Depression and Anxiety: An Integrated Approach

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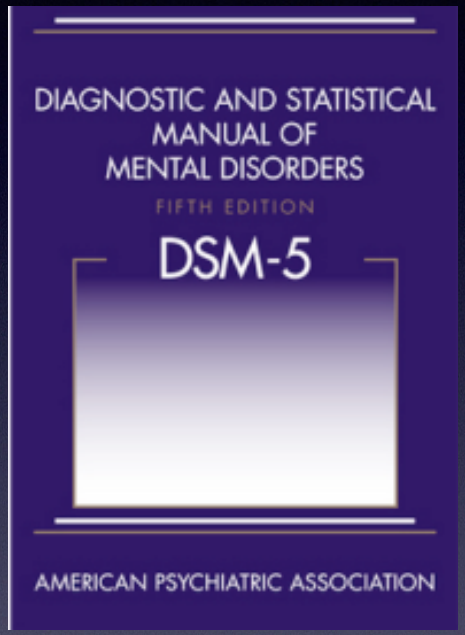
April 13, 2019

Outline

- Definition, Causes, Treatment of Depression
- Definition, Causes, Treatment of Anxiety
- Q and A

What is Depression?


DIAGNOSTIC AND STATISTICAL
MANUAL OF
MENTAL DISORDERS
FIFTH EDITION
DSM-5
AMERICAN PSYCHIATRIC ASSOCIATION

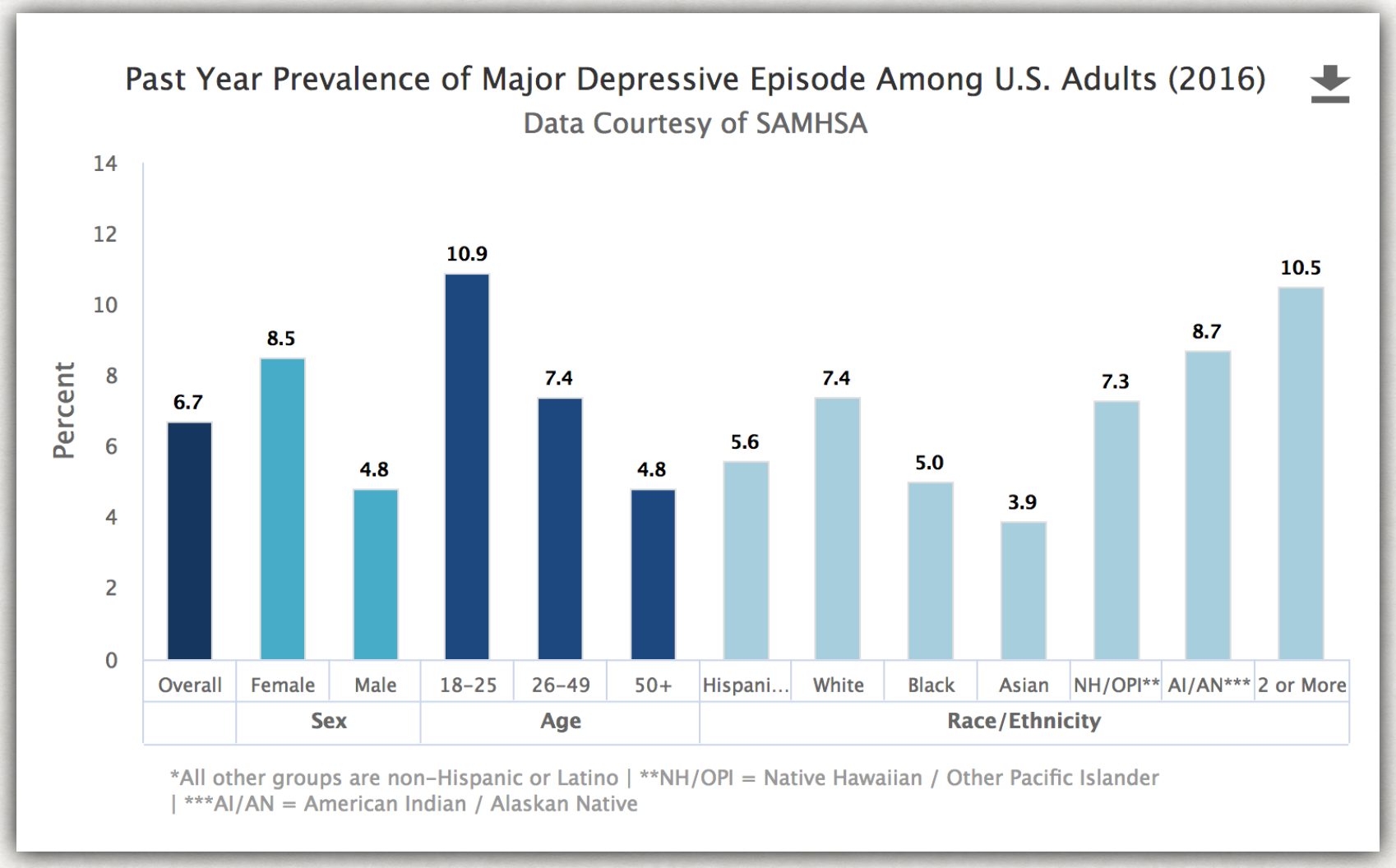
The Mood Disorders

- *Disruptive Mood Dysregulation Disorder* *(chronic persistent irritability in children)*
- Major Depressive D/O
- Persistent Depressive D/O (f.k.a. Dysthymia D/O)
- Premenstrual Dysphoric D/O
- Bipolar I Disorder
- Bipolar II Disorder
- Cyclothymic Disorder
- Mood (Depressive or Bipolar) D/O 2/2 GMC
- Substance-Induced Mood (Dep or BP) Disorder
- (Adjustment Disorder)

Major Depressive Disorder

- At least 5 of the following symptoms lasting 2 weeks, one symptom must be dysphoria or decreased in
  - Dysphoria (depressed mood, subjective or observed)
  - Decreased interests/pleasure most of the day, nearly every day
  - Change in appetite (increased or decreased, >5% change body weight in a month)
  - Change in sleep (hypersomnia or insomnia--initial, middle, terminal, nearly every day)
  - Psychomotor disturbance (slowed or restless/agitation, observed by others)
  - Decreased energy nearly every day
  - Feelings of guilt/worthlessness
  - Impaired concentration
  - Thoughts of death or suicide
- Causes significant functional life impairment (work, relationships, responsibilities)
- NOT due to substances, general medical condition, another mental d/o

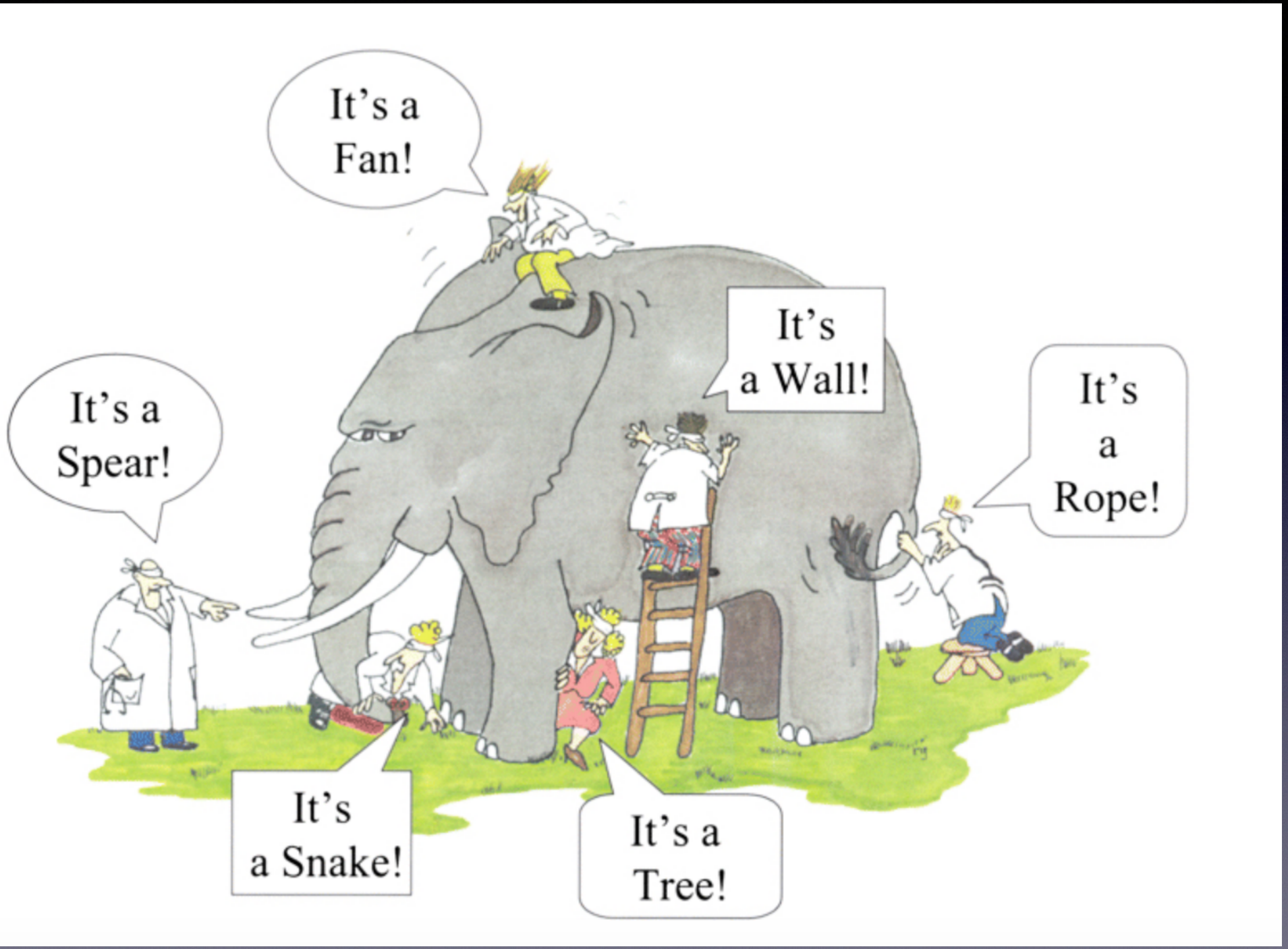
MDD STILL PREVALENT AND DISABLING



https://www.nimh.nih.gov/health/statistics/major-depression.shtml

Causes of Depression

- Many causes
- Will never be completely understood
- Paradigm-driven


It's a Fan!
It's a Spear!
It's a Wall!
It's a Rope!
It's a Snake!
It's a Tree!

- It’s genetics!
- It’s your childhood!
- It’s your chemical imbalance!
- It’s your unprocessed trauma!
- It’s your toxic marriage!
- It’s your lack of exercise and junky diet!
- It’s your drinking!
- It’s your unfulfilling job!
- It’s your lack of faith or prayer or confession!

The Three-Legged Causes of Mental Health/Dysfunction

- Brain/Body: Genetics, Neurobiology, Physical Body
- Mind: Memories, Attachments, Cognitions, Attention, Processing—Integration
- Soul: Being known by God, Mentalizing his emotions toward you, Purpose
- A wonderfully complex and individualized line of work

The Brain/Body

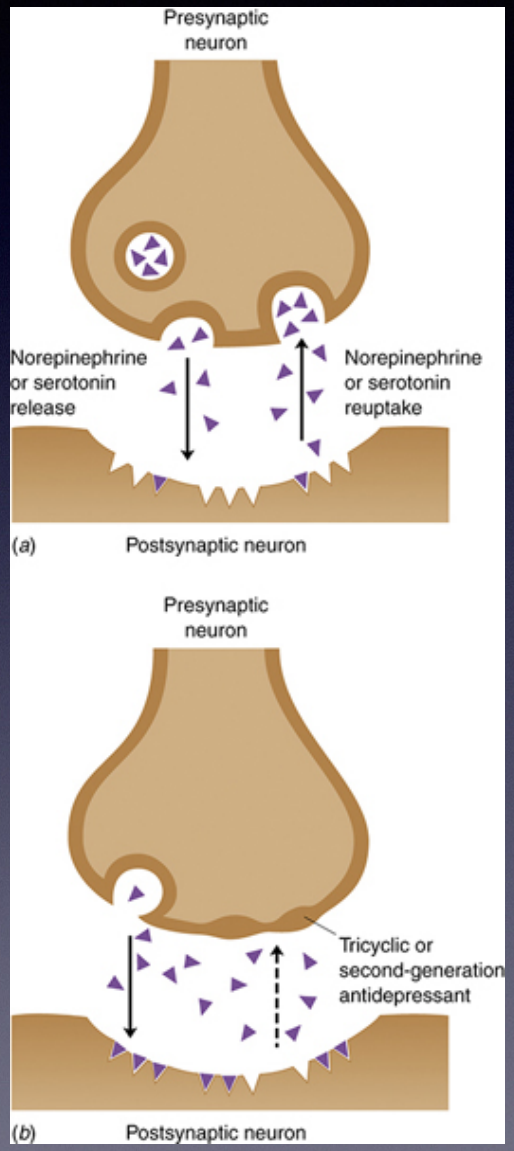
- Genetic Contributions
- Neurotransmitters
- Brain Imaging Differences
- Neuroendocrine Factors

Genetic Factors

- Genetic factors
  - Heritability estimates
    - –93% Bipolar Disorder (Kieseppa et al., 2004)
    - –37% MDD (Sullivan, et al., 2000)
      - Heritability estimates higher for women than men
  - Much research in progress to identify specific genes involved but the results of most studies fail to replicate (Kato, 2007)
- Not a single gene, but instead how genes may influence way people regulate emotions.

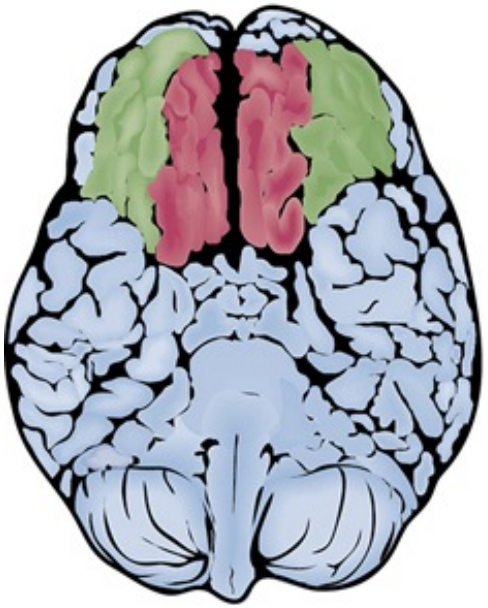
Neurotransmitters

- Serotonin
- Norepinephrine
- Dopamine
- Glutamate
- (Actually post-synaptic changes that enhance neuronal signalling)



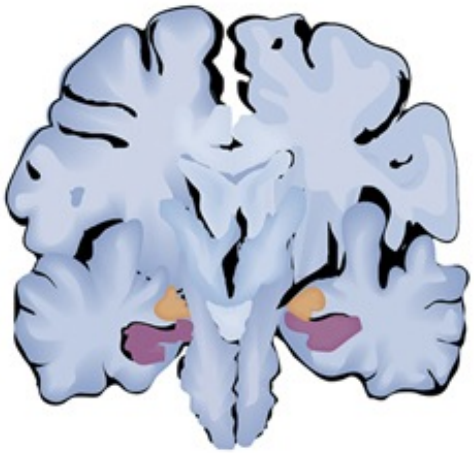
The Brain

A) Orbital prefrontal cortex (green) and the ventromedial prefrontal cortex (red)

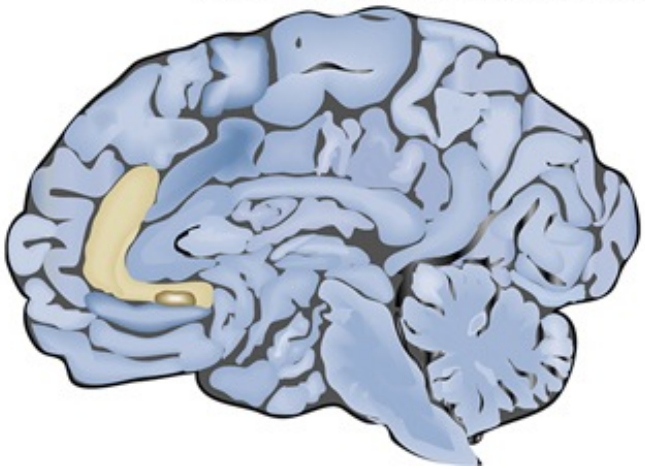


B) Dorsolateral prefrontal cortex (blue)

C) Hippocampus (purple) and amygdala (orange)



D) Anterior cingulate cortex (yellow) and subgenual anterior cingulate (brown)

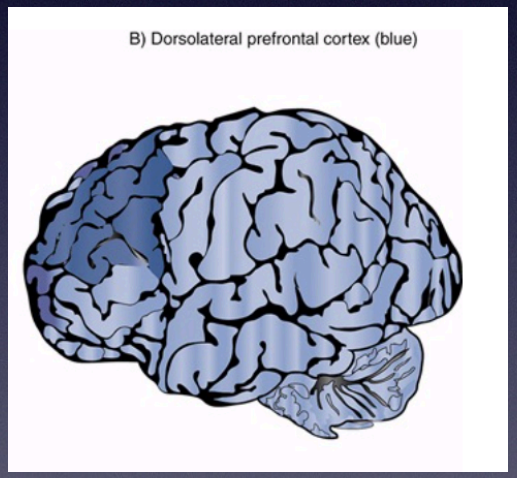


Prefrontal Cortex

- responsible for executive functioning, personality expression, decision making
- what makes humans human
- *Anatomy of a Soul* by Curt Thompson

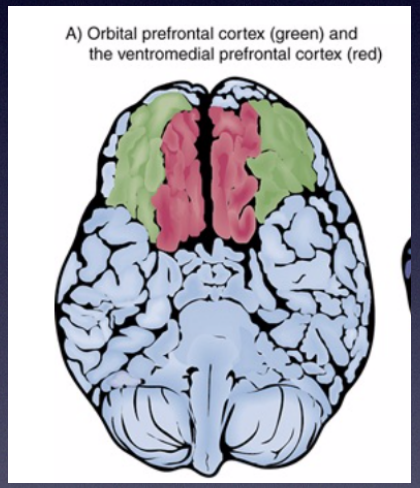
Dorsolateral PFC

- decide between conflicting thoughts and feelings
- activation of attention, multi-tasking
- create expectations and goal-making
- decreased in MDD



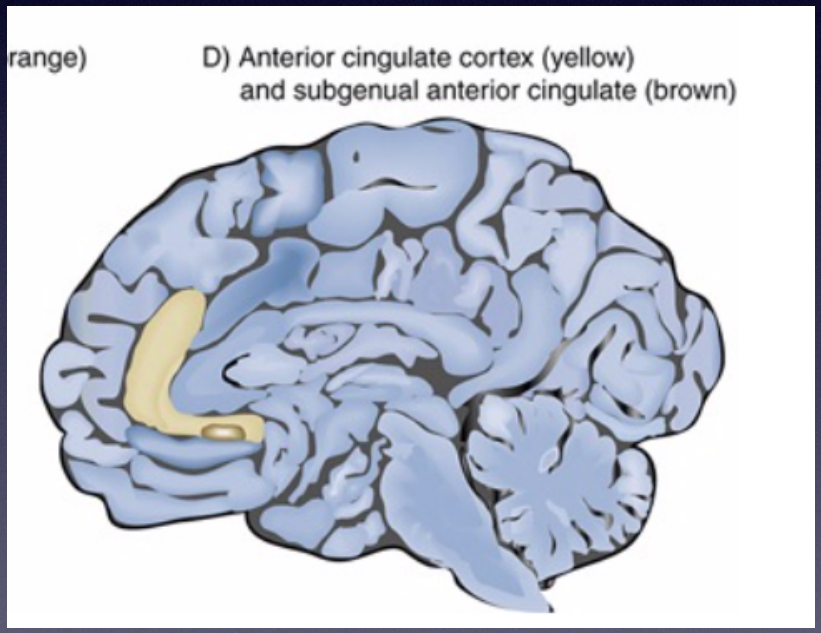
Orbitofrontal PFC

- sense of conscience and social judgment
- generates emotional states and cognition that regulate feelings
- restrain impulsive behavior
- reduced density of neurons and glial neurons in MDD
- stimulation of this area improves depressive symptoms



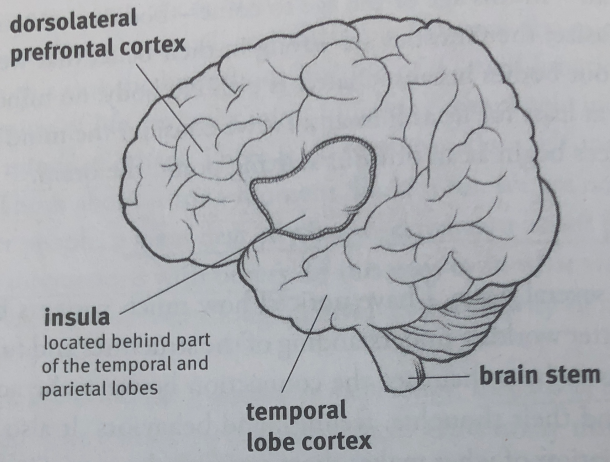
Anterior Cingulate Cortex

- Connects with limbic system (emotional) with cortex
- Involved with emotion formation, processing, memory
- decreased neuronal density in MDD
- depression improves with deep brain stimulation

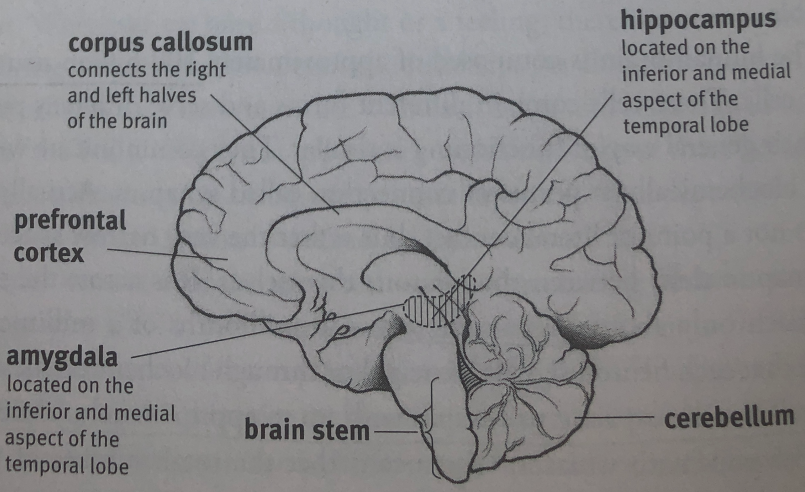


THE HUMAN BRAIN

Looking from the outside toward the lateral portion of the left side of the brain:



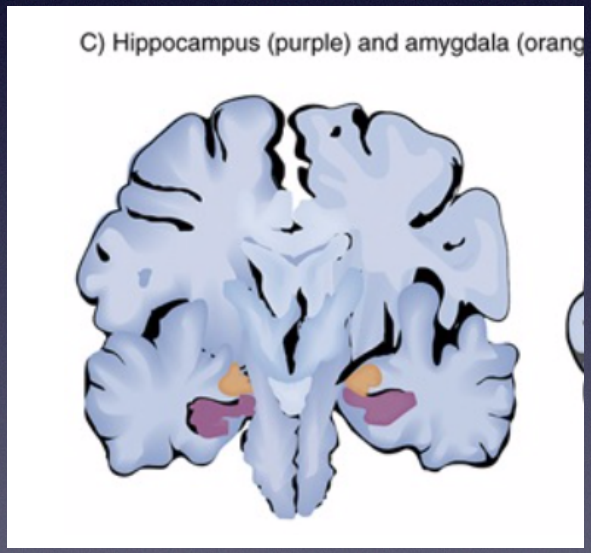
Looking from the middle to the right side of the brain:



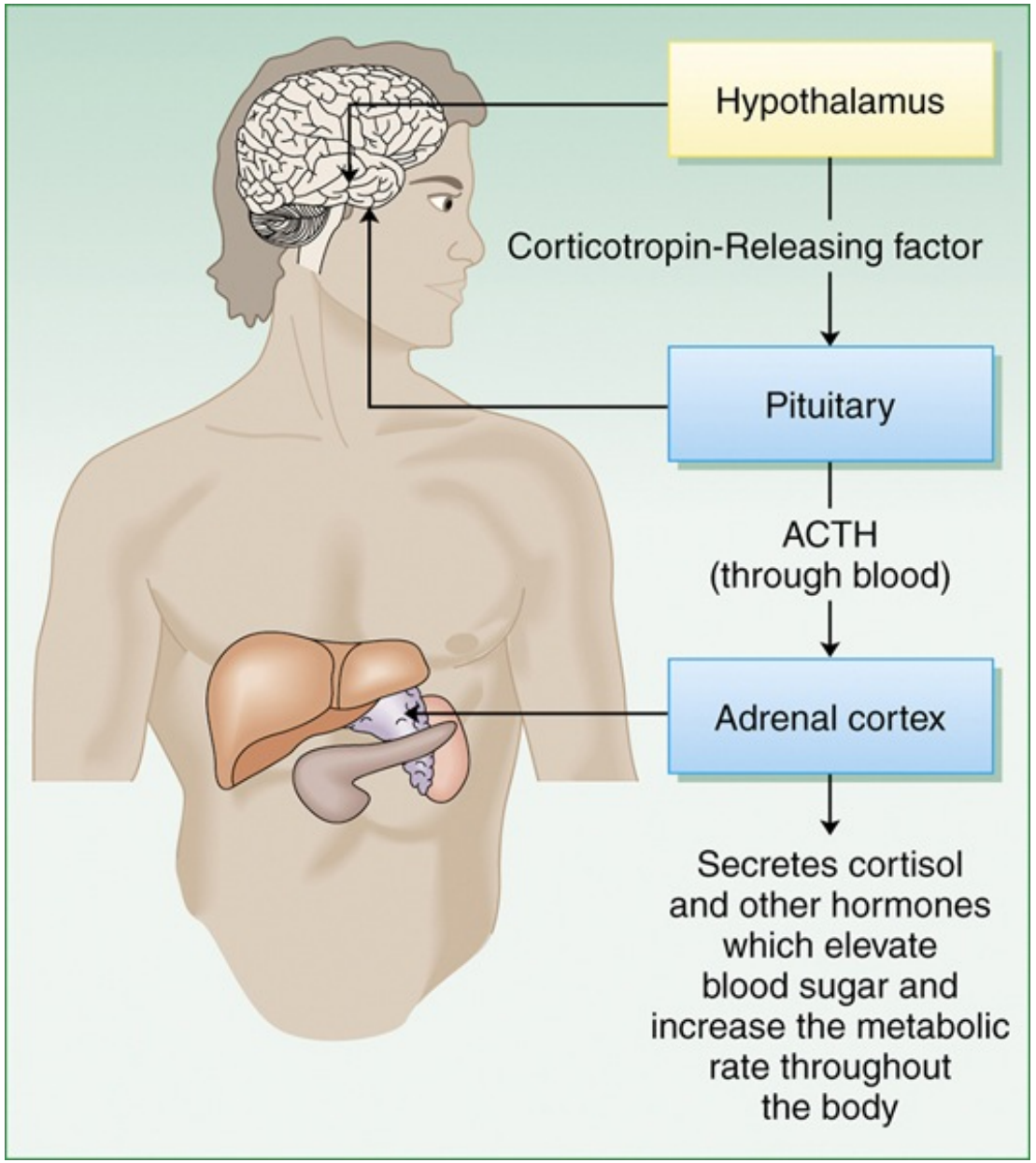
From Anatomy of the Soul, Thompson

Hippocampus and Amygdala

- Hippocampus—memory retrieval, details (esp long term)—decreased in MDD
- Amygdala—assigns broader associations of memory, assesses emotional importance—increased in MDD



Neuroendocrine Factors



- Overactive HPA axis in MDD—too much cortisol
- Excess cortisol linked with depression (Cushing's syndrome)
- Thyroid, estrogen, testosterone all also implicated in depression

The Body: Diet

- High sugar/refined foods lowers BDNF, increases cognitive decline
- Mediterranean diet recommended for lower rates of depression, increased rate of vegetable intake
- Gut inflammation hypothesis—probiotic
  - One Dutch study shows that clinically depressed are missing two strains of gut bacteria
  - more research needed

The Body: Exercise

- Both strength training and cardio associated with lower rates of depression, increased BDNF (neuroplasticity), sleep quality, mood scores, lower rate of cognitive decline

Medical Causes of Depression

- Hypothyroidism
- Sleep apnea
- Stroke, heart attack
- Frontal lobe tumor
- AIDS
- Hyponatremia (low sodium)
- Pancreatic carcinoma
- Cushing's syndrome (high cortisol)
- Addison's disease (adrenocortical insufficiency)
- Hyperparathyroidism/hypoparathyroidism
- Lupus
- Acute intermittent porphyria
- Hepatic encephalopathy
- Wilson's disease (high copper)
- Huntington's disease
- Vitamin deficiencies

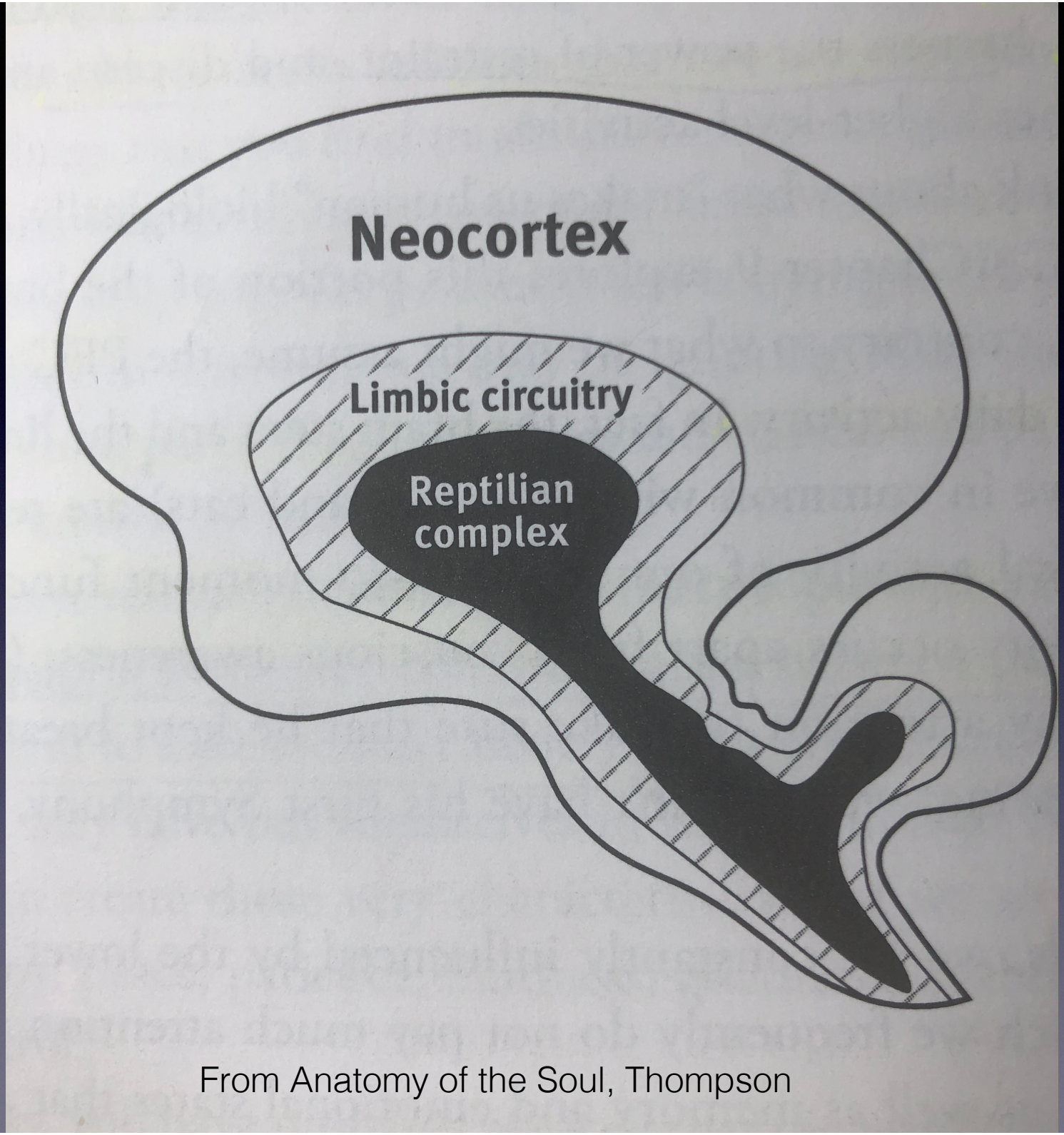
The Mind

Mind

- “The mind is an embodied and relational process, emerging within and between brains, that regulates the flow of energy and information.” —Daniel Siegal
- The mind of made up of many dynamic processes: Attachment style, attention, memory, emotion, regulation. All can contribute to dysfunctional thinking and depression.

Left-Right

- Left brain—logical, linear, literal processing, right vs wrong, resolve confusion (what we know)
- Right brain—body awareness, holistic experience, nonverbal communication, social-emotional context (what we feel)



From Anatomy of the Soul, Thompson

Top-Down

- Cortex (especially prefrontal cortex)—voluntary activation—higher complex tasks, abstract, creative, social, decision-making
- Limbic system (recognition, memory of fear, attention to salient stimuli, pleasure)—modulates and generates emotions
- Reptilian brain (brain stem, cerebellum)—automatic functions but also sensitive to threat

Many other ways to conceptualize the mind

- Stressful life event (with lack of social support)
- Interpersonal conflict (esp. marital, family)
- Cognitive errors about self, world, future
- Mood dysregulation
- Trauma/childhood/past experiences that shaped self
- Attachment theory

The Soul

- We are not disembodied souls, and what the mind/body matrix is telling us is often how God gets our attention.

- “The way you understand and try to make sense of Jesus will be filtered through your memory and your story” (Curt Thompson, *Anatomy of the Soul)*

The Soul

- Not just knowledge of God, but being known by God. Mentalizing what God feels about us through Scripture. Sitting and feeling it.
- Emotions are good! God-given, part of creation, and not debatable—you feel what you feel.
- Paying attention to emotions (early nonverbal signs and late cognitive awareness) can harness them, understand their origins (a.k.a. implicit and explicit memories), and ultimately increase our understanding and view of God.
- Emotions such as fear and shame bubble up, cortex dismisses in order to protect, leads to dysfunctional behaviors
- We try to integrate left/right brain, top/down brain.
- Careful questioning, observing, and listening is critical.

Mind/Soul-Body

- Mind/Soul —> Body (depressive episode leading to insomnia, lack of appetite, intense anxiety, nausea, diarrhea, etc)
- Body—> Mind/Soul (hypothyroidism, sleep apnea, premenstrual dysphoric disorder, chronic insomnia, poor eating, lack of exercise, etc)

The Three-Legged Treatment of Depression

- Mind: attachment, emotions, memories, telling your story, being known
- Body and Brain: limited but important, important but limited
- Soul: proper view and relationship with God, purpose in life, being in community
- You have to have all three!

Treatment of Depression

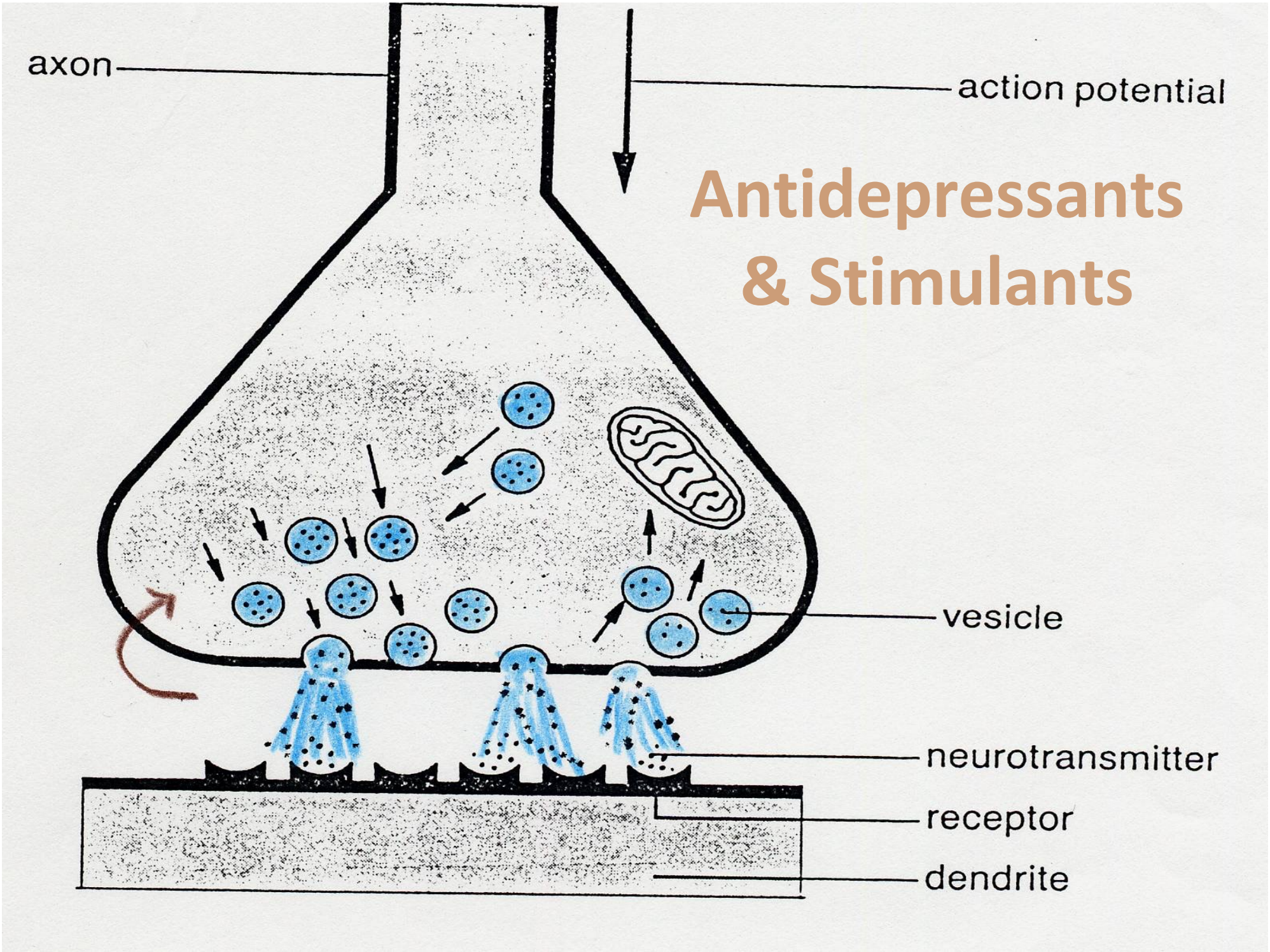
- 1. Psychotherapy
  - Individual--interpersonal, CBT, psychodynamic
  - Group, couples, family
  - Mindfulness training, DBT, EMDR
  - Spiritual guidance
- 2. Lifestyle changes—diet, exercise
- 3. Medications if needed
- 4. Spiritual Disciplines—prayer, meeting, reading, community
- 4. Hospitalization—safety is always paramount
- 5. ECT/TMS/ketamine

Many forms of psychotherapy

- Psychoanalytic
- Psychodynamic
- Interpersonal
- Motivational
- Cognitive-Behavioral
- Mindfulness, DBT
- EMDR
- Marriage and Family
- Play

"Of course you feel great. These things are loaded with antidepressants."

The Field: The Synapse


axon
action potential
Antidepressants
& Stimulants
vesicle
neurotransmitter
receptor
dendrite

The Players: Antidepressants

- Tricyclic Antidepressants (TCA's)
- Monoamine Oxidase Inhibitors (MAO-I's)
- Serotonin Reuptake Inhibitors (SSRI's)
- Serotonin-Norepinephrine Reuptake Inhibitors (SNRI's)
- Other Mechanisms
- Glutaminergic Agents (Ketamine)

The Ball: Neurotransmitters

- Serotonin—well being
- Norepinephrine—energy and mood
- Dopamine—reward, attention, energy
- Glutamate—excitatory, neuronal plasticity

Antidepressants

- TCAs—amitriptyline, nortriptyline, clomipramine, desipramine, imipramine, amoxapine, doxepin, clomipramine
- MAOIs—Nardil, Marplan, Parnate, Azilect, Mernix, Eldepryl, Emsam (transdermal)
- SSRIs—Prozac, Lexapro, Celexa, Zoloft, Paxil, Viibryd, Trintellix
- SNRIs—Cymbalta, Effexor, Pristiq, Fetzima
- Wellbutrin (NDRI), Remeron
- Ketamine/esketamine

Alternative Treatments

ECT

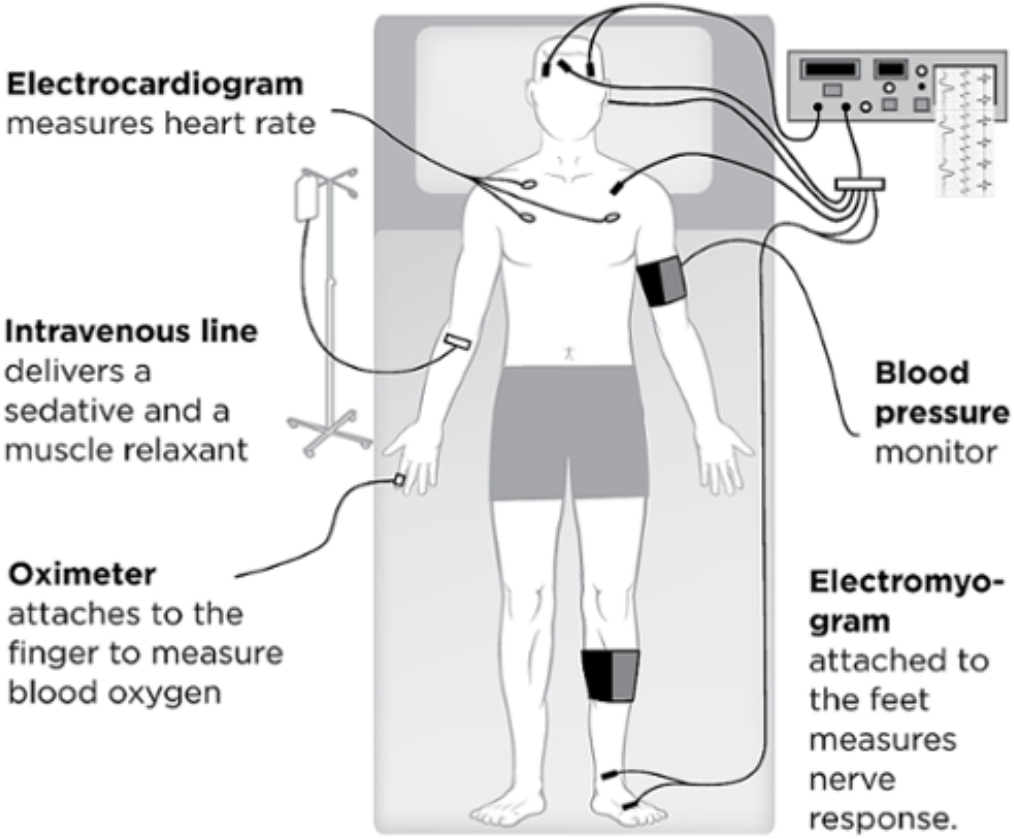
Biological Treatment of Mood Disorders

- Electroconvulsive therapy (ECT)
  - Reserved for
    - Severe depression with high risk of suicide
    - Depression with psychotic features
    - Treatment non-responders
  - Induce brain seizure and momentary unconsciousness
    - *Unilateral ECT*
  - Side effects
    - Memory loss

Electroconvulsive therapy: How it works

The use of ECT is on the rise in Texas as a treatment for severe depression. The procedure sends electrical current through the brain and induces a seizure, which usually lasts less than a minute. Patients are anesthetized during the process, and heart rate and blood pressure are monitored.

Electrodes are attached to the patient's head. They connect to wires from the ECT machine. The electrical current passes through these. **Electroencephalogram electrodes** attached to the head measure seizure activity.



SOURCE: *Electroconvulsive Therapy: A Guide for Professionals and Their Patients* by Dr. Max Fink

Michael Hogue/Staff Artist

State's ECT reports by the numbers

From Sept. 1, 2012, to Aug. 31, 2013:

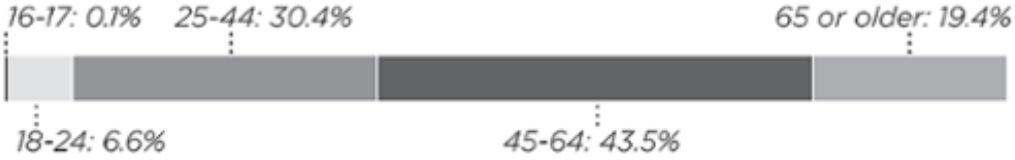
Total treatments: **14,176**

Total patients: **2,243**

Race/ethnicity of patients

Gender

Age



Primary source of payment

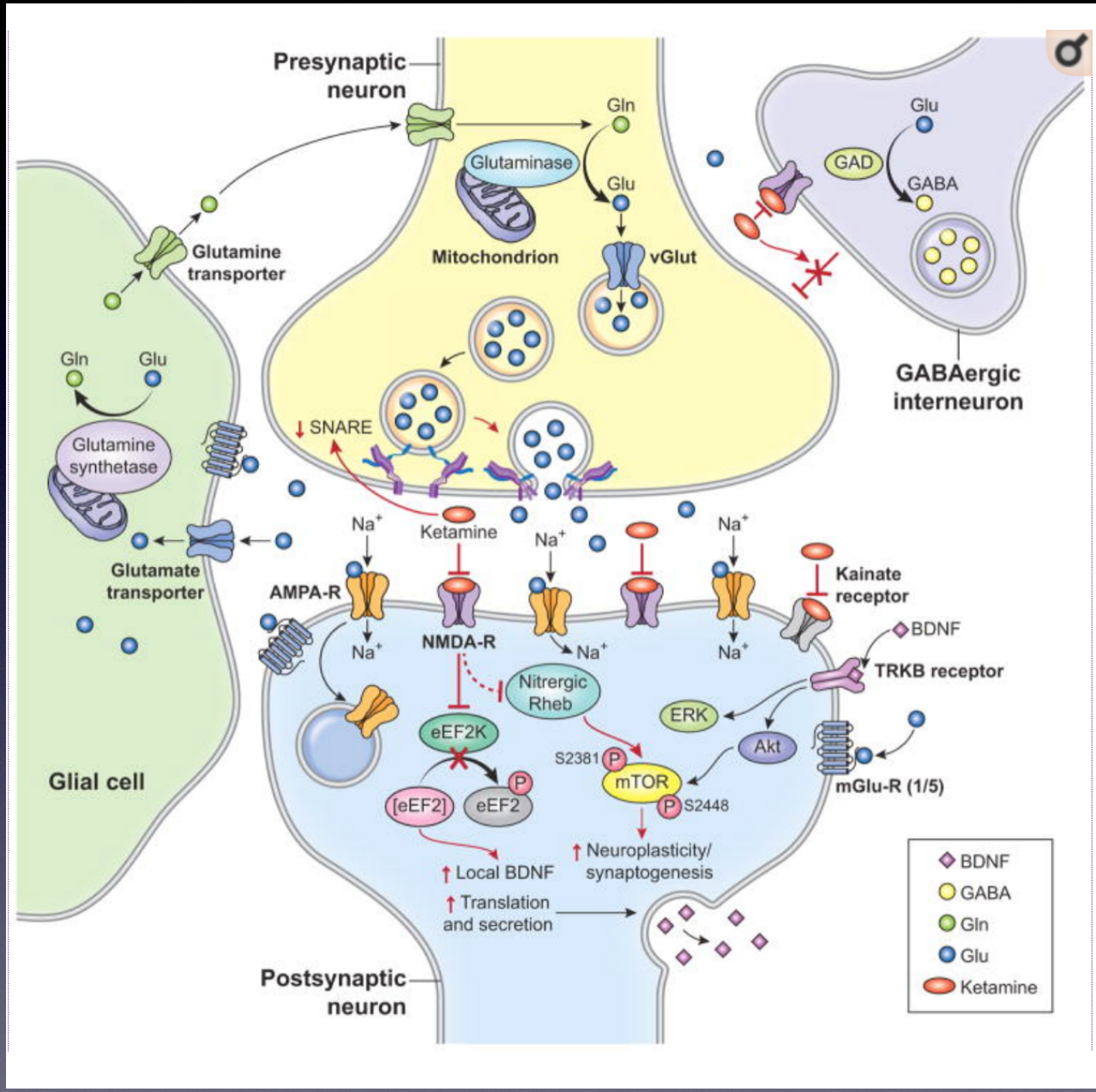
To access state ECT reports: dshs.state.tx.us/mhsa/bhmd/ect/

SOURCE: Texas Department of State Health Services

Staff Graphic

Other biological treatments

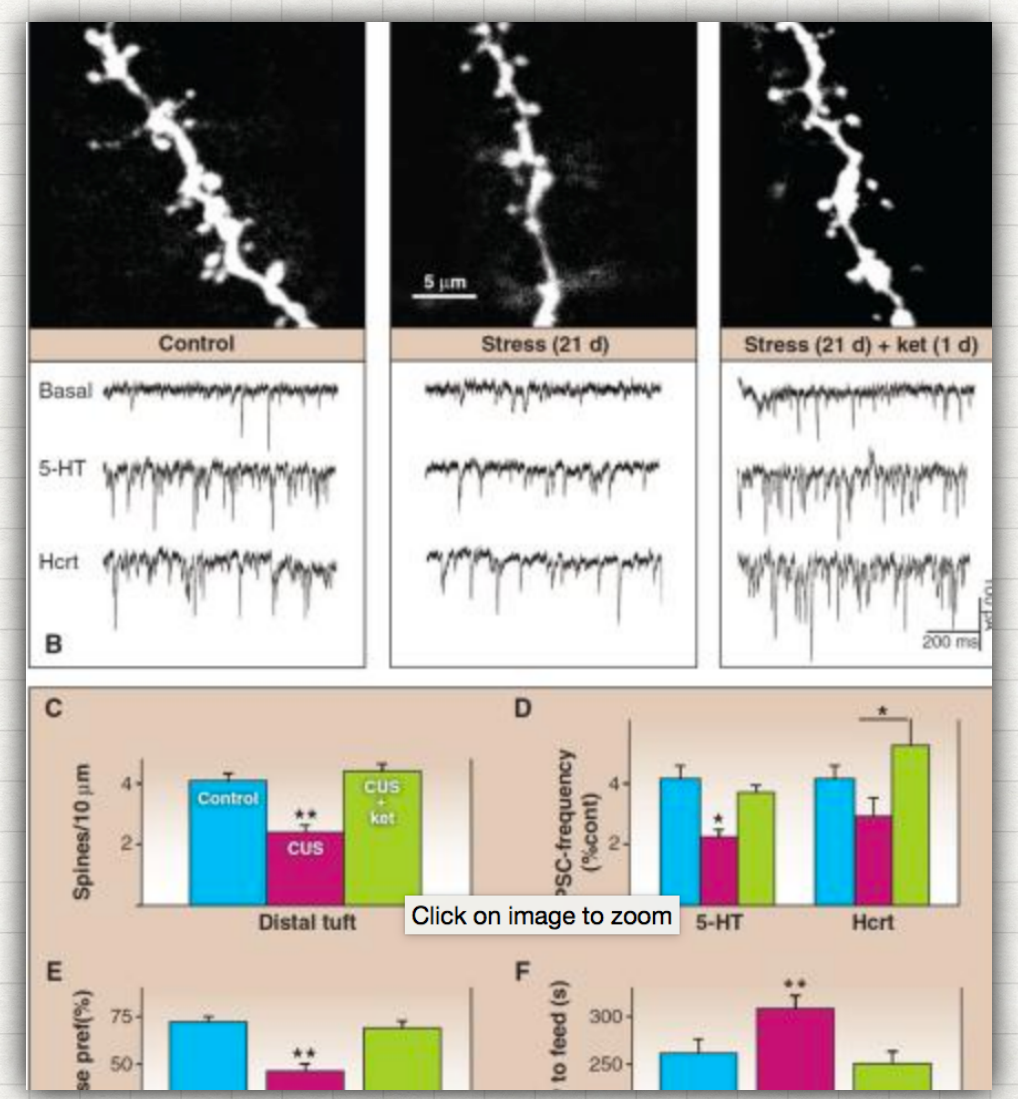
- TMS
- Ketamine infusions—rapidly increases BDNF
- esketamine nasal spray—FDA-approved 3/4/19


Presynaptic neuron
Gln
Glutaminase
Glu
Mitochondrion
vGlut
Glutamine transporter
Glu
GAD
GABA
GABAergic interneuron
Gln
Glu
Glutamine synthetase
SNARE
Ketamine
Na+
Glutamate transporter
AMPA-R
NMDA-R
Kainate receptor
BDNF
TRKB receptor
Nitrergic Rheb
ERK
Akt
eEF2K
S2381
P
mTOR
P
S2448
mGlu-R (1/5)
[eEF2]
eEF2
P
Glial cell
↑ Local BDNF
↑ Translation and secretion
↑ Neuroplasticity/ synaptogenesis
Postsynaptic neuron
BDNF
GABA
Gln
Glu
Ketamine

EFFECTS OF KETAMINE ON SYNAPSES

TAKEN FROM DUMAN & AGHAJANIAN 2012

- Chronic stress decreases synaptic connections and produces depressive-like behavior: rapid reversal by ketamine. (A) Confocal photomicrographs of labeled layer V pyramidal neurons in the medial PFC, showing the effects of CUS (21 days) on spine-synapses in layer V pyramidal neurons and reversal by a single dose of ketamine 1 day later. (B) Effects of chronic stress ± ketamine administration on 5-HT– or hypocretin (Hcrt)–induced excitatory postsynaptic potentials (EPSPs). (C and D) Quantitative analysis of the effects of CUS ± ketamine on spine density and the corresponding regulation of spine synapse function, 5-HT– or Hcrt-induced EPSP frequency (percentage of control). (E and F) Influence of CUS ± ketamine on behavior in (E) the sucrose preference test (measured by percentage of preference for a sucrose solution) and (F) novelty suppressed feeding, measured by latency to feed in an open field (measured in seconds). These models provide measures of anhedonia and anxiety, respectively, and are rapidly (1 day) reversed by ketamine, compared with the requirement for long-term administration (3 weeks) of a typical antidepressant. Error bars indicate SEM; asterisks indicate significance from control (C to F) or between CUS and CUS+ket (E, Hcrt).



Other important treatments

- Can’t neglect the body

You Gotta Sleep

- Healthy sleep is critical to all mental health/disorders
- Sleep hygiene
  - no caffeine after 3 pm
  - no alcohol (middle insomnia)
  - keep room cold
  - warm bath/shower shortly before bedtime
  - no screens—just non-exciting book and lamp
  - get out of bed if 15-30 minutes go by
- Cognitive-behavioral therapy for insomnia (free apps)
- Non-addictive sleeping aid if needed

"Most underutilized antidepressant"

- Regular exercise—
  - As effective as an antidepressant for mild-moderate depression
  - 2011 (UTSW) exercise administered to depressed pts already on SSRI shortened time to remission
  - Improves mood, anxiety, sleep, energy, BDNF
  - Recs: 45-60 min, 50-85% max heart rate, 3-5x/week
  - Brainstorm with patient: consider chronic pain, finances, schedules

“Most abused anti anxiety agent”




- Food—high sugar/processed foods leads to quick but temporary mood improvement, also leads to low energy, weight gain which worsens mood. Shown to lower BDNF as well. Carbs are important to mood but the right ones. Proteins important for amino acids to build neurotransmitters.
- Vitamins: Omega-3 fatty acids, B complex, B vitamins, folate, calcium, magnesium, selenium—take a MVI!
- Supplements is a new field, varied research, unregulated in quality, but research is starting to be done. Beware the miracle supplement.

- Limit or ideally eliminate drugs and alcohol

Relationships

- Depressed people avoid interacting with people because of poor energy, low motivation, apathy, and lack of interest.
- But we are created to be in community. It's a fundamental human need. This creates a vicious cycle.
- Christians should continue to go to church and meet with believers.
- Behavioral activation: Just do it.
- Therapy/counseling is a vital way to get depressed people to connect again—to start process of being known, to reflect, to learn where their mind is disintegrated

Spiritual Disciplines

- Prayer, fasting, Scripture reading, meditation, confession
- “Do not give up meeting together as some are in the habit of doing”
- In community we are developing trust, feedback, encouragement, re-writing our story as we tell it

Sunshine—Seasonal Affective Disorder

- Phototherapy light box for fatigue, especially in winter months, even in states with more sunshine (lots of office workers)
- $50-$150 on Amazon, 10,000 LUX, 30 minutes in the AM
- Evidence to suggest it works in depression not associated with seasonal affective disorder
- Beware of potential bipolar patients

For the supporter

- Pray, pray, pray!
- Notice changes in mood/life patterns—you are our eyes and ears
- Notice isolation—call and text and visit and knock
- Notice dangerous thinking/words (passive, active)
- (Talking about suicide does not increase the risk of suicide)
- Be specific in offering help—health, carpool, social outings, meals, laundry, etc
- Have your own self-care, therapy, and support group—caring for depressed person is a life stressor, and can cause another case of depression!
- Try teamwork and know your limits—you can't be everything for everyone at all times
- Suggest professional help (various levels) and offer to go with them

The Anxiety Disorders:

Definition
Causes
Treatments

“Excessive anxiety and worry”

—DSM-V

Mild anxiety is adaptive

- increases alertness
- enhances our survival
- motivates us to accomplish things and be productive

PSYCHOLOGICAL SYMPTOMS OF ANXIETY

- Intense fear, worrying
- Worry something awful or tragic will happen, out of proportion to actual threat
- Feeling that one might die (panic disorder)
- Feeling that one might be going crazy (panic disorder)
- Irritability, poor concentration, distractibility
- Derealization/depersonalization

PHYSICAL SYMPTOMS OF ANXIETY

- Trembling, shakiness, restlessness, muscle tension
- Shortness of breath, smothering sensation
- Increased heart rate
- Sweating, cold hands and feet
- Light-headedness and dizziness
- Paresthesias (tingling of skin)
- Diarrhea, frequent urination
- Initial insomnia
- Nervousness, edginess, tension

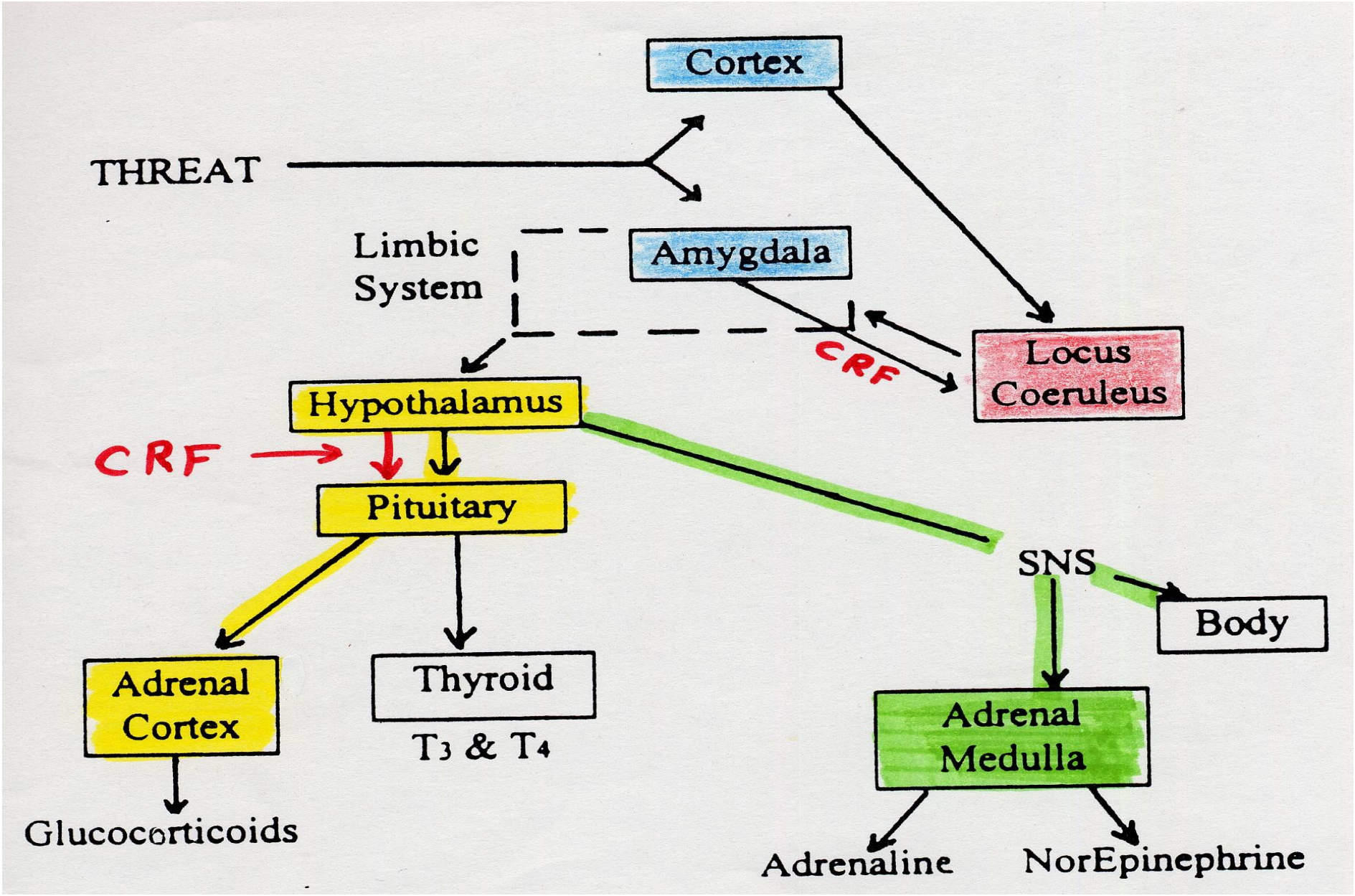
THE ANXIETY DISORDERS

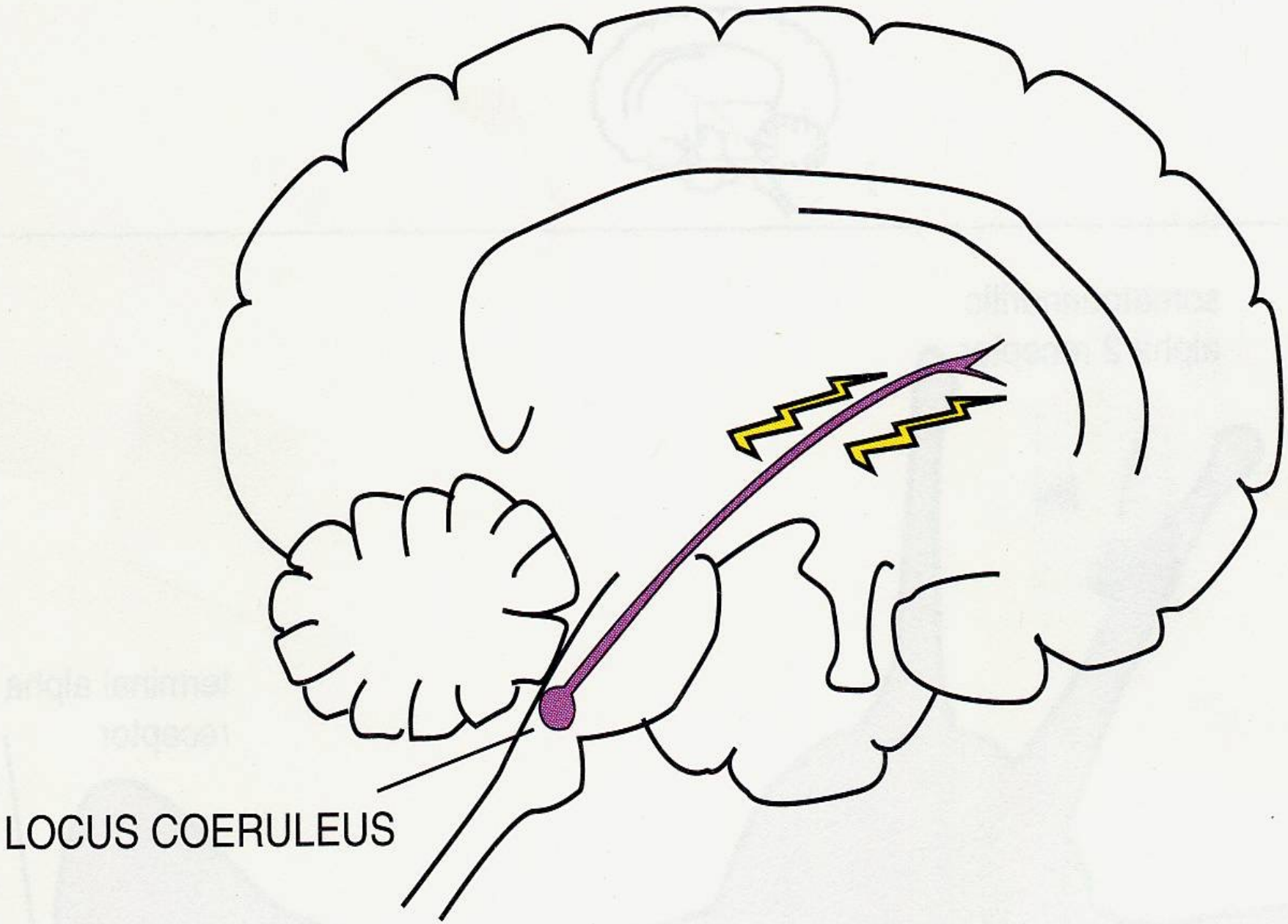
- Generalized Anxiety Disorder
- Specific Phobia
- Social Anxiety Disorder
- Agoraphobia
- Panic Disorder
- Due to General Medical Condition
- Due to Substances
- Adjustment disorder
- Acute Stress Disorder
- PTSD

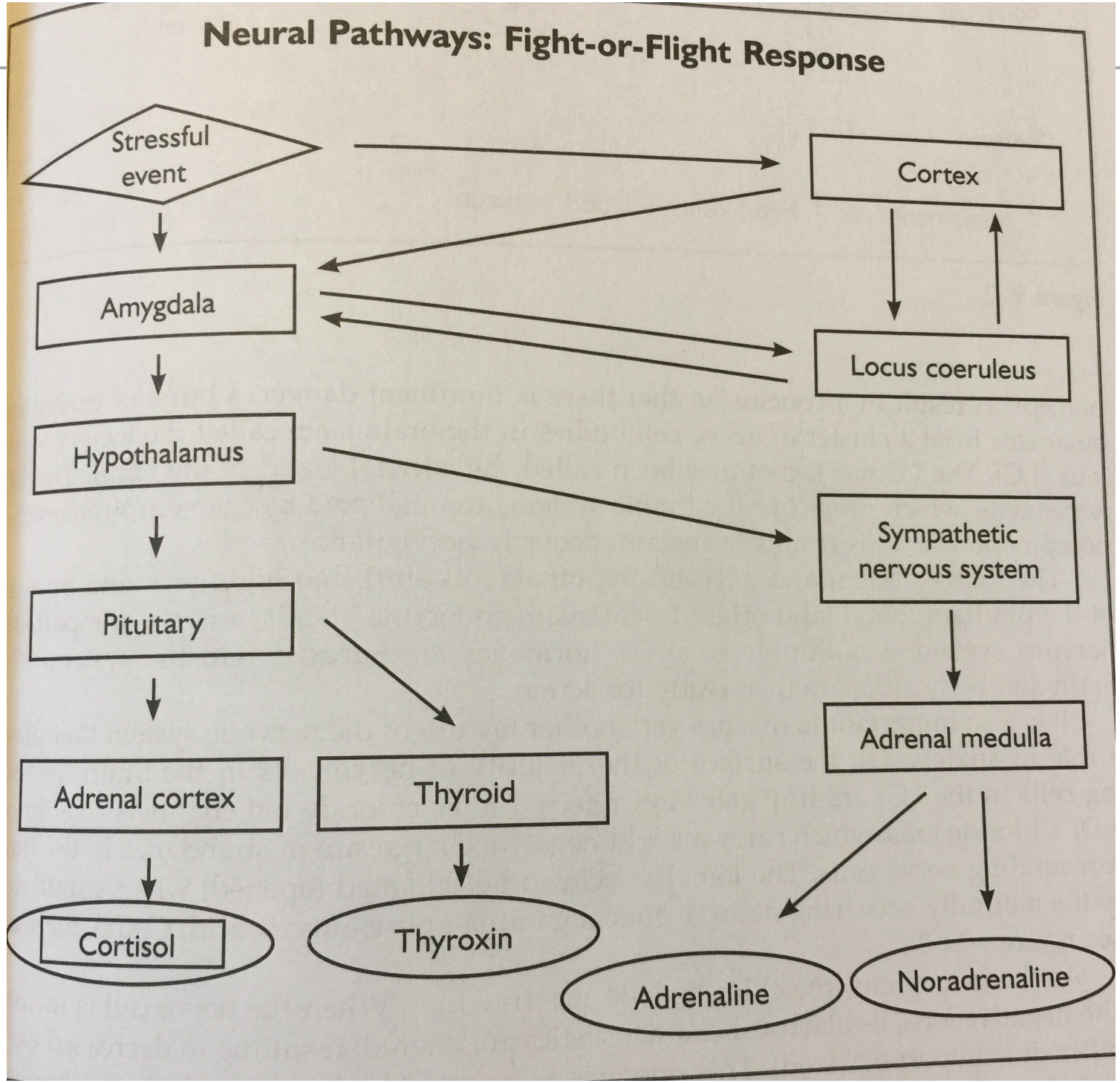
ETIOLOGY OF ANXIETY

- Biological Theories
  - Imminent danger—sympathetic NS for fight or flight
  - Acquired fears—amygdala learns, tough to extinguish, can generalize to stimuli that resembles original stimulus
  - Genetics: not strong heritability rates, much is modeled or learned
- Psychological: Core beliefs of perfectionism and people-pleasing
- Insecure Attachment: unreliable, inconsistent parental attention that did not match child's needs, flooded with emotions

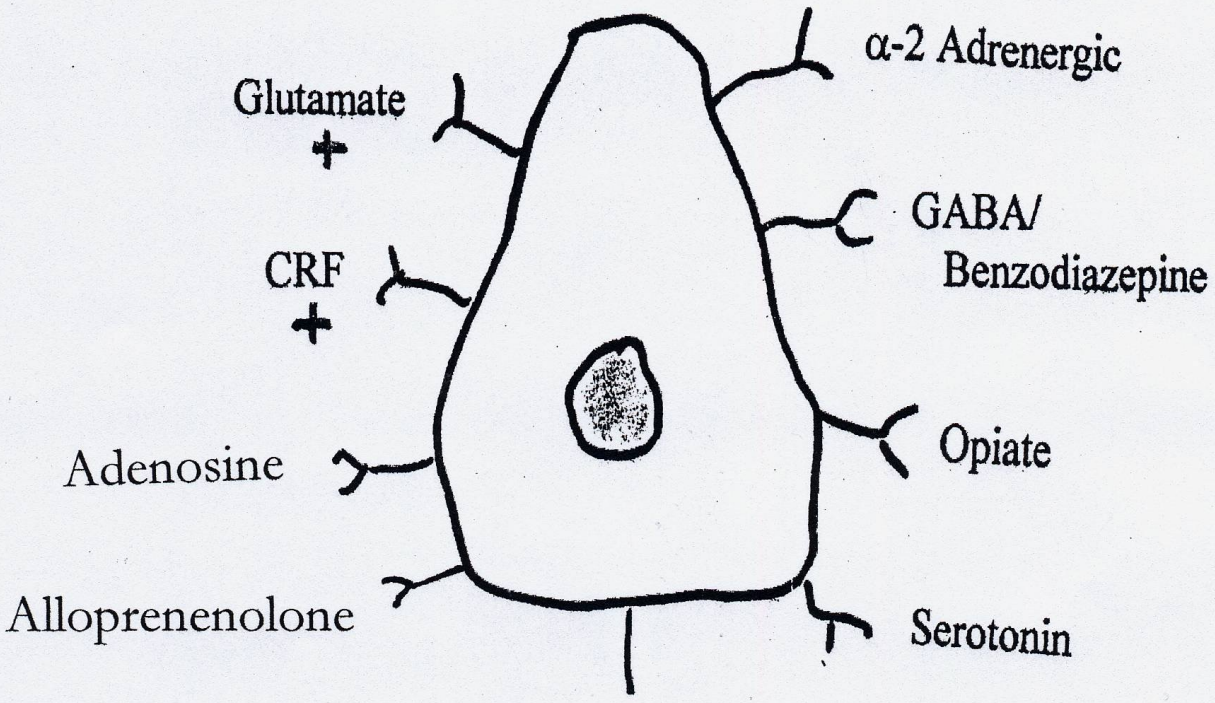
Impact on Fear Appraisal




LOCUS COERULEUS


Neural Pathways: Fight-or-Flight Response
Stressful event
Cortex
Amygdala
Locus coeruleus
Hypothalamus
Sympathetic nervous system
Pituitary
Adrenal medulla
Adrenal cortex
Thyroid
Cortisol
Thyroxin
Adrenaline
Noradrenaline

Norepinephrine Cell:
Locus Coeruleus



Treatment of Anxiety Disorders

Therapy—1st line treatment

- Still paying attention, attending to memories, emotions, attachments, but also:
- CBT (regular, panic control)
- Exposure Therapy
- Systematic Desensitization
- DBT (mindfulness)
- Relaxation techniques

Medications—2nd line treatment

- Antidepressants (SSRIs, SNRIs)
- Benzodiazepenes (potential tolerance and dependence)
- Buspirone for worry
- Off-label: clonidine, hydroxyzine, gabapentin, propranolol for social anxiety disorder
- Always recommended for use in conjunction with 1st line treatment (can help lower symptoms to improve therapy)

Lifestyle Changes

- **Regular Sleep**
- Healthy Diet
- Cardio Exercise
- Yoga
- Limit alcohol
- Journaling
- Spiritual Disciplines
- Social supports/community
- Volunteering
- Pets

Thank you