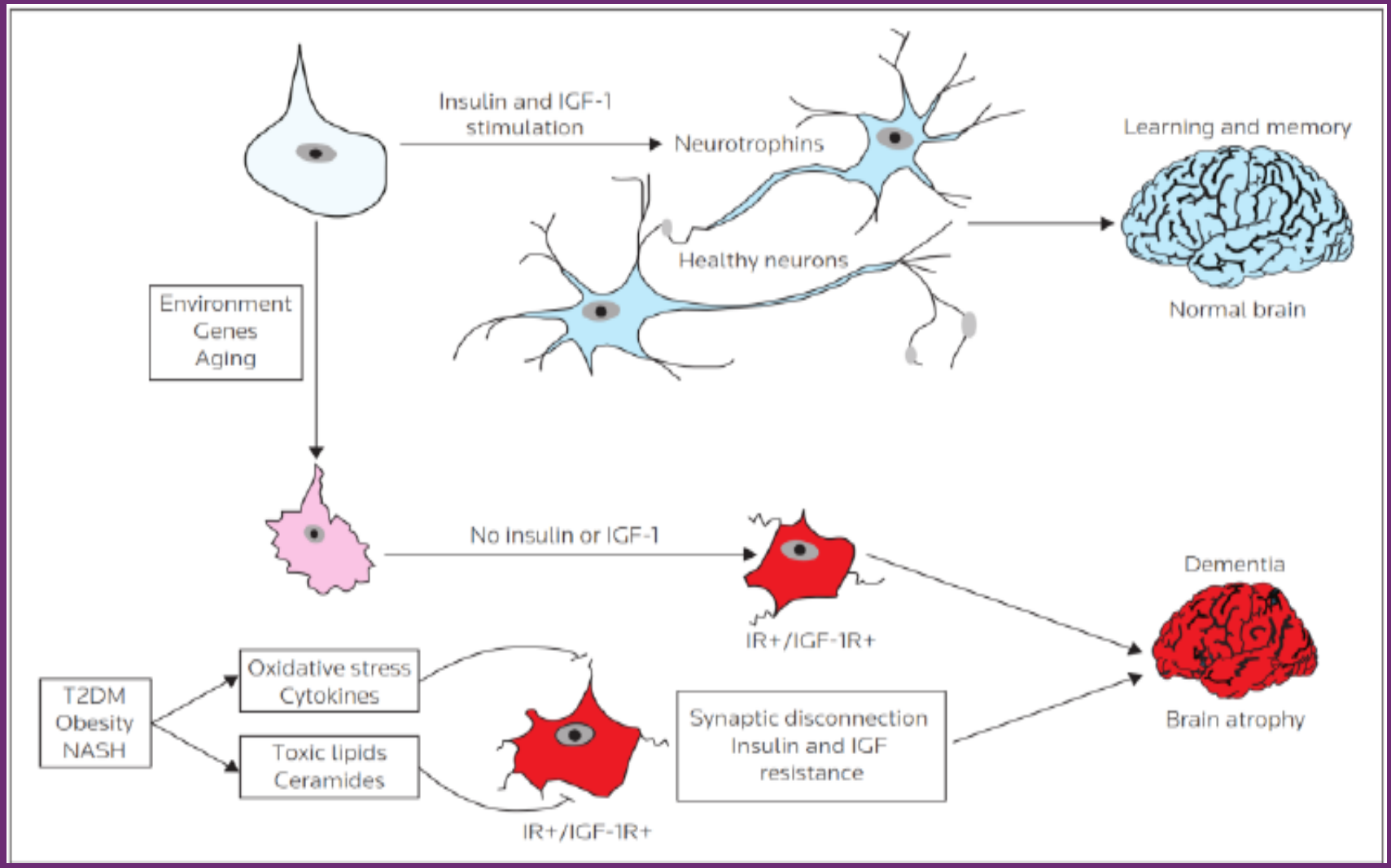


LaSalle et al., 2005

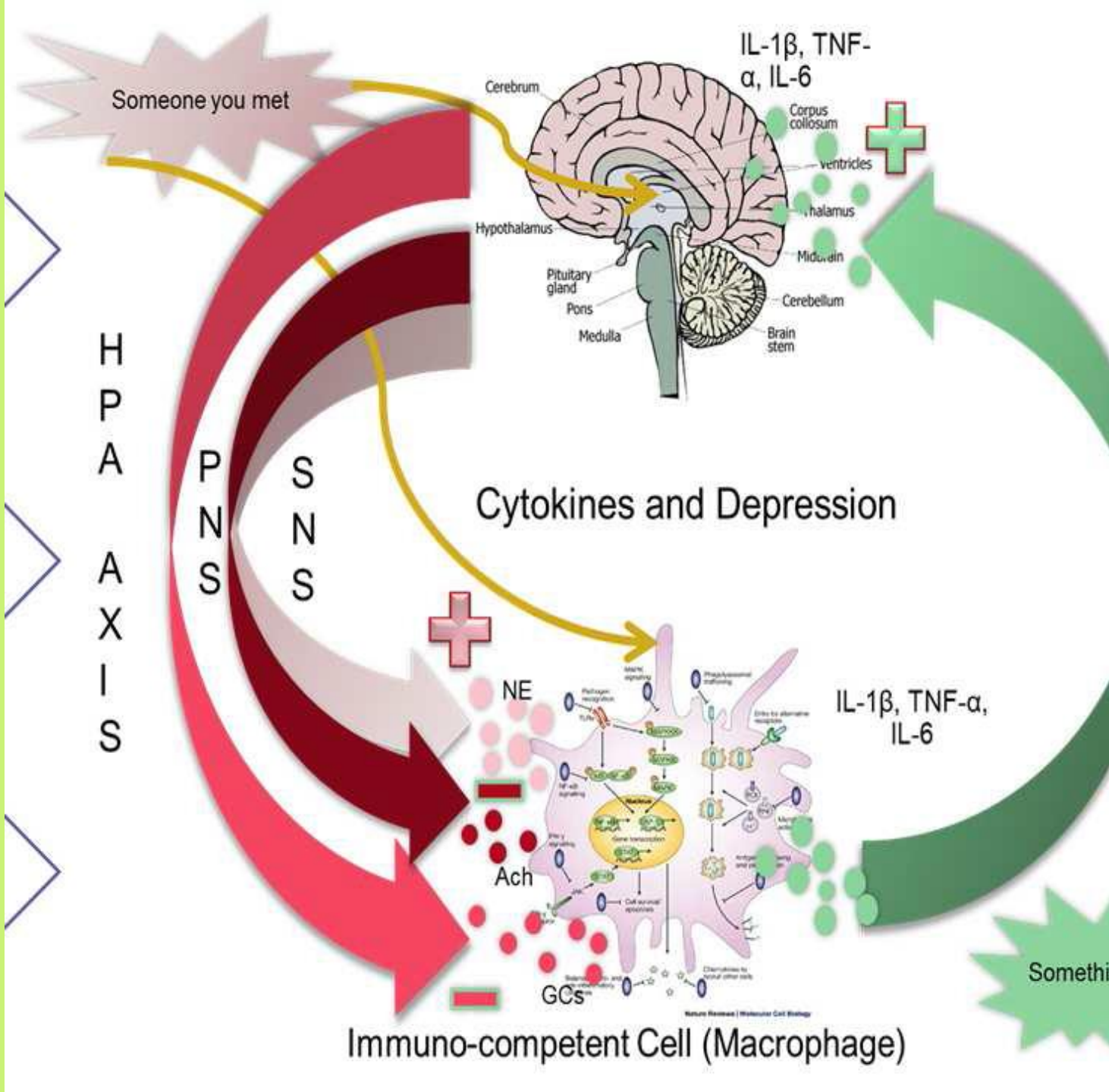
The PNI of Social Medicine

- ↓ 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)

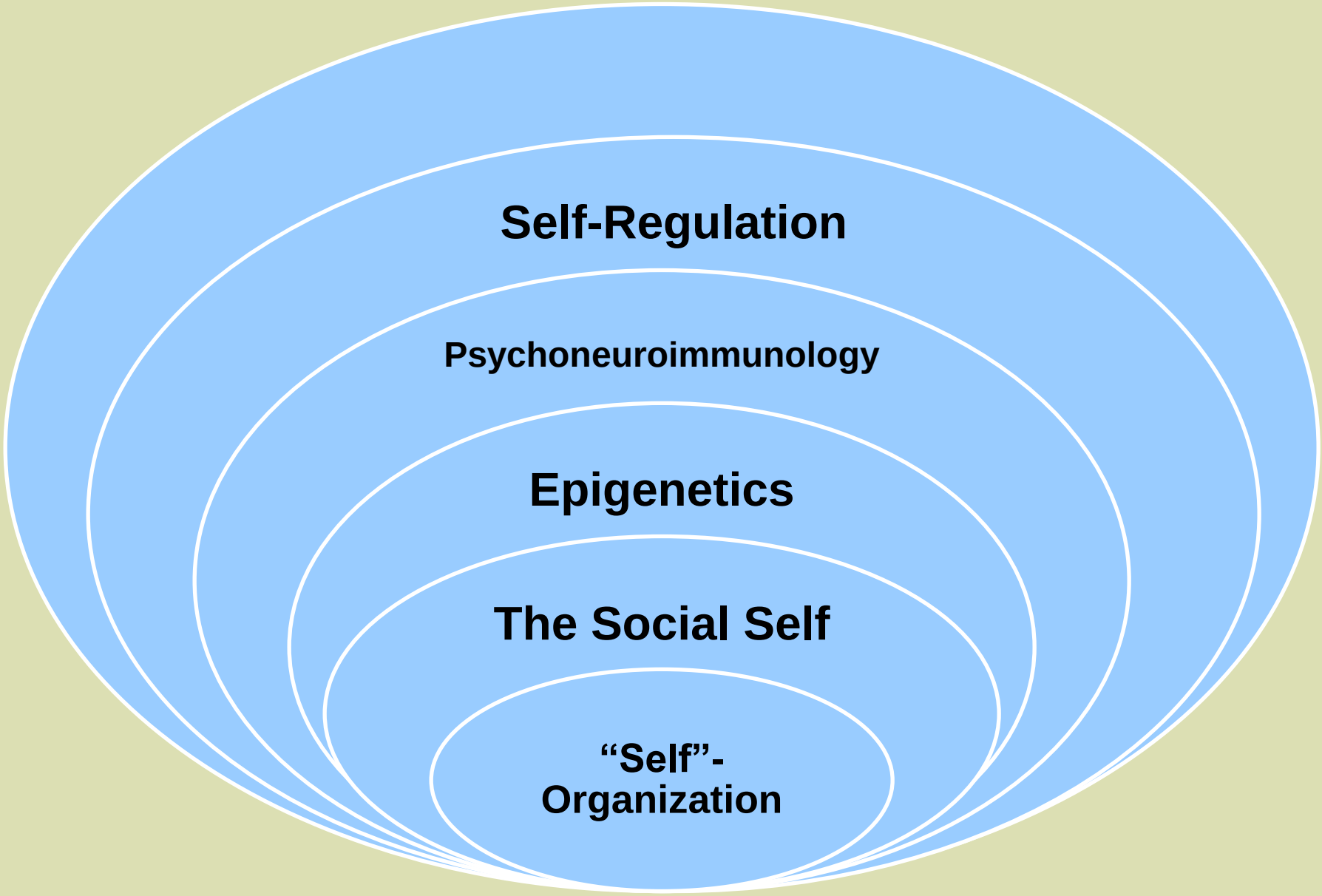
Diabetes and Brain Shrinkage



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



Mind-Brain-Gene Feedback Loops



Self-Regulation Factors

- **Social**
- **Exercise**
- **Education**
- **Diet**
- **Sleep**

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





Socialise

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

Exercise

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

Education

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

Diet

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

Sleep

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

…AND MUCH MORE…

SEEDS Epigenetics

- Fruits, vegetables, --polyphenols found to epigenetically reduce stress and depression by modulating inflammatory responses and synaptic plasticity in the brains of those with depression.
- Epigenetic changes increase inflammation across tissues in response to sleep loss. --that the adipose tissue is attempting to increase its capacity to store fat following sleep loss
- Physical inactivity deactivates genes associated with inflammation and activates genes associated with lower inflammation
  - Muscle movement activates anti-inflammatory genes

Mind-Brain-Gene Spectrum

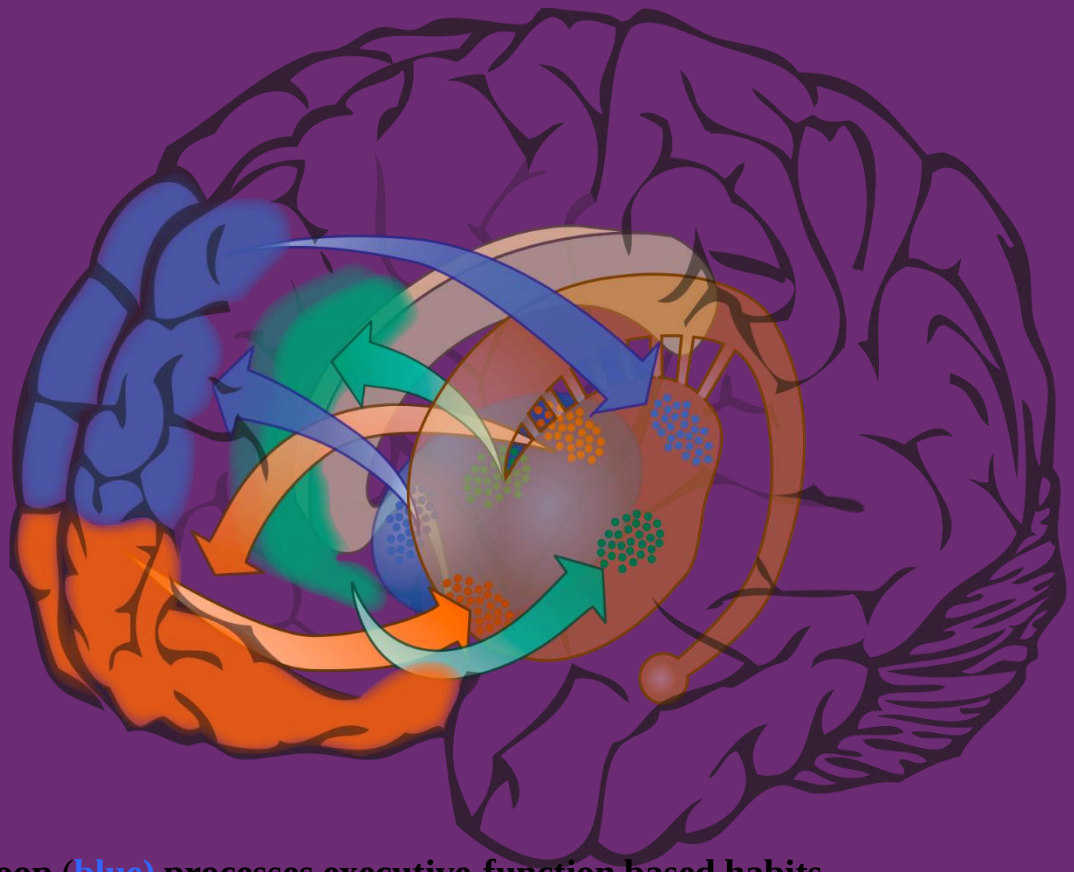
Wanting vs. Liking

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

The Middle Path

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

The Habit Circuits

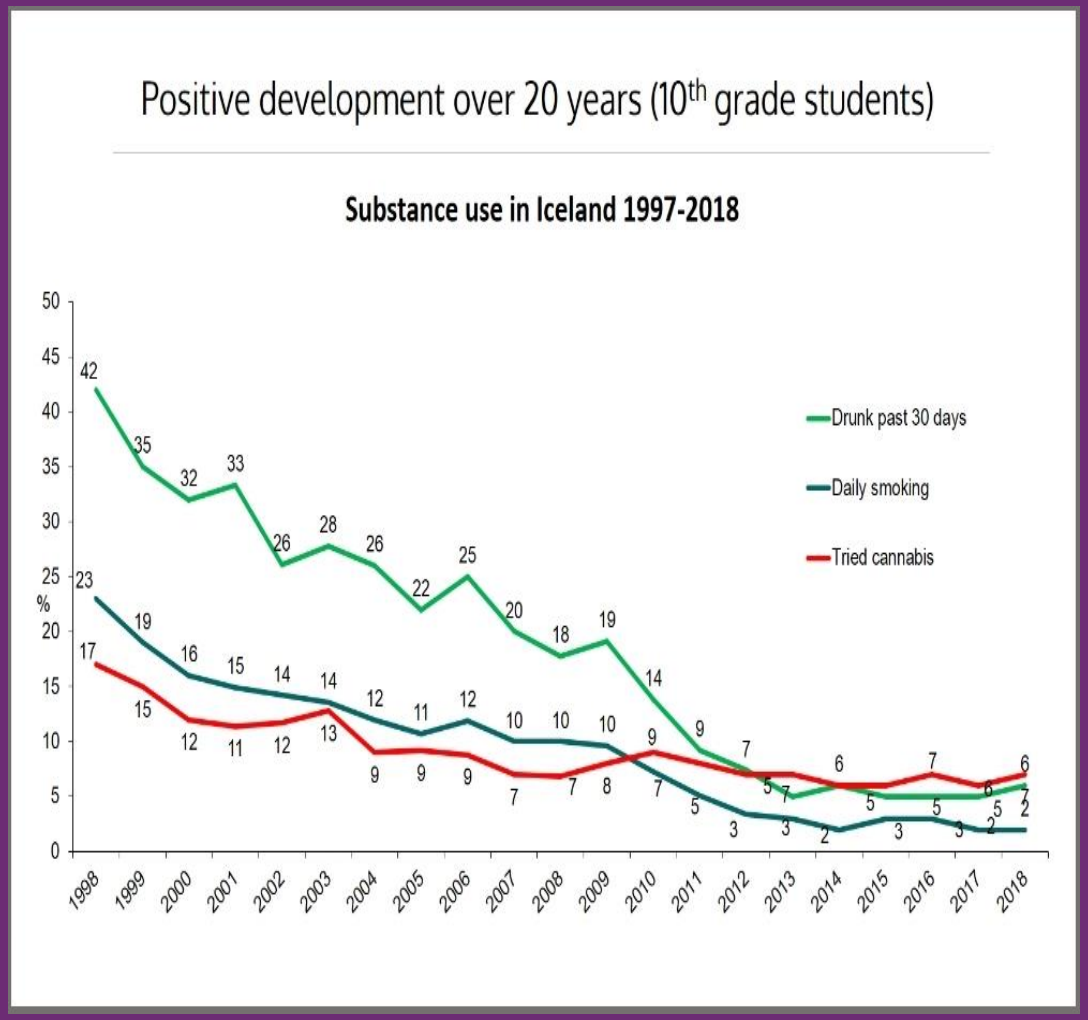


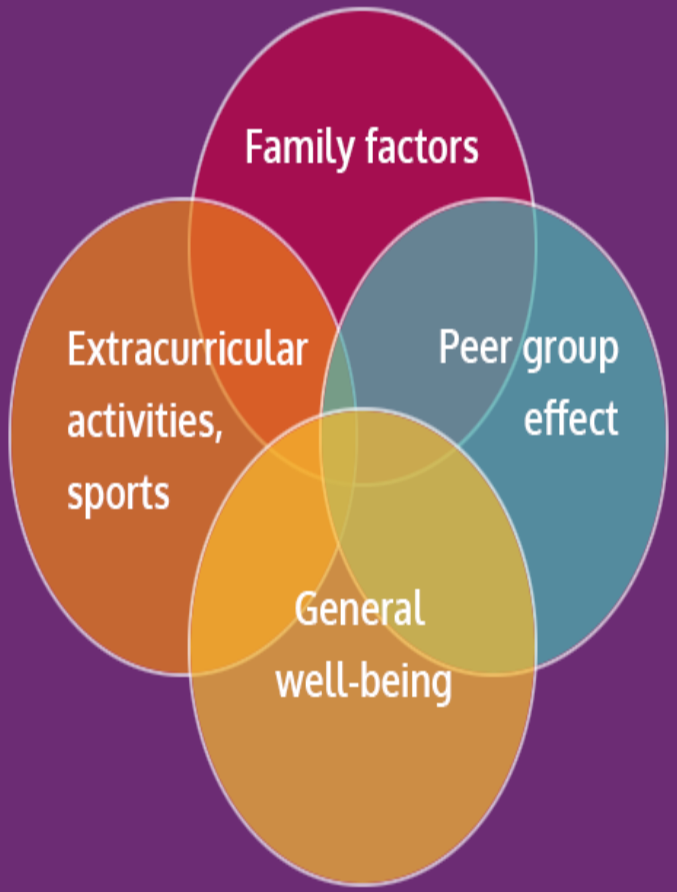
The upper loop (blue) processes executive-function based habits.

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

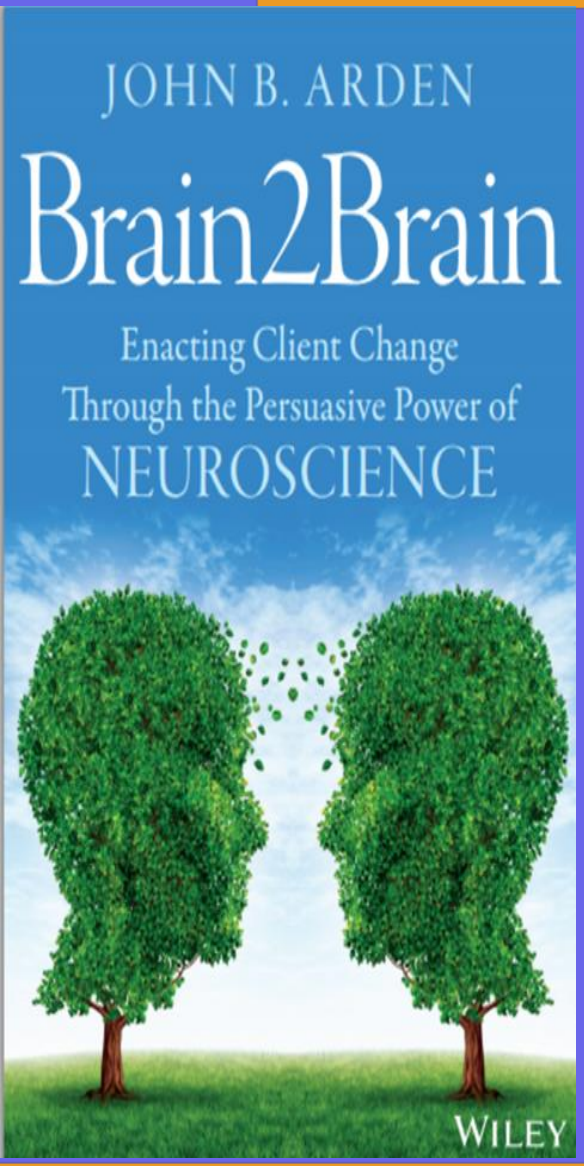
The lower loop (orange) processes social-emotional and reward-based habits

The Iceland Project





References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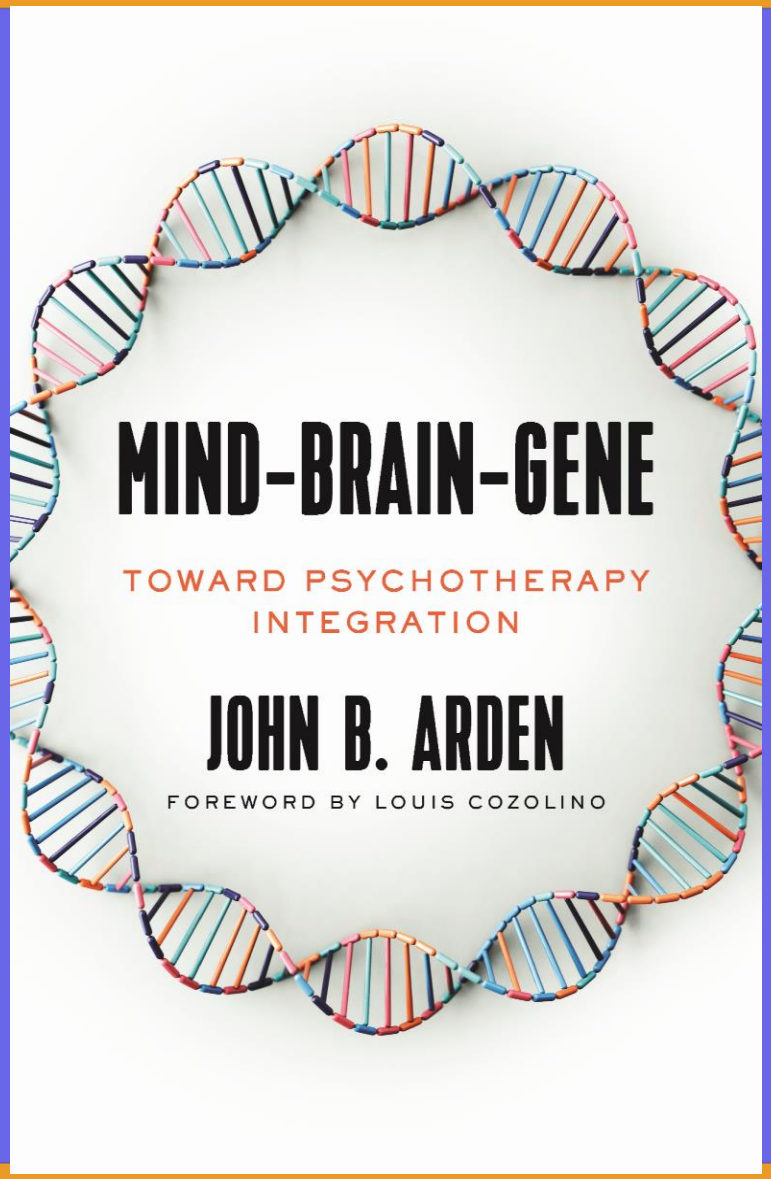
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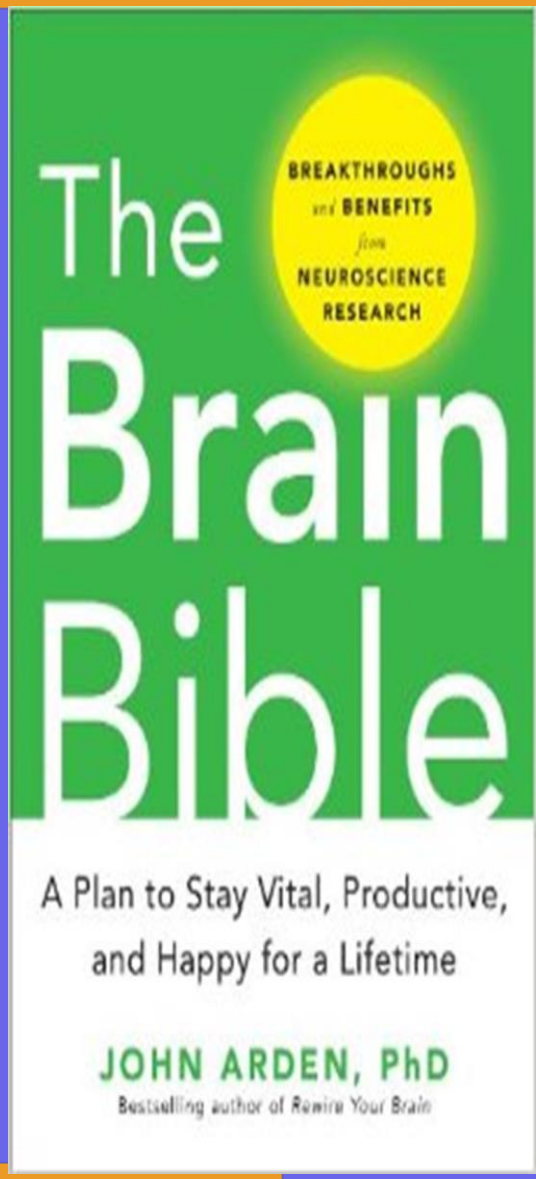
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drjohnarden@gmail.com

www.drjohnarden.com