

Neuroplasticity in the Aging Brain

Jack B. Nitschke

Departments of Psychiatry and Psychology
University of Wisconsin-Madison

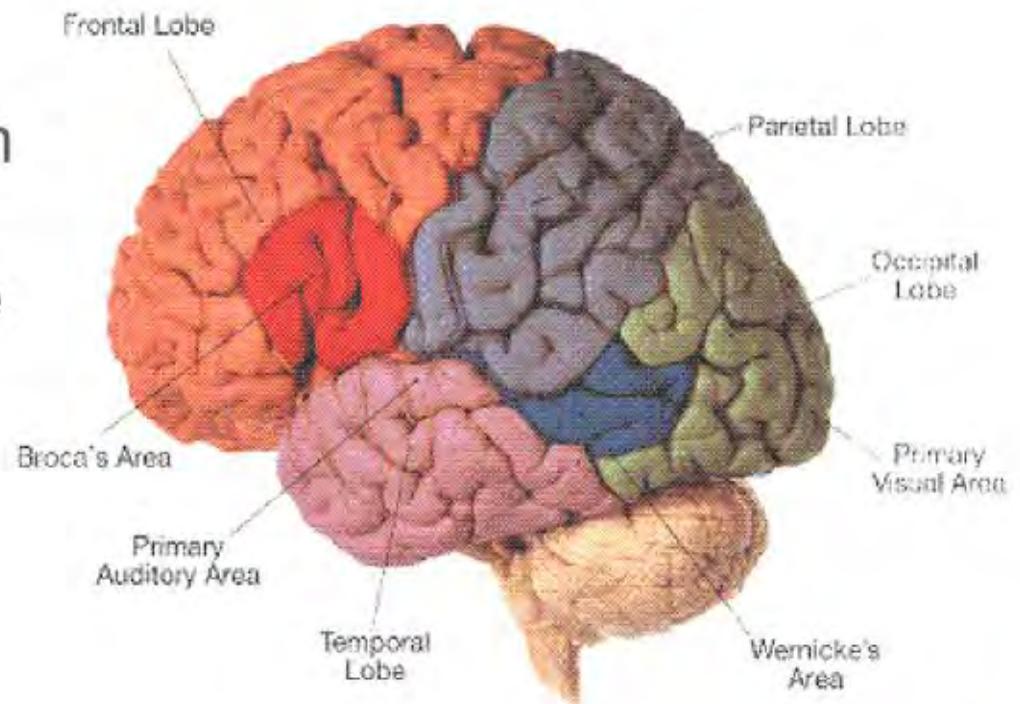


The Older, More Mature Brain



Normal Changes in the Healthy Aging Brain

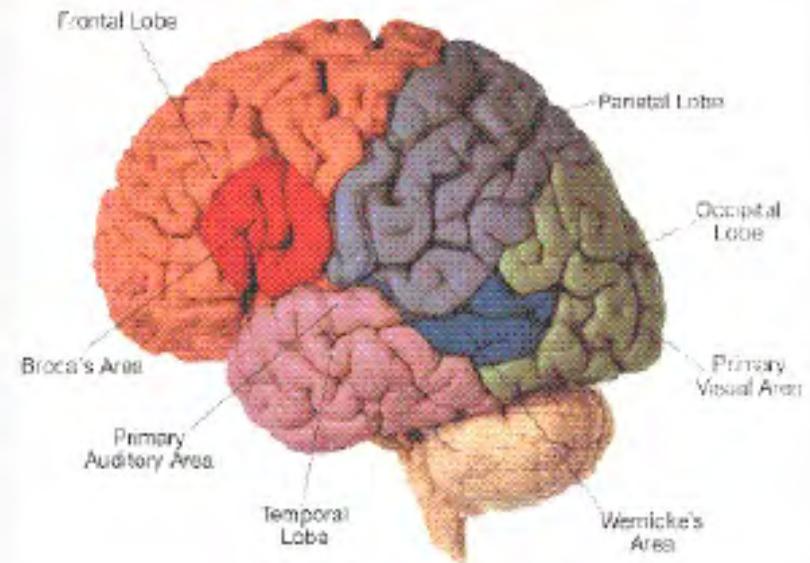
- Prefrontal cortex and the hippocampus will start shrinking.
- Communication between neurons and neurotransmitters will be reduced.
- Blood flow can be reduced because arteries will start to narrow.



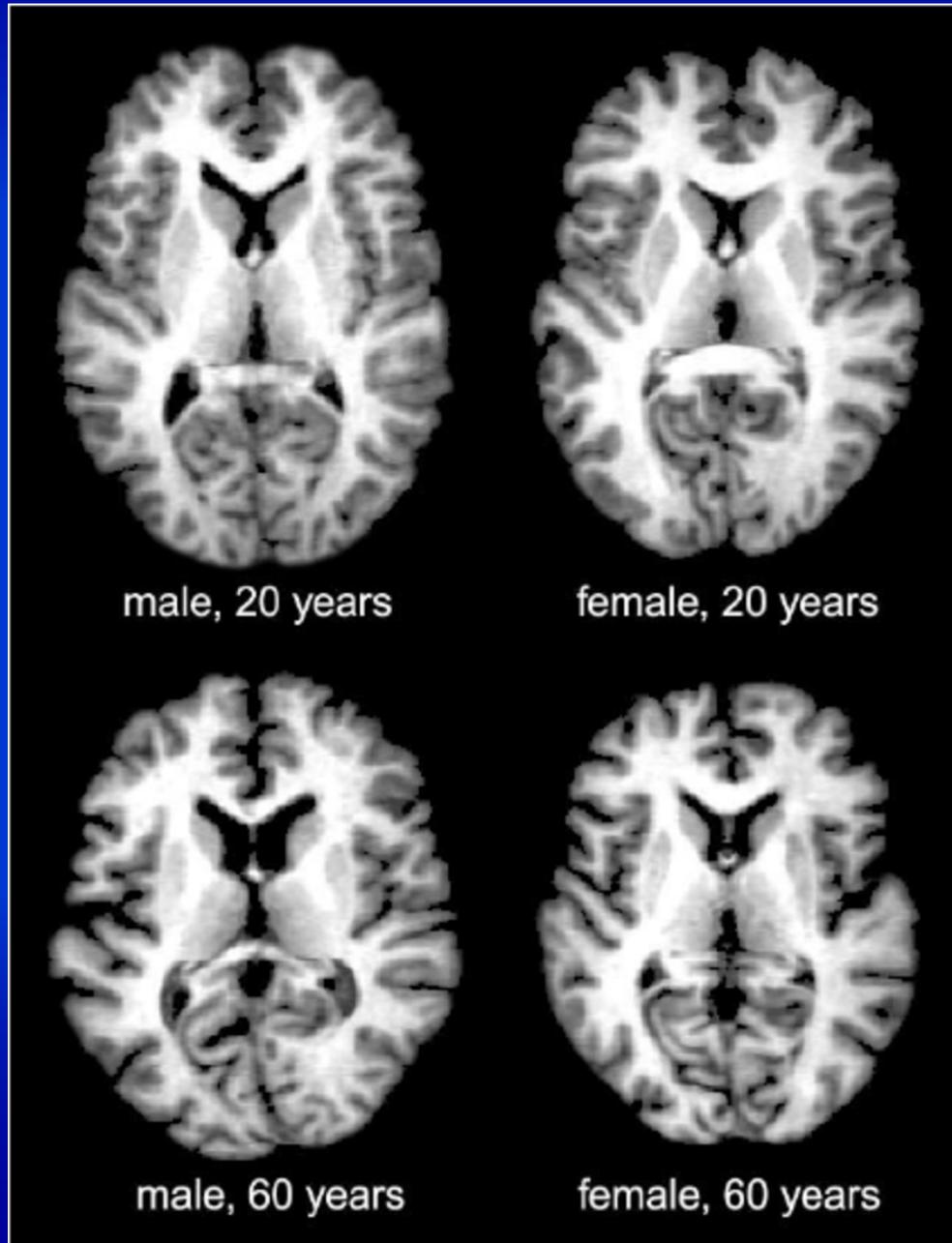
<http://www.nia.nih.gov/alzheimers/publication/pat-t-1-basics-healthy-brain/changing-brain-healthy-aging>

Symptoms of normal brain aging

- Difficulty recalling a word or name
- Trouble understanding the “jabbering” of a child or the “mumbled” conversation of a friend when in background noise.
- Difficulty remembering verbal instructions
- Slower mental processing
- Keeping up with quick firing speech



The Older, More Mature Brain



Teenage Brain



The Older Brain When Cognitive Loss

YOUNG VERSUS OLD BRAIN



Healthy
25-year-old

Loss of
hippocampus

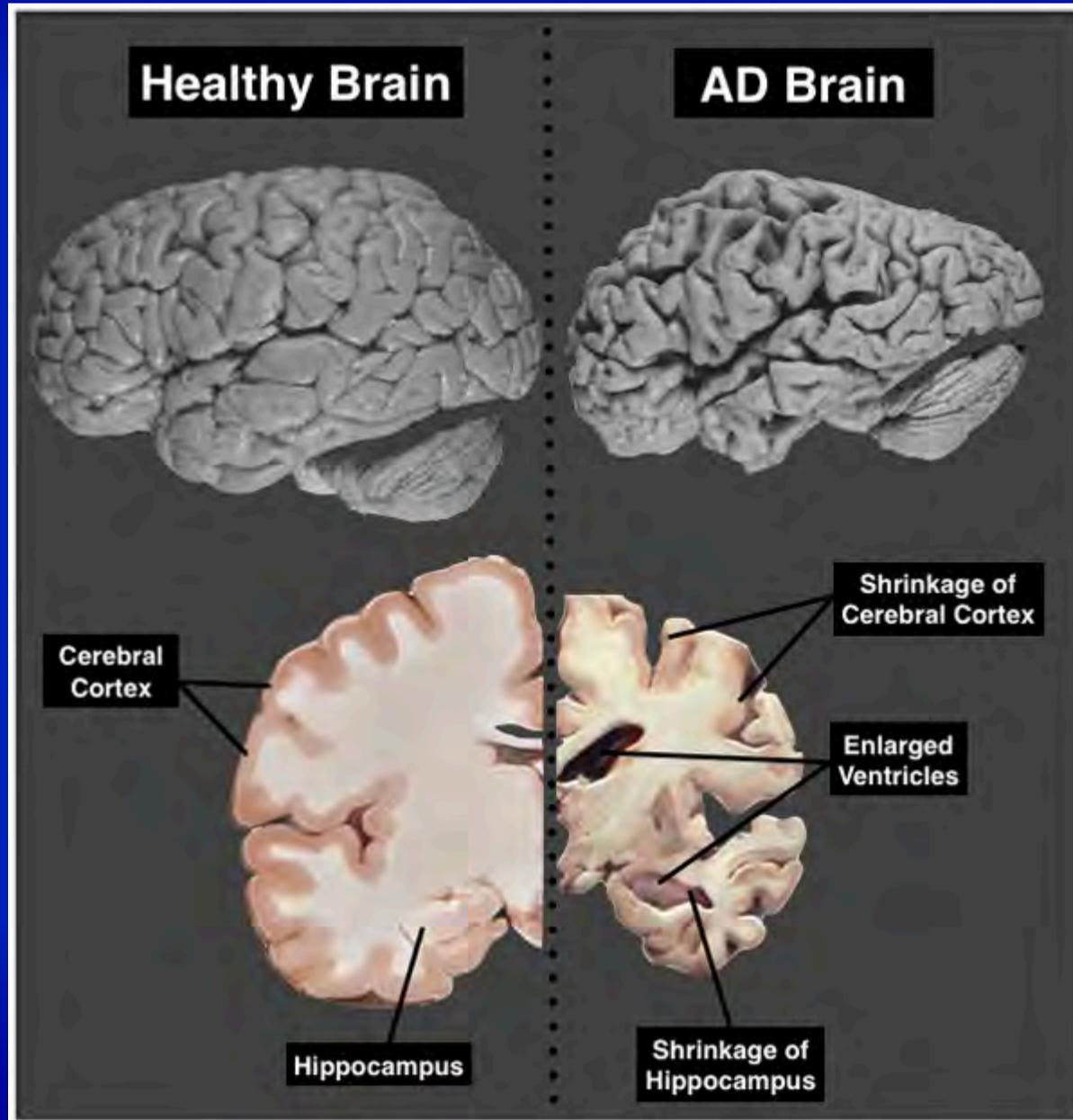
axons

gyri

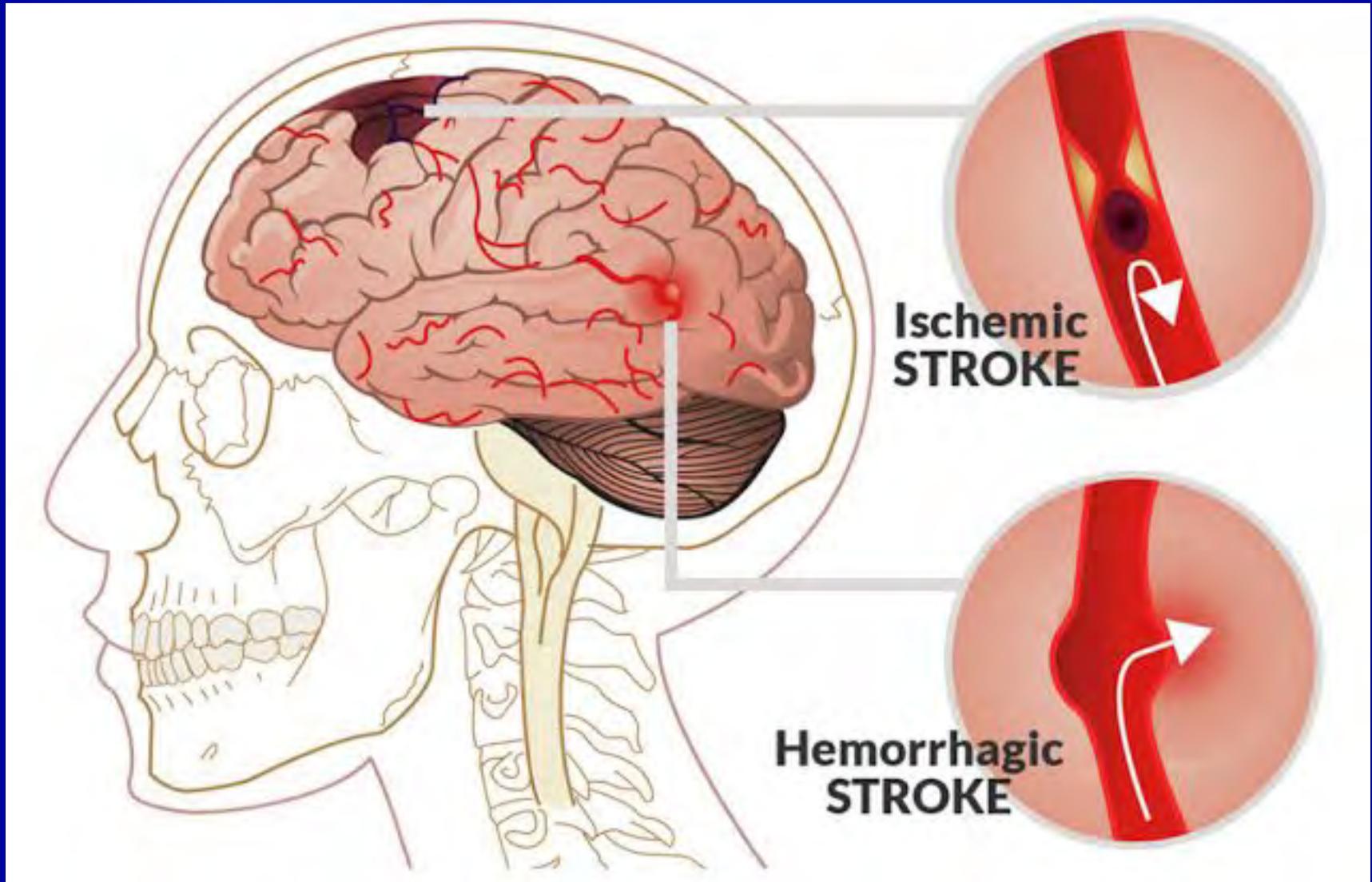


80-year-old with
cognitive losses

The Older Brain With Alzheimer's



Stroke

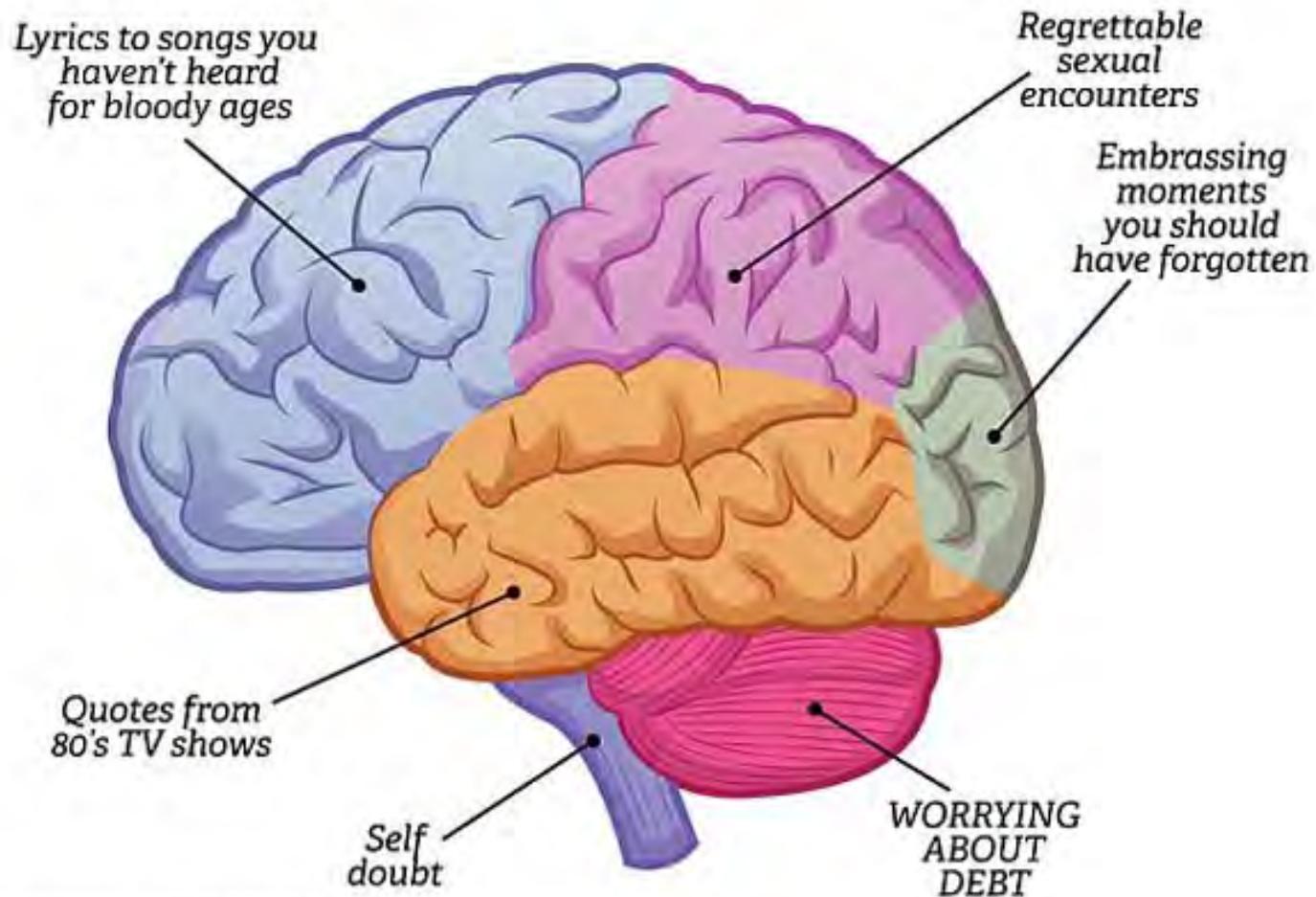


Depression



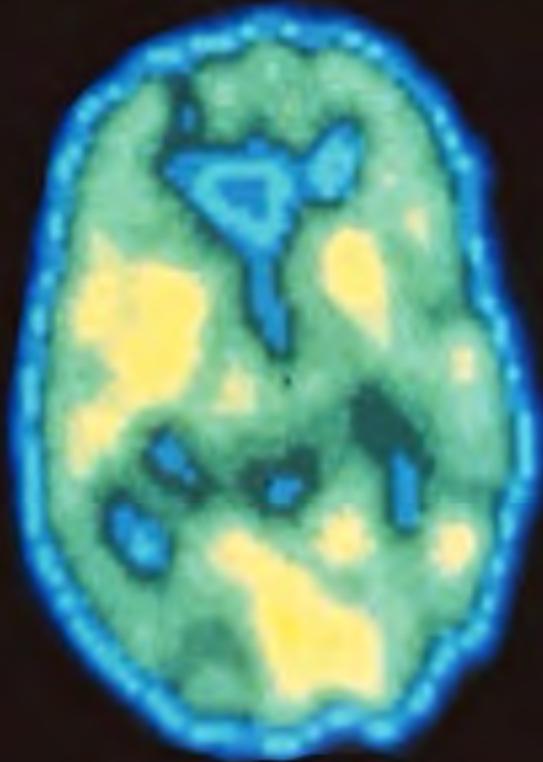
Depression

The average brain of a depressive

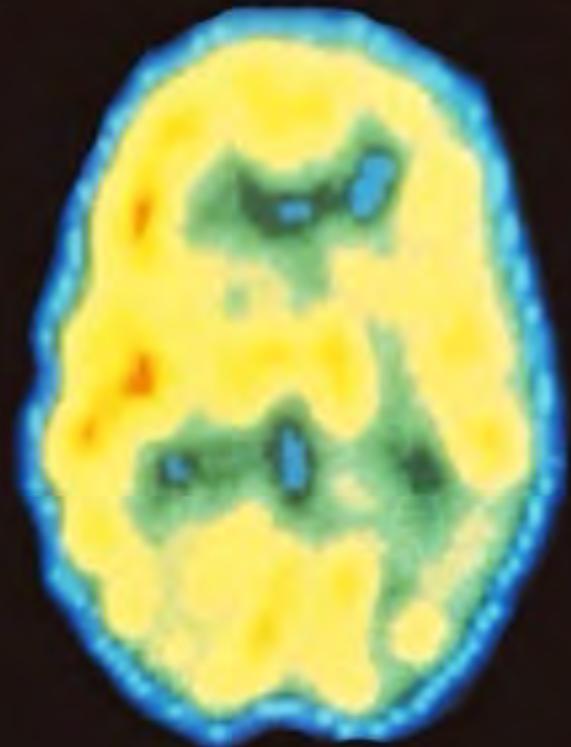


Depression

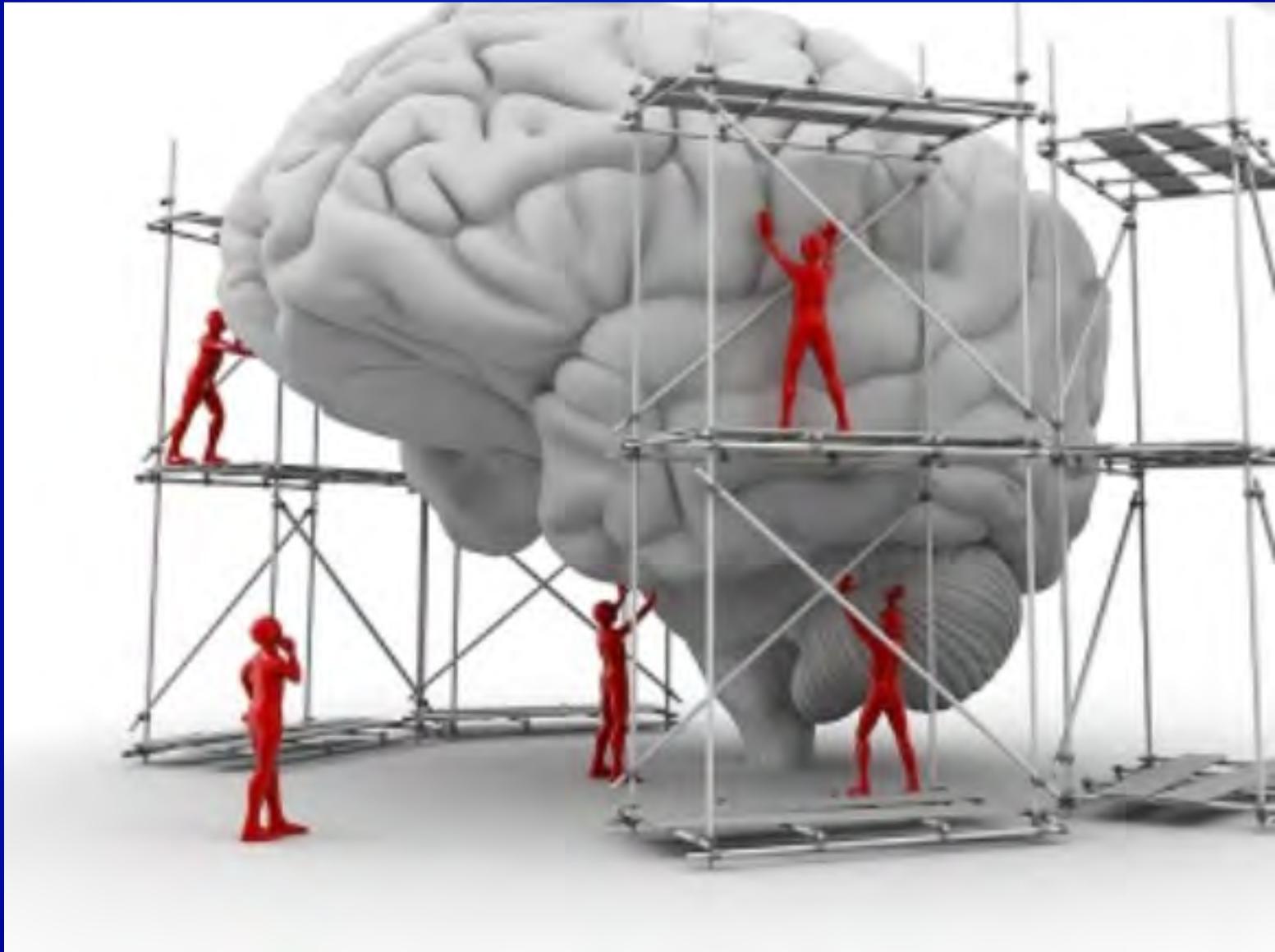
Depressed



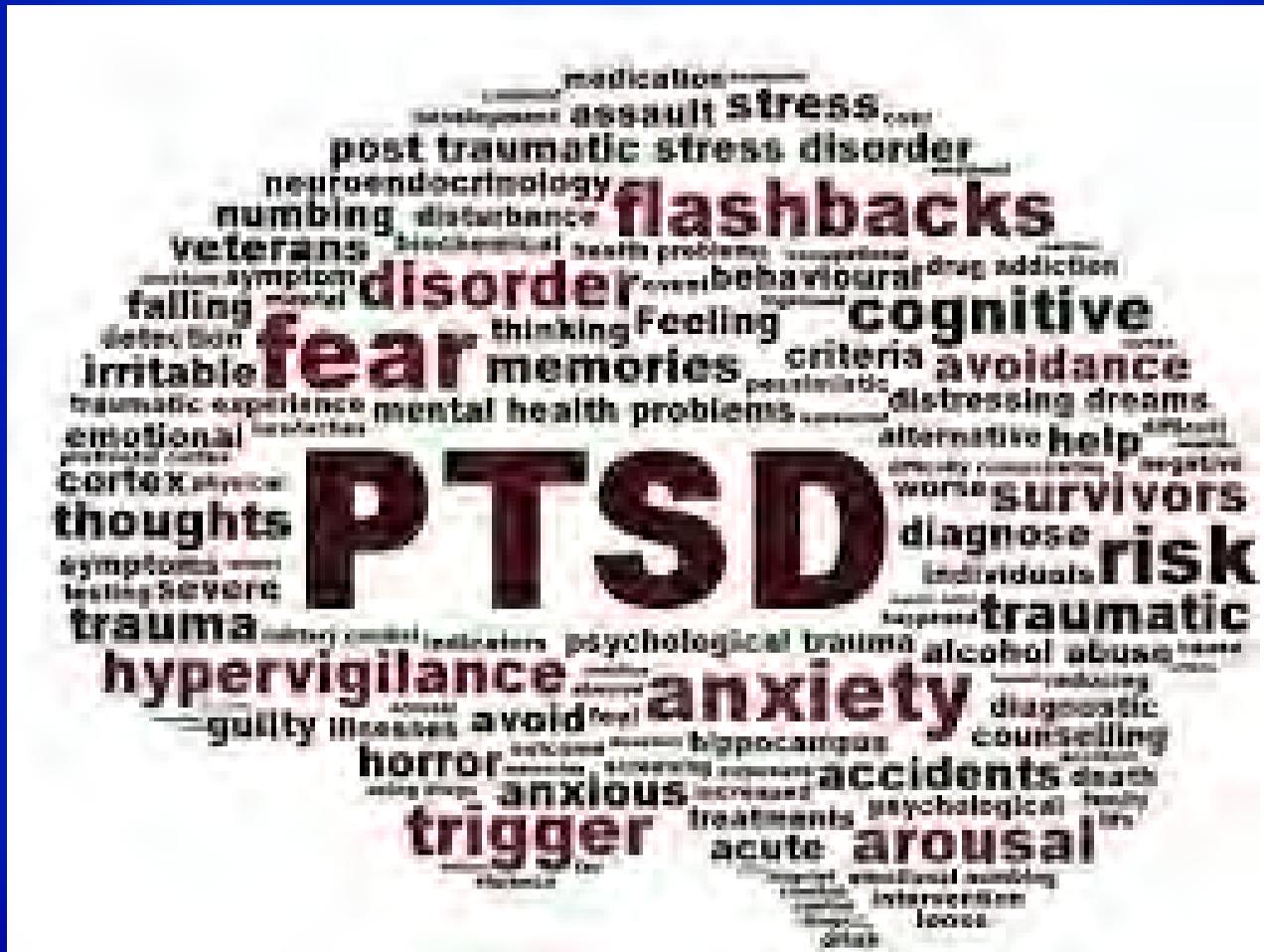
Not depressed



Depression – Psychotherapy



PTSD



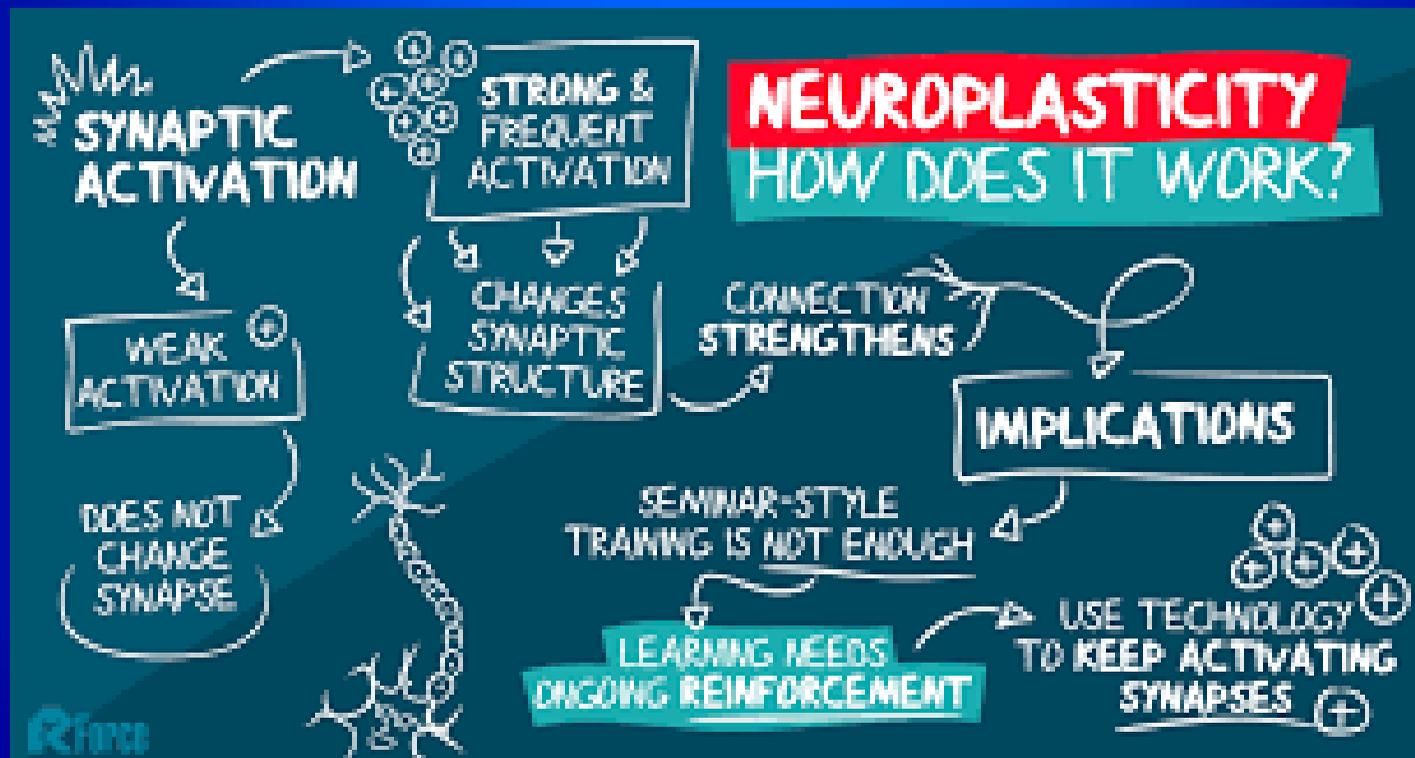
**Your brain helps you get really
good at whatever you spend
your time doing.**

The Aging Brain and Mental Health

- **Neural connections that support bad stuff (problematic thinking and behaviors)**
 - Anxiety, panic, worries, phobias, obsessions, avoidance
 - Depression, self-critical thoughts, suicidal thoughts
 - PTSD, self-blame, safety concerns, trust issues
 - Anger, irritability, outbursts, abusive behavior
 - Substance use
 - Practice/repetition strengthens these neural connections
 - Same brain mechanisms as in learning math, chess, basketball, piano, or sudoku
- **The *bad news* is that these neural connections do not go away, even if they are no longer “practiced”**
- **The *good news* is **neuroplasticity****
 - Psychotherapy, caretakers, and nursing staff can help you build neural connections that support accurate thinking and adaptive behaviors
 - Same brain mechanisms as above

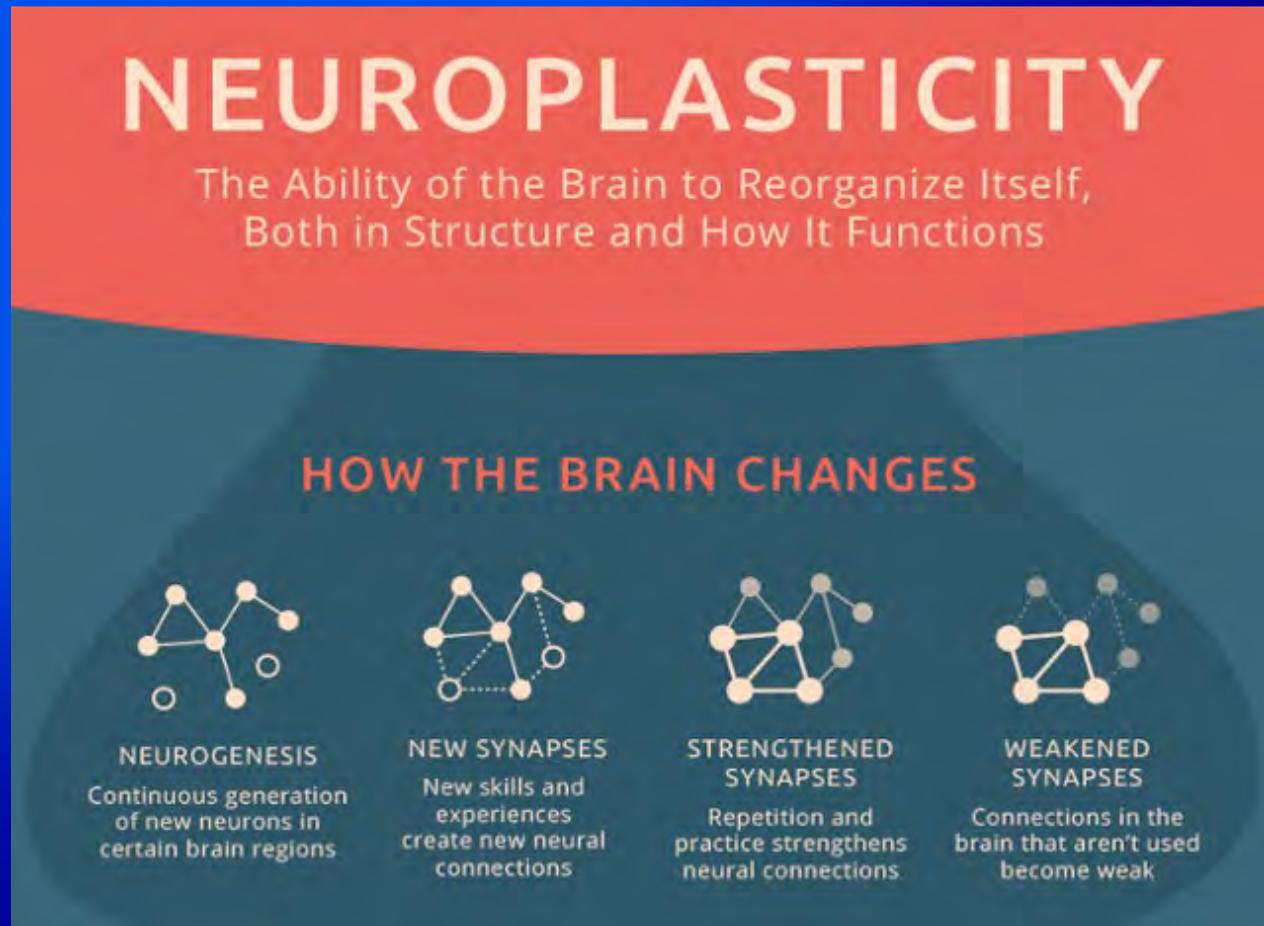
The Aging Brain and Mental Health

- Neural connections that support bad stuff (problematic thinking and behaviors)
- The *bad news* is that these neural connections do not go away, even if they are no longer “practiced”
- The *good news* is **neuroplasticity**



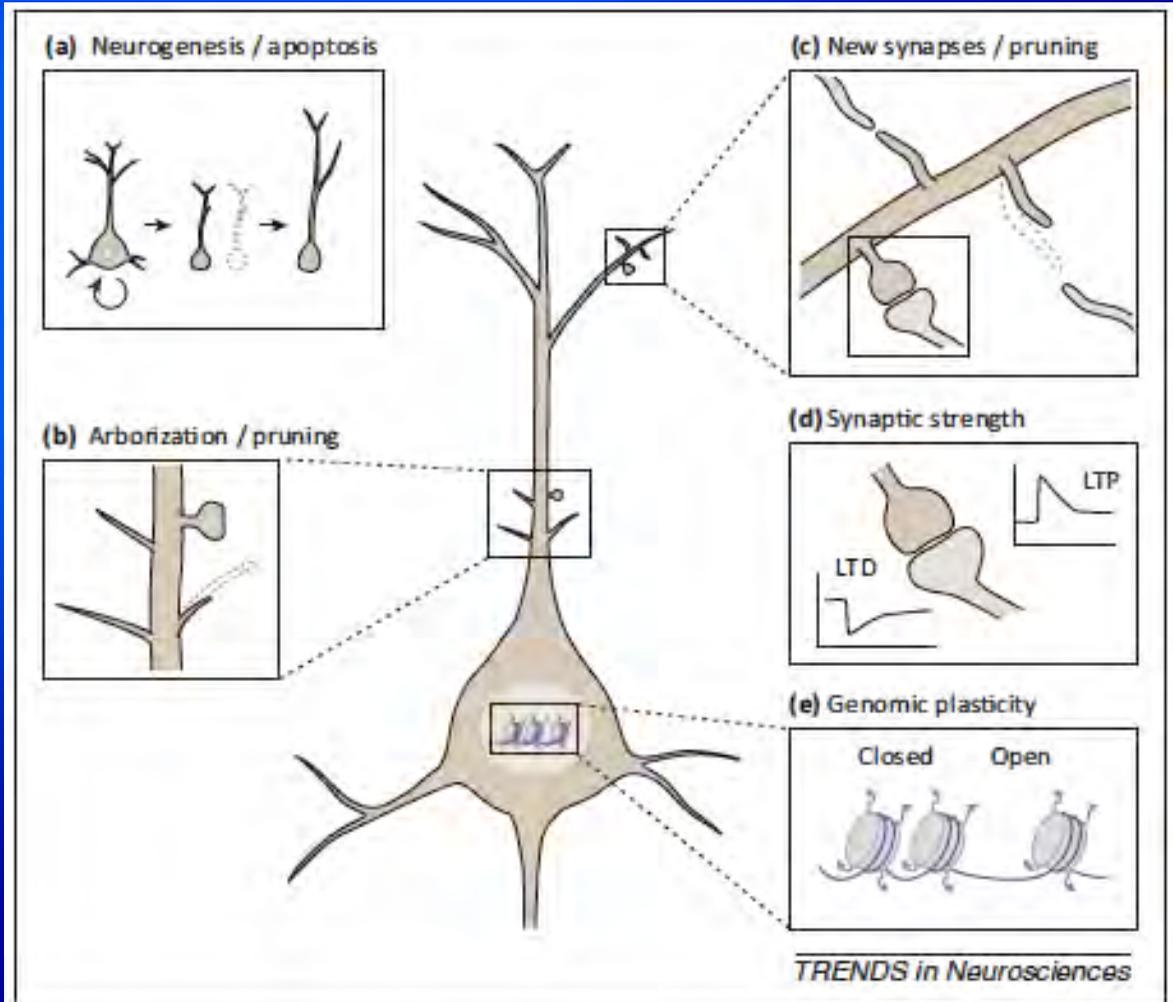
Neuroplasticity

- **Neuroplasticity – experience-dependent changes in the structure and function of neuronal networks**
- **The mechanisms of neuroplasticity**
 - **Neurogenesis**
 - **Arborization**
 - **Synaptogenesis**
 - **Synaptic strength**
 - **Genomic plasticity**
 - **Role of sleep**

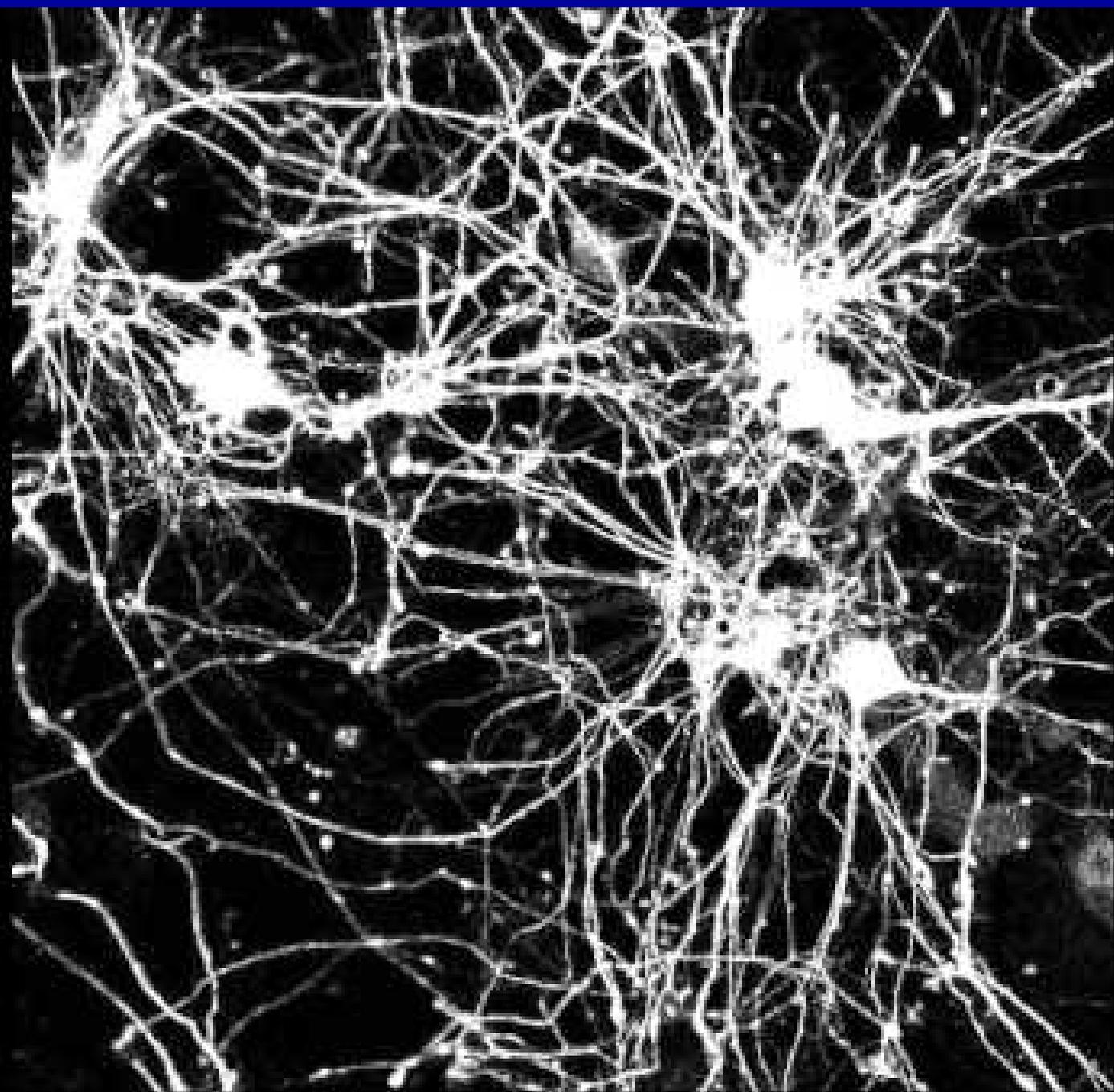


Neuroplasticity

- Neuroplasticity – experience-dependent changes in the structure and function of neuronal networks
- The mechanisms of neuroplasticity
 - Neurogenesis
 - Arborization
 - Synaptogenesis
 - Synaptic strength
 - Genomic plasticity
 - Role of sleep



RECORDED WITH
SCREENCAST  MATIC



9 DIV

73 Hours

Neurogenesis

- Neurogenesis – the birth of new neurons
- Adult neurogenesis – the birth of new neurons in adulthood
 - In most mammals: hippocampus and olfactory bulb
 - In humans: hippocampus and striatum

NEUROPLASTICITY

The Ability of the Brain to Reorganize Itself,
Both in Structure and How It Functions

HOW THE BRAIN CHANGES



NEUROGENESIS

Continuous generation
of new neurons in
certain brain regions



NEW SYNAPSES

New skills and
experiences
create new neural
connections



STRENGTHENED SYNAPSES

Repetition and
practice strengthens
neural connections

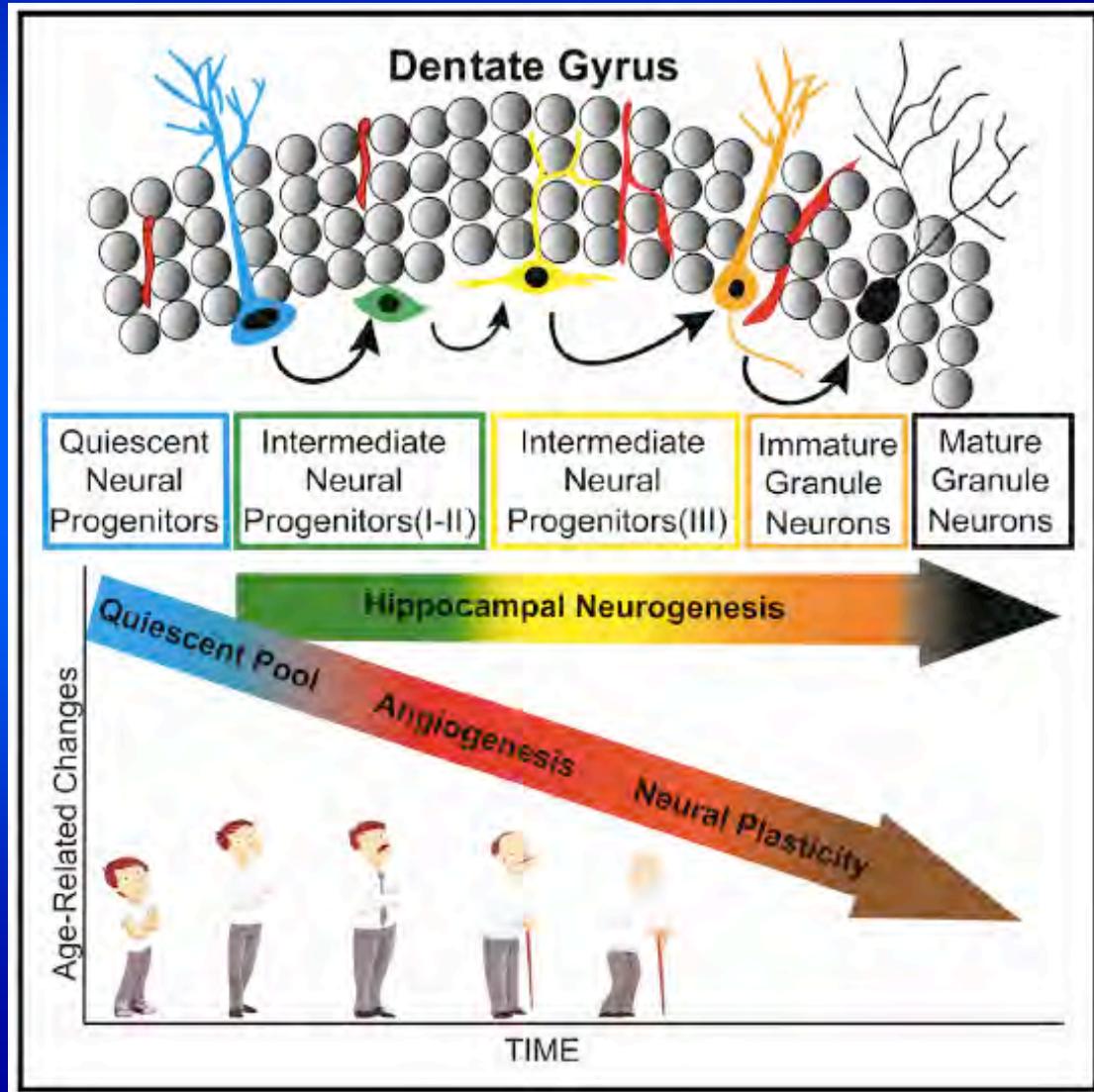


WEAKENED SYNAPSES

Connections in the
brain that aren't used
become weak

Adult Neurogenesis

- 700 new neurons in each hippocampus every day
- Documented from adolescence through 70's
- Stimulated by enriched environments, exercise, learning, antidepressant drugs, and electroconvulsive shock treatment
- Inhibited by chronic stress and aging



Ready for the punchline?

Your brain helps you get really good at whatever you spend your time doing.

“I used my neuroplasticity, and things got better.”

-Anonymous patient

Neural Mechanisms of Clinical Depression

- **There are neural connections that support clinical depression**
 - **Once someone has a Major Depressive Episode, being depressed most of the day nearly every day for at least 2 weeks straight, that person has robust neural connections supporting that**
 - **Even 2 weeks is already a lot of practice and repetition**
 - **The more they are depressed, the more their brains strengthen the neural connections supporting the many facets of depression**
 - **People with recurrent Major Depressive Disorder and those with Persistent Depressive Disorder are **Olympians of depression****
 - **They have often logged thousands of hours with the constellation of depression symptoms (lot of practice and repetition with depressed mood, anhedonia, sleep and appetite disturbance, self-critical thoughts, feelings of worthlessness, fatigue and low energy, lack of motivation and initiative, indecisiveness, poor concentration, guilt, hopelessness, and suicidal ideation)**
 - **Each of these symptoms is represented neurally – the more they are practiced, the more those neural connections are strengthened, and the better these people get at being depressed**

Neural Mechanisms of Suicidality

- **There are neural connections supporting suicidal ideation**
 - **The more someone thinks about being dead or taking one's own life, the more one's brain strengthens the neural connections supporting such thoughts and the better one gets at contemplating, considering, and committing suicide**
 - **Can people become **suicidality Olympians**?**
 - **Many folks have logged thousands of hours wanting to be dead and thinking of how to do it, perhaps even attempting it**
 - **Psychotherapy cannot get rid of the neural pathways supporting suicidality**
 - **However, psychotherapy can build and strengthen neural pathways supporting one's strengths, reasons for living, and hope for the future**
 - **Psychoeducation can build and strengthen neural pathways that support knowledge about the impact of suicide on family, friends, and other survivors, which can be a potent deterrent**
 - **Psychotherapy can build and strengthen neural pathways for drawing on available resources to get through times of suicidality and to stay safe**

Neural Mechanisms of Psychotherapy for Depression

■ Cognitive Behavioral Therapy

- Identify inaccurate, negative views of self and cease repeating/practicing them
 - Allow old neural pathways supporting them to lie dormant
- Identify accurate, positive views of self, based on evidence from the patient's life thus far, and *practice/repeat* them
 - Use neuroplasticity to build new neural pathways that support these accurate views and then to strengthen those pathways
 - The old pathways supporting the depressogenic thinking have been activated *ad nauseum*, so these new pathways require ongoing, extensive practice to stand a chance and hold off relapse

Neural Mechanisms of Psychotherapy for Depression

■ Behavioral activation

➤ Get out of bed

- Strengthen neural pathways that support this multi-faceted behavior

➤ Exercise

- Strengthen neural pathways that support *initiating* exercise and then establishing a routine

➤ Social activities

- Strengthen neural pathways that support this multi-faceted behavior

➤ Going to work, going to school, doing course work, etc.

- Strengthen neural pathways that support these multi-faceted behaviors

Neural Mechanisms of Worry

- There are neural connections that support worry
 - Worries about health, family members, work, school performance, money, climate change, state of our world, etc.
 - The more we worry, the more our brains strengthen the neural connections supporting worry, to the point of worry becoming automatic and eventually crossing threshold of GAD
 - People with GAD are **worry Olympians**
 - They practice their sport 8+ hours per day, every day
 - Their brains transport them into the future to spend time on fabricated events, 90-95% of which will never come to pass
 - With worry comes muscle tension, irritability, fatigue, etc.
 - Psychotherapy cannot get rid of the neural pathways supporting worry
 - However, mindfulness strategies can be effective for helping people return to the present and disengage from future-oriented worry, with *new neural connections* supporting the ability to return to and stay in the present (requiring *lots* of practice)
 - Acceptance strategies can help people develop a new way of relating to worries, with *new neural connections* supporting that

Treating Worry, Stress, and Anxiety

■ Techniques to reduce worry, stress, and anxiety

- Not ‘
- CBT,
- relax



WORRIER POSE

Gemma CORRELL

traction,
rior Pose

Healthy Aging

- **Neuroplasticity can limit cognitive decline, but you have to use it: crossword puzzles, word searches, sudoku, reading, playing musical instruments, social interactions, exercise, healthy diet**
- **These activities build up neural pathways that support these healthy behaviors**
- **Even in the face of normal brain aging and cognitive decline, these activities use neuroplasticity to strengthen their own neural pathways that directly counter the normally occurring brain and cognitive changes that accompany aging**

Remember...

Your brain helps you get really good at whatever you spend your time doing.

Use your neuroplasticity, and aging will go better.

Treatment – Neural Mechanisms of

- **There are neural mechanisms for psychotherapy treatment: behavioral activation, exercise, sleep hygiene, accurate views of oneself, exposure to safety, coping skills, stress management, anger management, mindfulness, acceptance, relaxation, breathing exercises, new insights, taking meds as prescribed**
- **Using these psychotherapy techniques and treatment adherence strategies build up neural pathways that support these healthy behaviors**
- **Even in the face of years of practice and training in psychiatric symptoms that have so strengthened the neural pathways supporting these symptoms and made them so resistant to change, these psychotherapy and treatment practices build up their own neural pathways that compete with and maybe one day send inhibitory projections to the robust pathways that support the symptoms**

Neural Mechanisms of Psychotherapy for Depression

- Neural connections that support depression and its symptoms
 - Depressed mood, anhedonia, lack of motivation/initiative, low energy and fatigue, sleep and appetite disturbance, self-critical thoughts, feelings of worthlessness, suicidal ideation, etc.
 - Practice/repetition strengthens these neural connections
- The *bad news* is that these neural connections do not go away, even if they are no longer “practiced”
 - Even after successful treatment, depression symptoms can return when stress or negative life events – **Relapse**
- The *good news* is **neuroplasticity**
 - Psychotherapy develops and strengthens neural connections that are antidotes to depression and its symptoms
 - Neural connections supporting behavioral activation, cognitive restructuring, emotion regulation, interpersonal functioning
 - Practice/repetition strengthens these neural connections
 - Thanks to the exact same mechanisms that created the depression symptoms in the first place

Neural Mechanisms of Psychotherapy for Depression

■ Interpersonal Therapy

➤ Complicated bereavement (grieving loss)

- Build and strengthen neural pathways that support recognizing the loss and processing the emotional impact on oneself
- Build and strengthen neural pathways that support acceptance of this transition to a life without the physical presence of this being

➤ Role dispute (interpersonal struggle)

- Build and strengthen communication skills for addressing and resolving the dispute

➤ Role transition (mourning loss of old role and assuming new one)

- Build and strengthen neural pathways that support recognizing the loss and the impact on oneself
- Build and strengthen neural pathways that support acceptance of the change and the transition
- Build and strengthen neural pathways that support the skills and attitudes required for the new role

Neural Mechanisms of Psychotherapy for Depression

- **Interpersonal Therapy (continued)**
 - **Interpersonal deficits (improving social skills and decreasing social isolation)**
 - **Build and strengthen neural pathways that support new interpersonal skills**
 - **Strengthen neural pathways that support skills for initiating interpersonal contacts, maintaining friends, and getting out on regular basis**

Suicide Prevention in Teens

■ Suicide rates and facts

- 800,000 per year worldwide
- 45,000 per year in the US
- 10th leading cause of death in the US
- 2nd leading cause of death in teens
- Among teens, rate of completed suicide is 4 times higher in males than females (despite females having more attempts)
- Quarter million people each year become suicide survivors
 - Suicide survivors themselves become 9 times more likely to commit suicide as a result

■ How to prevent suicide

- PALS (or SLAP) – Plan, Access, Lethality, Support
- Get help (school counselor, role model, professional)
- Other resources (exercise, healthy behaviors)
- Sleep
- National Suicide Prevention Lifeline: 1-800-273-TALK (8255)

Neural Mechanisms of Clinical Depression

- **There are neural connections that support clinical depression**
 - **Once someone has a Major Depressive Episode, being depressed most of the day nearly every day for at least 2 weeks straight, that person has robust neural connections supporting that**
 - **People with recurrent Major Depressive Disorder and those with Persistent Depressive Disorder are **depression Olympians****
 - **They have often logged thousands of hours with the constellation of depression symptoms (lot of practice and repetition with depressed mood, anhedonia, sleep and appetite disturbance, self-critical thoughts, feelings of worthlessness, fatigue and low energy, lack of motivation and initiative, indecisiveness, poor concentration, guilt, hopelessness, and suicidal ideation)**
 - **Each of these symptoms is represented neurally, and the more they are practiced, the more those neural connections are strengthened, and the better these people get at being depressed**
 - **No wonder relapse is so prominent**
 - **And, by “practicing” relapses, these folks get even better at having relapses, with research consistently showing that each successive relapse is less and less likely to be caused by a negative life event**

Neural Mechanisms of Self-critical Thoughts

- There are neural connections supporting self-critical thoughts
 - Thoughts about being no good, not good enough, failure, stupid, fat, don't deserve to be happy, etc.
 - The more someone engages self-critical thoughts, the more one's brain strengthens the neural connections supporting inaccurate, negative views of oneself
 - People with MDD and PDD are **self-criticism Olympians**
 - They have logged thousands of hours being critical of themselves, often stretching back as far as they can remember
 - The source may be statements from others, often a parent, at a very young age, which are then repeated until they become internalized, such that the external source is no longer needed
 - Psychotherapy cannot get rid of the neural pathways supporting the inaccurate, negative views of self-criticism
 - CBT instead builds new pathways that support new accurate (positive) views of oneself, based on evidence from the patient's life thus far, and these accurate (positive) views now require extensive practice

Neural Mechanisms of Panic

- There are neural connections that support panic
 - Once a panic attack occurs, the neural circuit has been created
 - The more panic attacks we have, the more our brains strengthen the neural connections supporting panic attacks
 - People with panic disorder and other anxiety disorders can become **panic Olympians**
 - Some people have had multiple panic attacks each day and have been doing that for years before they get treatment
 - Their brains have made them experts at having panic attacks and sometimes not even leaving home (agoraphobia)
 - Again, psychotherapy cannot get rid of the neural pathways supporting panic attacks
 - Instead, CBT and exposure are fabulously effective in *cop*ing with panic attacks and thus *building neural connections* that support people knowing that they can survive panic attacks
 - The decreased frequency and intensity of the panic attacks reinforces these neural connections that support coping with panic, allowing people to leave the home, go shopping, stay at work, go on dates, attend social events, etc.

Neural Mechanisms of Social Anxiety

- There are neural connections that support social anxiety
 - Neural circuits for *feeling* shy, embarrassed, and humiliated, and then *fearing* evaluation and scrutiny
 - The more we experience these components of social anxiety, the more our brains strengthen the neural connections supporting it
 - People with social anxiety disorder are also **Olympians**
 - They practice social anxiety thoughts and avoidance of social situations, strengthening the neural connections supporting social anxiety
 - Their brains get so good at social anxiety that they even have social anxiety about their social anxiety, fearing that they will display anxiety symptoms that will be viewed negatively by others and thus be humiliating or embarrassing
 - Again, psychotherapy cannot get rid of the neural pathways supporting social anxiety
 - Instead, exposure and CBT *build neural connections* that support people tolerating different social situations, developing social competence, and ultimately reducing their social anxiety

Symptoms – Neural Mechanisms of

- There are neural mechanisms of suicidal ideation, self-blame, eating disorder thoughts, self-harm urges and acts, panic attacks, obsessions and compulsions, delusions, substance abuse
- Our patients have been practicing these symptoms sometimes for decades, and are practicing them often many times a day, beefing up the neural pathways supporting these symptoms
- As a result of all this practice, it is no wonder that these symptoms are resistant to change, and then can return even after successful treatment

Treatment – Neural Mechanisms of

- There are neural mechanisms for behavioral activation, exercise, sleep hygiene, accurate views of oneself, exposure to safety, coping skills, stress management, anger management, mindfulness, acceptance, relaxation, breathing exercises, new insights, taking meds regularly as prescribed
- Our patients can now practice these psychotherapy techniques and treatment adherence strategies, building up neural pathways that support these healthy behaviors
- Even in the face of years of practice and training in psychiatric symptoms that have so strengthened the neural pathways supporting these symptoms and made them so resistant to change, these psychotherapy and treatment practices build up their own neural pathways that compete with and maybe one day send inhibitory projections to the robust pathways that support the symptoms

Neural Mechanisms of Eating Disorders

- Neuroplasticity is required for restricting, purging and other compensatory behaviors to prevent weight gain, and bingeing
 - Food is a frequently encountered stimulus in our daily lives, such that once the neural connections for restricting, purging, and bingeing are built, there is ample opportunity for *practice*
 - Significant emotional consequences become integrally linked to these maladaptive eating behaviors, implicating neural connections to emotion centers in our brains
 - Patients' visual perceptions of their own bodies become warped, implicating neural feedback on visual cortex
 - Eating disorder thoughts are pernicious and relentless; through neuroplasticity, they come to dominate patients' internal dialogue
 - Neuroplasticity allows this necessary ingredient for life – food – to be so manipulated to the point even of death
 - Tragically, being the ultimate **Olympian** in this domain may result in death (also true for depression, PTSD, and others)
 - That neuroplasticity can be co-opted to work against our own survival is astounding

Neural Mechanisms of Self-harm

- There are neural connections supporting self-harm
 - The more patients with BPD engage/“practice” cutting and other self-harm *acts*, the more their brains strengthen the neural connections involved, including motor neurons
 - The “practice” of self-harm *urges* strengthens those neural connections, likely including the self-same motor neurons even in the absence of the actually cutting or other self-harm act
 - Patients with BPD are often **self-harm Olympians**
 - They have logged thousands of hours wanting to hurt themselves, thinking they deserve that, actually hurting themselves, and having it feel good when they do
 - Psychotherapy cannot rid our patients of the neural pathways supporting self-harm
 - However, DBT strongly discourages the “practice” of self-harm and its associated neural connections, while strengthening new neural connections that support distress tolerance skills
 - Psychotherapy can also build and strengthen neural pathways supporting reasons for not hurting themselves and the realization that they don’t deserve the pain

Neural Mechanisms of Substance Use Disorders

- Alcohol and other drugs affect the self-same neurotransmitters involved in synaptic connections that support emotions, moods, thoughts, and behaviors
- In addition, there are neural connections supporting various other aspects of substance abuse and dependence
 - Neural connections support urges and behaviors for drinking
 - At certain times of the day (after work, 7 pm)
 - In specific situations (dinner, social events, football games, alone)
 - When certain emotions/moods arise (anxiety, depression)
 - In alcoholism and addiction, these neural connections have been activated so much that “the bottle” becomes the #1 priority, even over one’s children
 - The negative impact of this on children is enormous and life-long
 - **AODA Olympians** even get active support for their training through codependency
 - Spouses especially develop quite elaborate and secretive patterns of collusion that dupe so many others, including themselves (as they have slowly built neural highways supporting codependency)

Neural Mechanisms of Attention Deficit Disorders

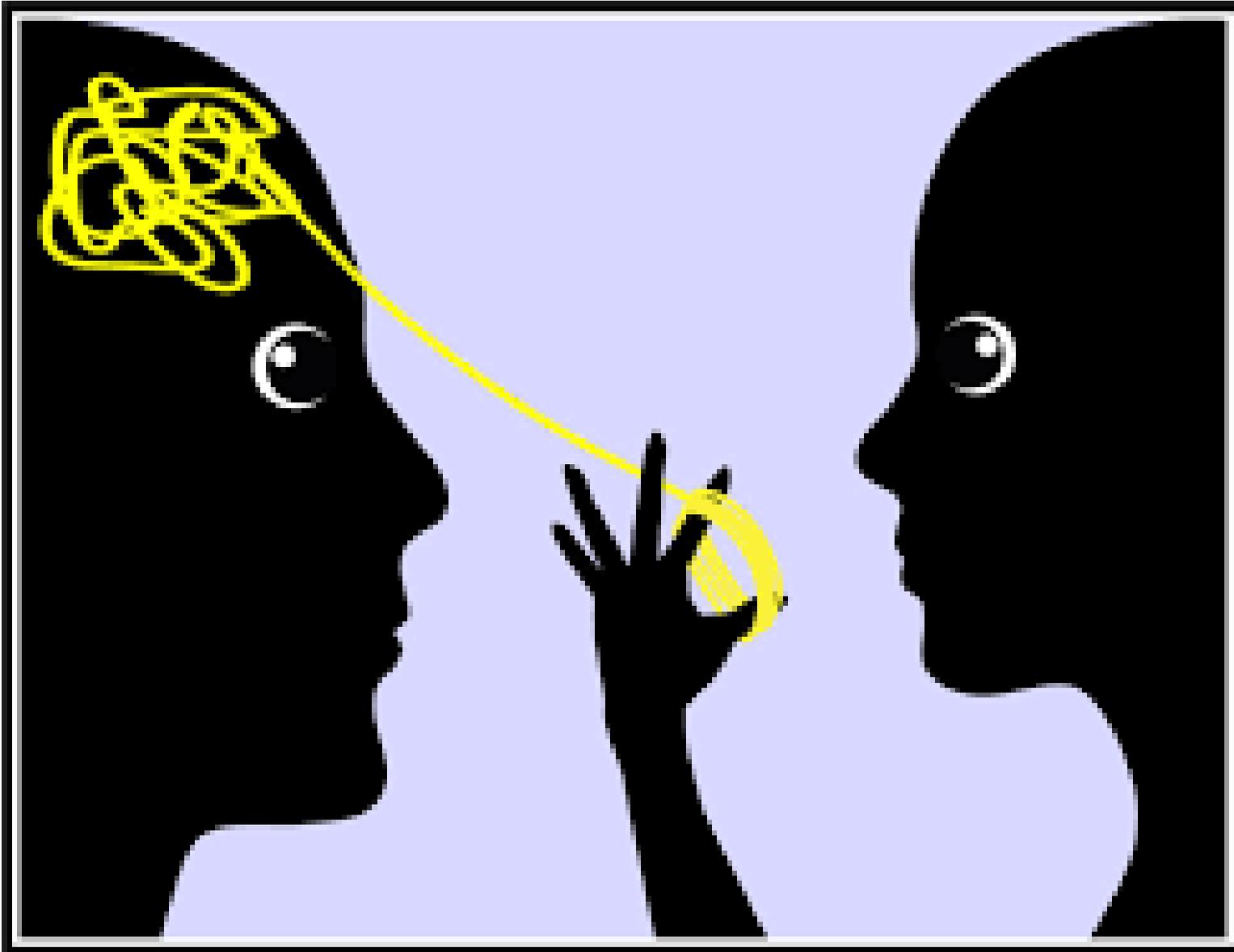
- **There are neural connections supporting ADD/ADHD behaviors**
 - **The more that distractibility, inattention, hyperactivity, and impulsivity are practiced, the stronger the neuronal connections supporting them become**
 - **Patients with ADD/ADHD become Olympians of distractibility, inattention, hyperactivity, and impulsivity, with significant consequences for school, work, family, and the downstream effects on self-image (“lazy”, “stupid”)**
 - **Again, psychotherapy cannot rid people of the neural pathways supporting ADD/ADHD features**
 - **Stimulants activate neural connections that support concentration and sustaining attention – the more practice, the better**
 - **Neural connections support behavioral and coaching strategies to help people stay on task, remember commitments, and slow down – the more practice, the better**
 - **With stimulants and/or the practice of these compensatory strategies, the neural circuits supporting the various components of ADD/ADHD can increasingly lie dormant**

Neural Mechanisms of Anger and Anger Management

- **There are neural connections supporting the experience of anger and overlapping neural circuitry supporting the various ways of expressing anger (e.g., facial expressions, yelling, hitting)**
 - **The more that unhealthy, abusive expressions of anger are practiced, the stronger their neuronal connections become**
 - **Many people with anger control problems go from 0 to 60 in milliseconds – neural connections operate on that timeline too**
 - **Living with these Olympians isn't much fun – the anger outbursts can happen so fast, leaving family members feeling terrorized and walking on egg shells (and targets of the abuse)**
 - **Again, psychotherapy cannot rid people of the neural pathways supporting maladaptive expressions of anger**
 - **However, anger management builds neural connections that support counting to 5 or taking a deep breath, which buy time and allow emotion regulation strategies time to come on line**
 - **With practice of anger management, the neural circuits supporting the “out-of-control” anger behaviors may increasingly lie dormant**

Neural Mechanisms of Gaslighting

- T
- ▶
- ▶
- ▶
- ▶
- ▶
- ▶
- ▶



s the
ions
ns,

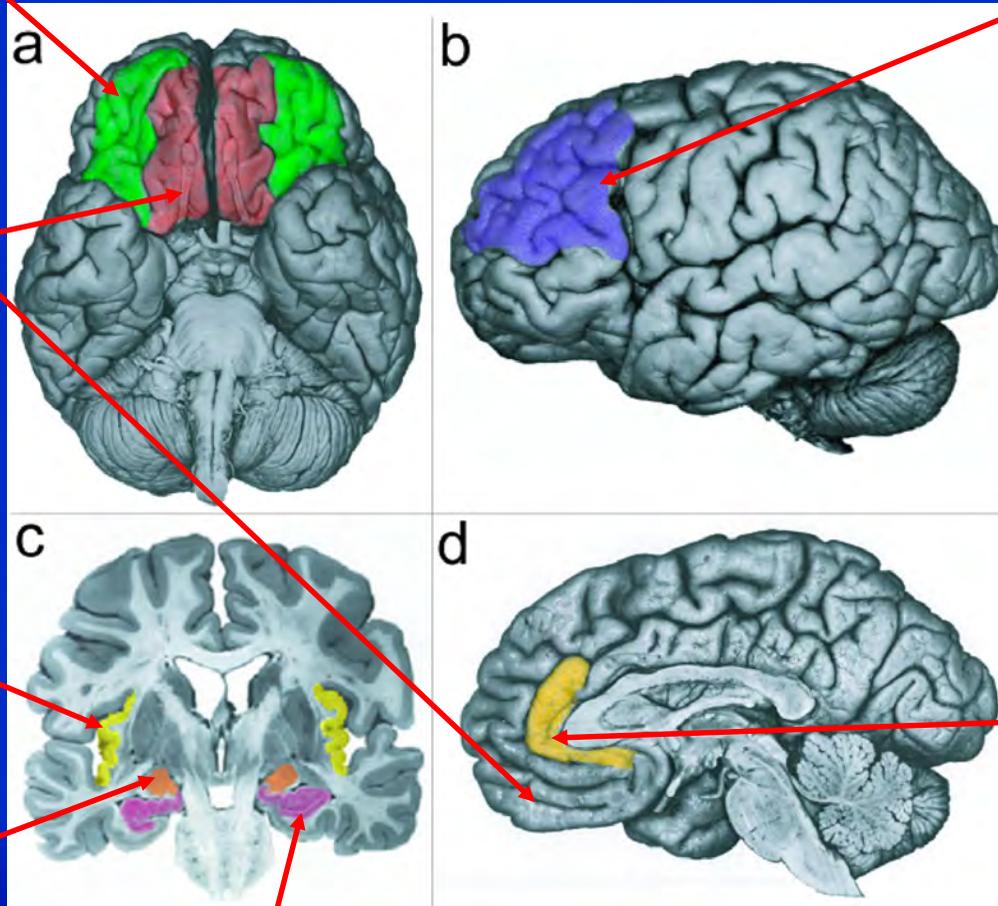
The Brain and Teen Mental Health

Key Brain Areas

Orbitofrontal cortex (OFC)

Dorsolateral prefrontal cortex (dlPFC)

Ventromedial prefrontal cortex (vmPFC)



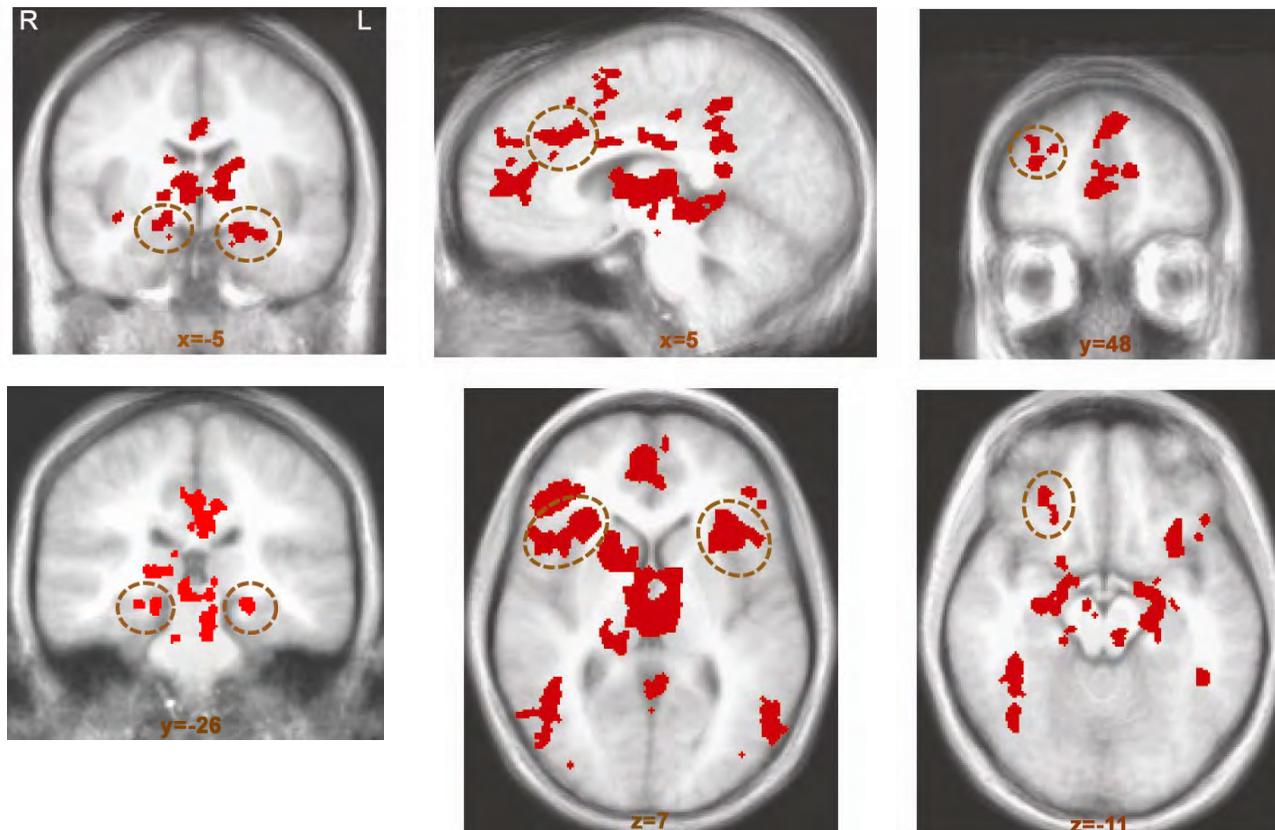
Insula

Amygdala

Hippocampus

Anterior cingulate cortex (ACC)

Brain Areas and Anticipating Bad Things



$n = 21$

Nitschke et al. (2006) *NeuroImage*

Psychotherapy, Learning, and Neuroplasticity

■ Learning

- **Acquiring new information and/or skills: emotional regulation, coping strategies, cognitive restructuring, mindfulness**
- **Changing behavior**
- **Repetition and practice**

■ Neuroplasticity

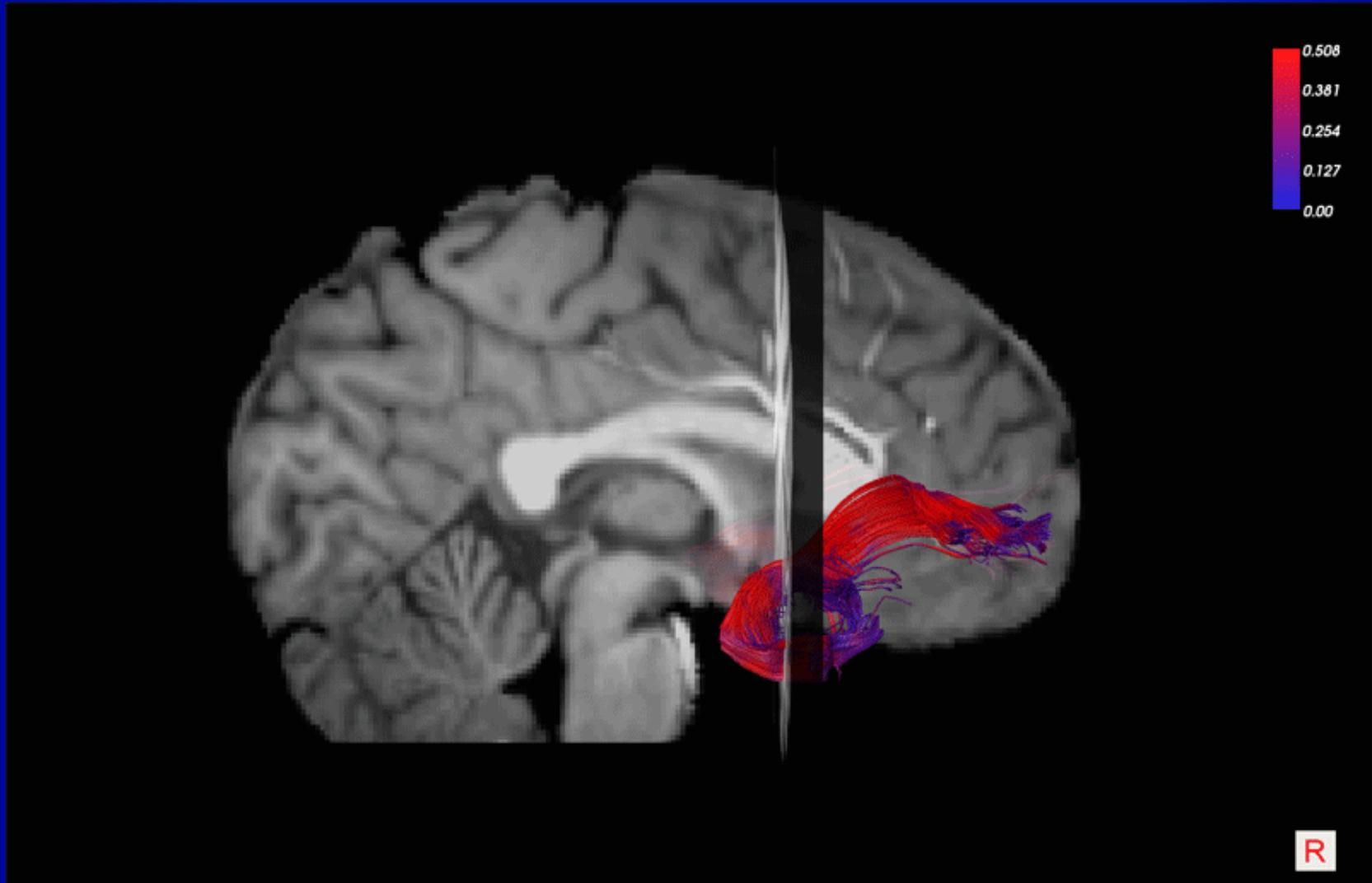
- **Changes in brain structure and function**
- **Neurogenesis**
- **Repetition and practice**

Psychotherapy, Learning, and the Brain

- **Prefrontal cortex**
 - Emotional regulation, coping strategies, cognitive restructuring, mindfulness, directing behavioral activation (e.g., exercise)
- **Hippocampus**
 - Learning and memory related to therapeutic techniques
- **Amygdala**
 - Emotional salience related to therapeutic learning
- **Insula**
 - Moment-to-moment awareness and mindfulness to effect therapeutic learning

Uncinate Fasciculus

DTI-based Tractography



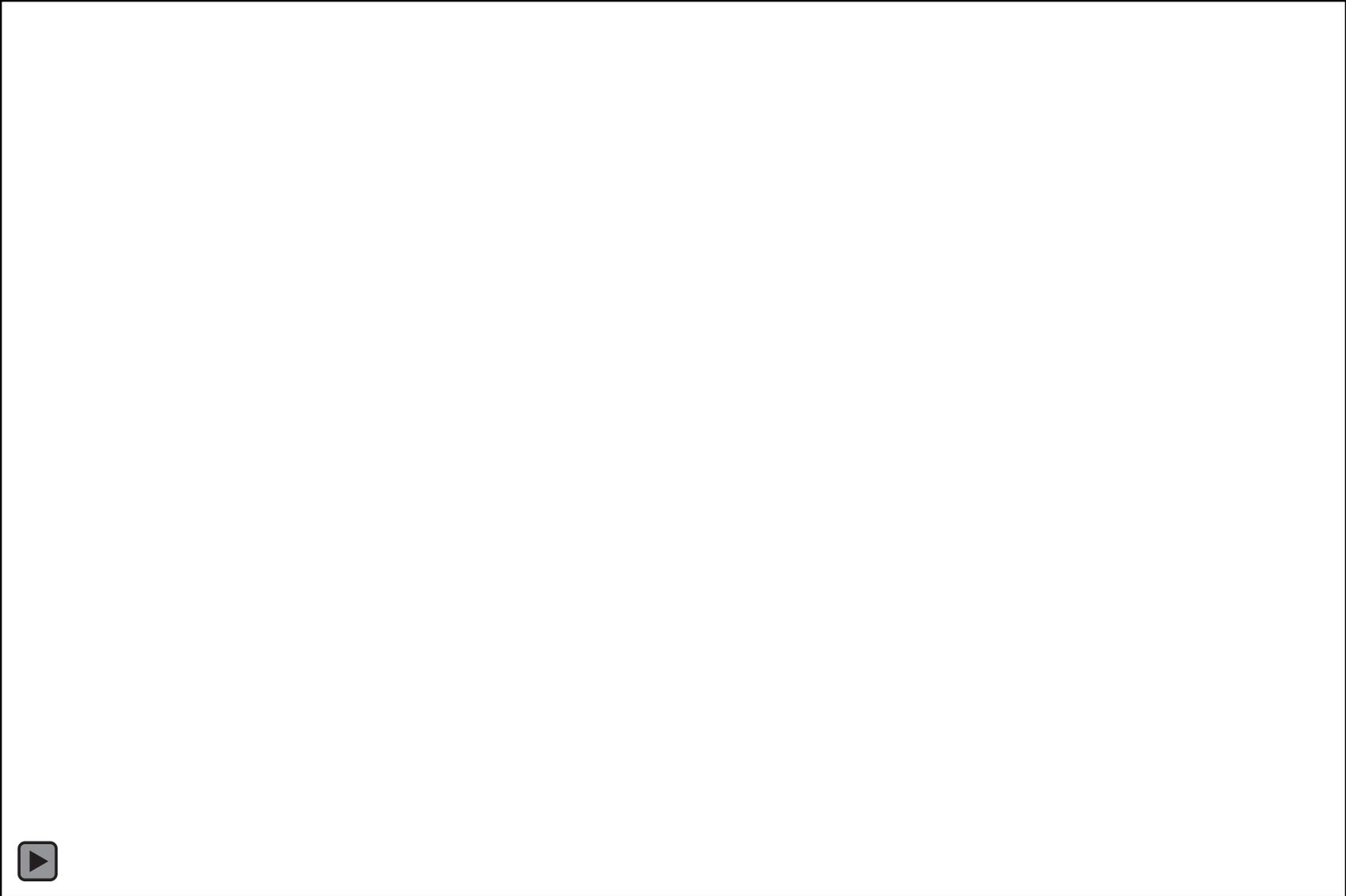
Your Questions







Nitschke et al. (2004) *NeuroImage*





Anticipation Paradigm

Event-related fMRI

