

The Stellate Ganglion Block: New Paradigms and New Treatments

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Disclosure

There are no relevant conflicts of interest to disclose

Objectives

- Review ACES study findings and implications
- Understand sequelar diseases related to ACEs events
- Explore pathophysiological links between ACEs events and chronic illness
- Identify therapies that restore normal physiological function and reverse the chronic effects of the physiological response to ACEs events

ACEs Study

- Fellitti, Vincent, *et al.* "Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults, The Adverse Child Experiences Study". *American Journal of Preventative Medicine*. Vol 14:4, P245-256, May 01, 1998.

Landmark study that began to change the medical and social conception as to how child abuse may result in not only chronic psychological illness, but also chronic physical disease.

ACEs Study

- CDC and Kaiser Permanente collected survey data of 17,000 patients in the Oakland, CA area:
 - Data collected included:
 - Childhood experiences of maltreatment
 - Childhood experiences of family dysfunction
 - Adult risk Behavior
 - Adult health status
 - Identified correlation between specific childhood experiences and certain adult diseases

ACEs Study: Specific Adverse Childhood Experiences

Personal exposure to:

- Emotional neglect
- Emotional abuse
- Physical neglect
- Physical abuse
- Sexual abuse

Household exposure to:

- Domestic violence
- Substance abuse
- Mental illness/ suicide attempt
- Parental separation or divorce
- Incarceration of family member

Prevalence of ACEs

- ACE score of
 - 0 : 36%
 - 1-3: 52%
 - 4+: 13%
- Sample demographics:
 - Female: 54%, Male: 46%
 - White: 74.8%, Black: 4.5%, Asian 7.2%, Hispanic: 11.2%
 - 19-29yrs: 5.3%, 30-39yrs: 9.8%, 40-49yrs: 18.6%, 50-59yrs: 19.9%, 60+yrs: 46.4%
 - Non-HS grads: 7%, HS grads: 18%, Some college: 36%, College grad or higher: 39%

ACEs Study: Prediction of **Adult Behaviors**

(Odds ratio for individuals with an ACEs score of 4 or greater)

- Current smoker: 2.0
- Considers self alcoholic: 7.4
- Ever used illicit drugs: 4.7
- Severe obesity: 1.6
- No leisure-time physical activity: 1.3
- 2+ weeks of depressed mood in past year: 4.6
- Ever attempted suicide: 12.2

ACEs Study: Prediction of **Adult Diseases**

(Odds ratio for individuals with an ACEs score of 4 or greater)

- Ischemic heart disease: 2.2
- Stroke: 2.4
- Chronic bronchitis/emphysema: 3.9
- Hepatitis: 2.4
- Any variety of cancer: 1.9
- Skeletal fracture: 1.6
- Diabetes: 1.6

ACEs Study: Prediction of **Adult Diseases**

(Odds ratio for individuals with an ACEs score of 4 or greater)

- Fair or poor self-rated health: 2.2
- There is a dose-dependent relationship with increased risk for 7/10 of the leading causes of death in the United States
- For those with ACEs scores of 6+, there is a **20-year** decrease in life expectancy⁽²⁾

Pathophysiology of ACEs

- Current theories regarding development of disease related to ACEs include:
 - Acute Stress Response Theory (Fight or Flight or freeze or faint) 1932
 - Allostatic load theory 1993
 - Argument that PTSD is more oriented towards SNS than HPA axis
 - Unknown processes resulting in shortened telomere-length and Horvath DNA methylation. (3)
 - Epigenetic changes may also result in multi-generational trauma (4)

Stress Response

Threat perceived by the senses → **Thalamus** (sensory/motor relay switchboard)
Amygdala/Frontal cortex

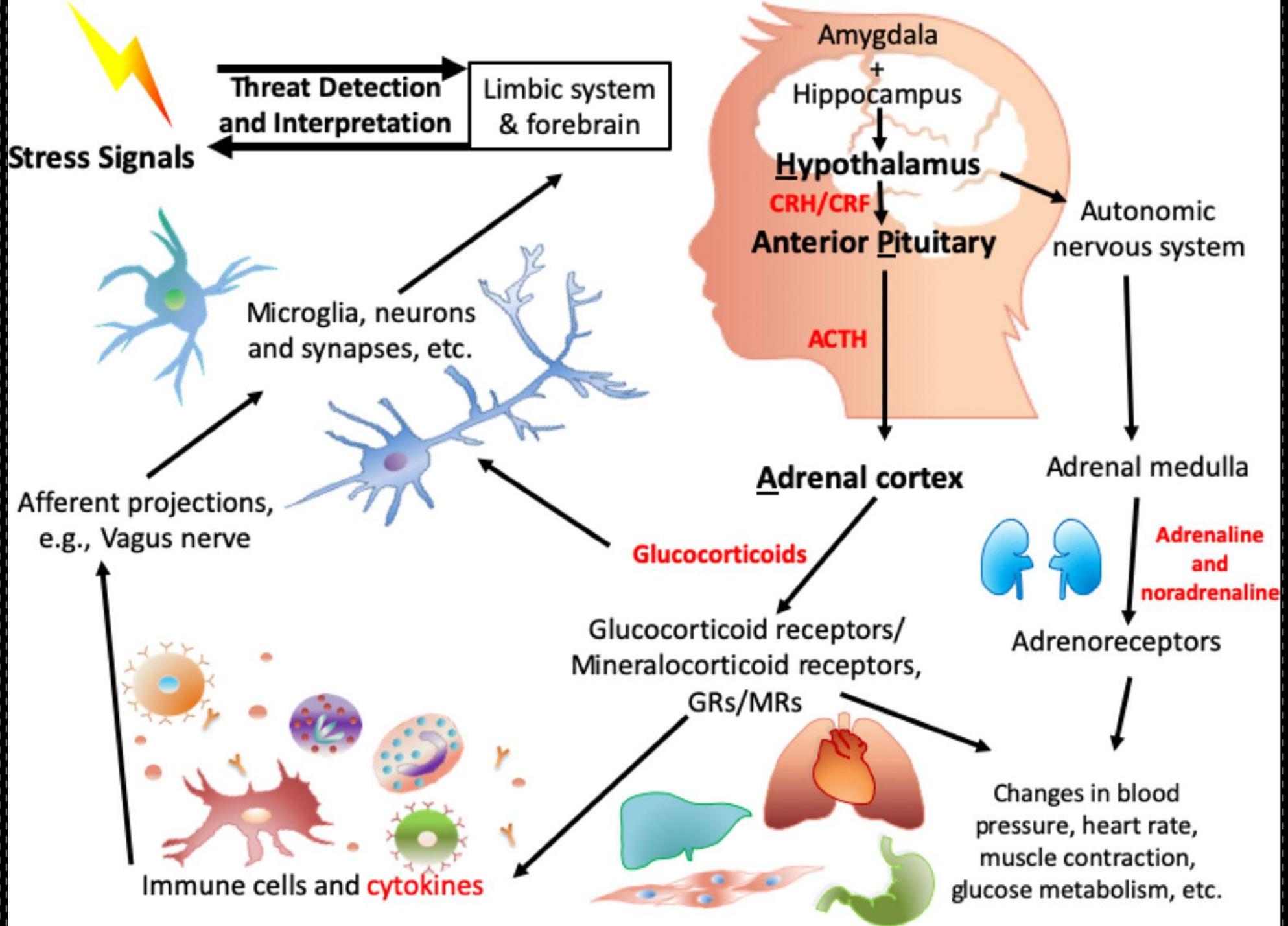
Hypothalamus (Paraventricular nucleus)

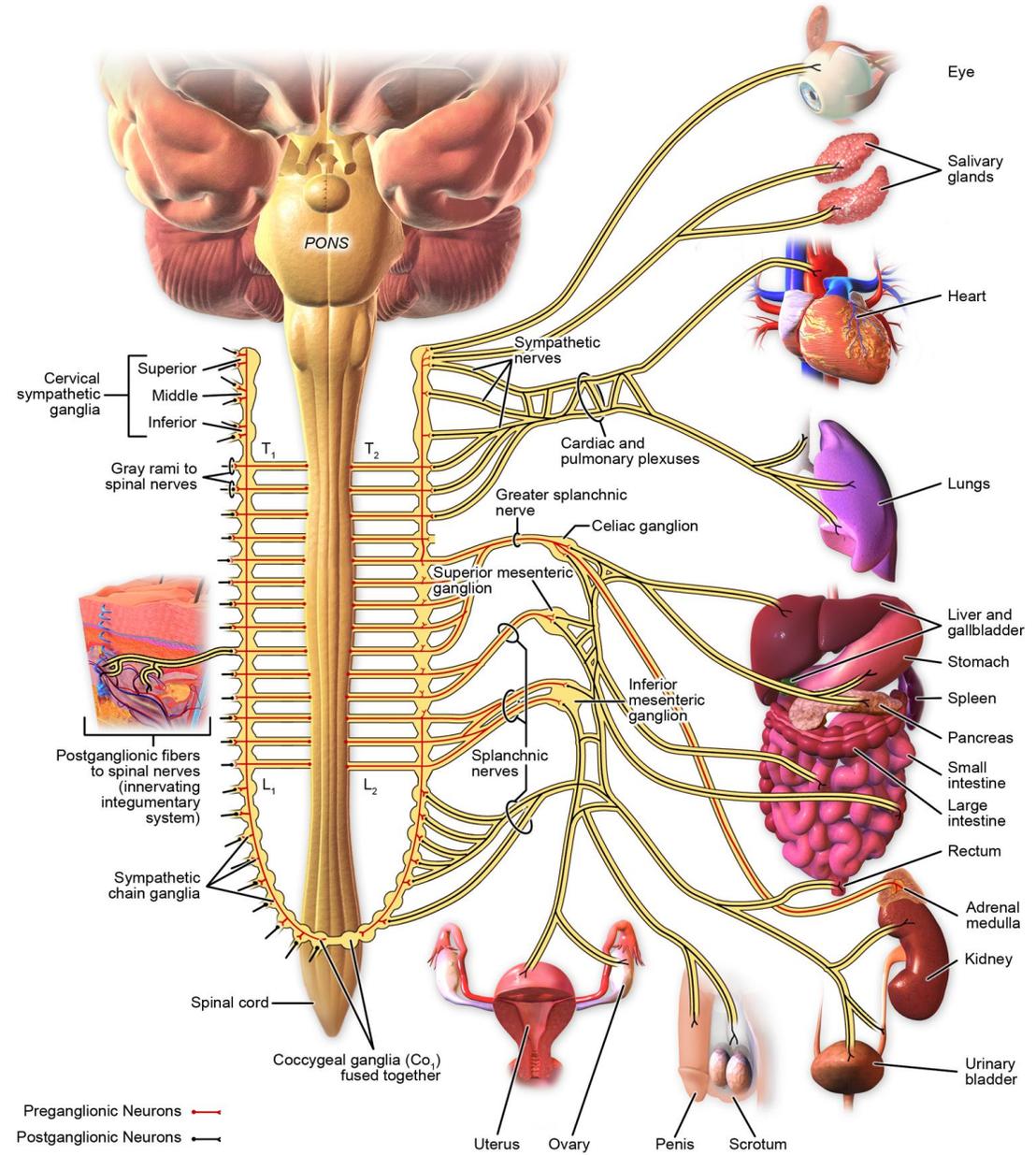
Sympathoadrenal Medullary System

- Immediate/short term stress response
- Vagal tone withdrawal
- Sympathetic stimulation of target tissue
- Adrenals release Epi into the blood
- Onset: immediately to seconds

Hypothalamus-Pituitary-Adrenal-Axis

- PVN releases ADH/CRH into ant. Pituitary
- Pituitary releases ACTH, which activates the adrenal cortex
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- Onset: minutes to hours





Sympathetic Innervation

Blausen.com staff (2014). "[Medical gallery of Blausen Medical 2014](#)". *WikiJournal of Medicine* 1 (2).

Stress Response

- Short term (minutes to hours) SAM-mediated response
 - Cardiovascular: Increased contractility and heart rate
 - Vascular shunting from skin/organs to muscles
 - Decreased vascular compliance
 - Respiratory: Bronchial dilation
 - GI: Increased motility and secretions in digestive organs, glucose produced/released from liver
 - Renal: Increased angiotensin II
 - MSK: Increased muscle contractility
 - Immune system: Increased antibody production and pro-inflammatory shift

Allostatic Load

- **Allostasis:** The ability to maintain homeostasis via stress-mediating systems
- **Allostatic load:** Theory presented in 1993 as “the wear and tear on the body which accumulates as an individual is exposed to repeated or chronic stress.”
- **3 Physiological processes increase allostatic load:**
 - **Frequent stress:** The magnitude and frequency of response to stress.
 - **Failed shut-down:** The inability to shut off compensatory processes
 - **Inadequate response:** Failure of systems to respond to challenge

Allostatic Load Theory

- Developed by Hans Selye in 1993
- Argues that in order to maintain homeostasis in the face of multiple/long-term stressful insults an organism incurs costs that may result in chronic disease through the mechanisms employed to achieve this homeostasis
 - Phase 1--Alarm Reaction: Adrenal glands are activated to release catecholamines (medulla) and glucocorticoids (cortex) to restore homeostasis
 - Phase 2—Resistance: Defense and adaptation are sustained/optimized
 - Phase 3—Exhaustion/Allostatic overload: If the stressor persists, increased “wear and tear” occurs throughout the individual as a result of the adaptive measures of phases 1 and 2.

The Threat Response System

The threat response system energizes the body preparing it to fight or flee a perceived threat. Every non-essential system shuts down and we lose the ability to think rationally.

Vision Changes

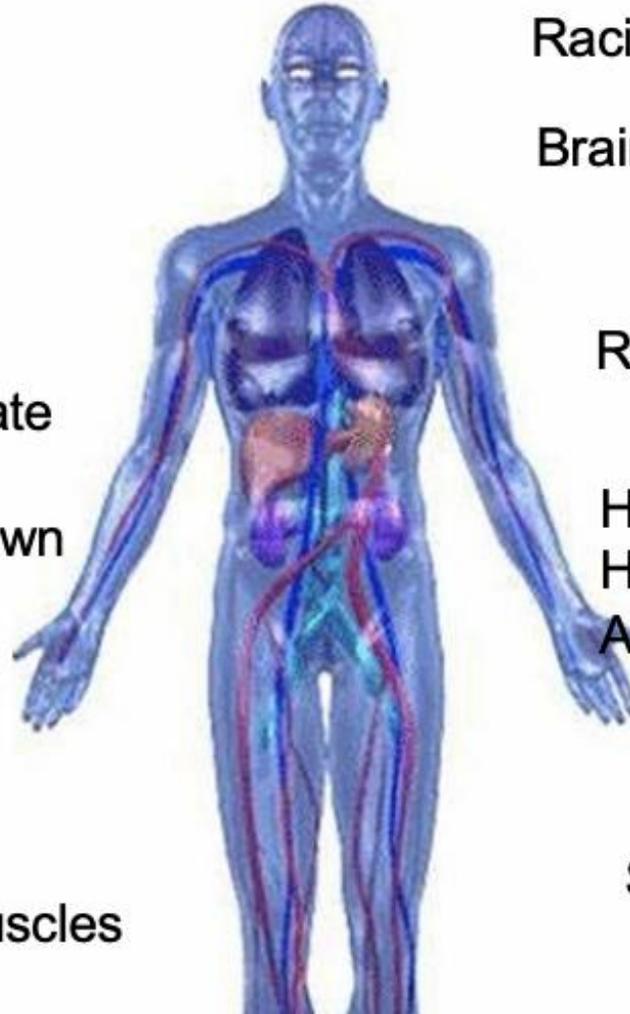
Dry Mouth

Increased heart rate

Digestive Shutdown

Cold hands

Tensed Muscles



Racing Negative Thoughts

Brain Fog

Rapid Breathing

HPA Axis

Hypothalamus, Pituitary

Adrenal (gasoline)

Bladder urgency

Sweaty Palms

Stress Response: What could possibly go wrong?

- Long-term
 - Cardiovascular:
 - Respiratory:
 - GI:
 - Renal:
 - MSK:
 - Immune system:
 - Psych:

Results of Prolonged Stress Response

- Cardiovascular: Hypertension, CAD
 - Respiratory: COPD, Pulmonary hypertension
 - GI: IBS, Peptic ulcer
 - Renal: CKD is not only the result of HTN. Renin-Angiotensin II SNS modulator, decreased systemic NOS.
 - MSK: Increased contractility, decreased motor variability, increased pain sensitization (FMS)
 - Immune system: HPA suppresses B-cell activity, favors inflammation (IL-6, TNF) Autoimmune disorders

“You’ve only got the symptoms. You haven’t got the whole disease”

-Elvis Costello

Treatments

- ACEs
 - Prevention
 - Social Programs
- Sequelar diseases
 - Medical prevention/treatment of sequelar diseases
 - Mitigate sympathetic hyertonicity
 - DHEA ⁽⁶⁾
 - Adrenergic blockers when appropriate (prazosin vs. Lasix, etc.)
 - Stellate ganglion block

Wasn't this talk supposed to be about PTSD?

Effects of prolonged hypercortisolism

- Epigenetic changes with DNA methylation in fetuses, neonates, and children
- Over-exposure to stress results in structural changes in limbic-cortical areas and with chronic exposure, decreased dendritic complexity in the hippocampus and pre-frontal cortex, and hypertrophy of the amygdala ⁽⁷⁾
- Higher cortisol levels increase likelihood of MDD⁽⁸⁾

Is There a Link Between Stress and Mental Illness?

- Increased cortisol correlates with MDD
 - ACh (PNS) inhibits release of TNF, IL-1, IL-6 (inflammatory cytokines)
- Increased SNS tone Increased cortisol (HPA) and catecholamines (SAM) and decreased PNS tone create an inflammatory milieu which pushes tryptophan towards conversion to Kynurenine rather than serotonin (9)

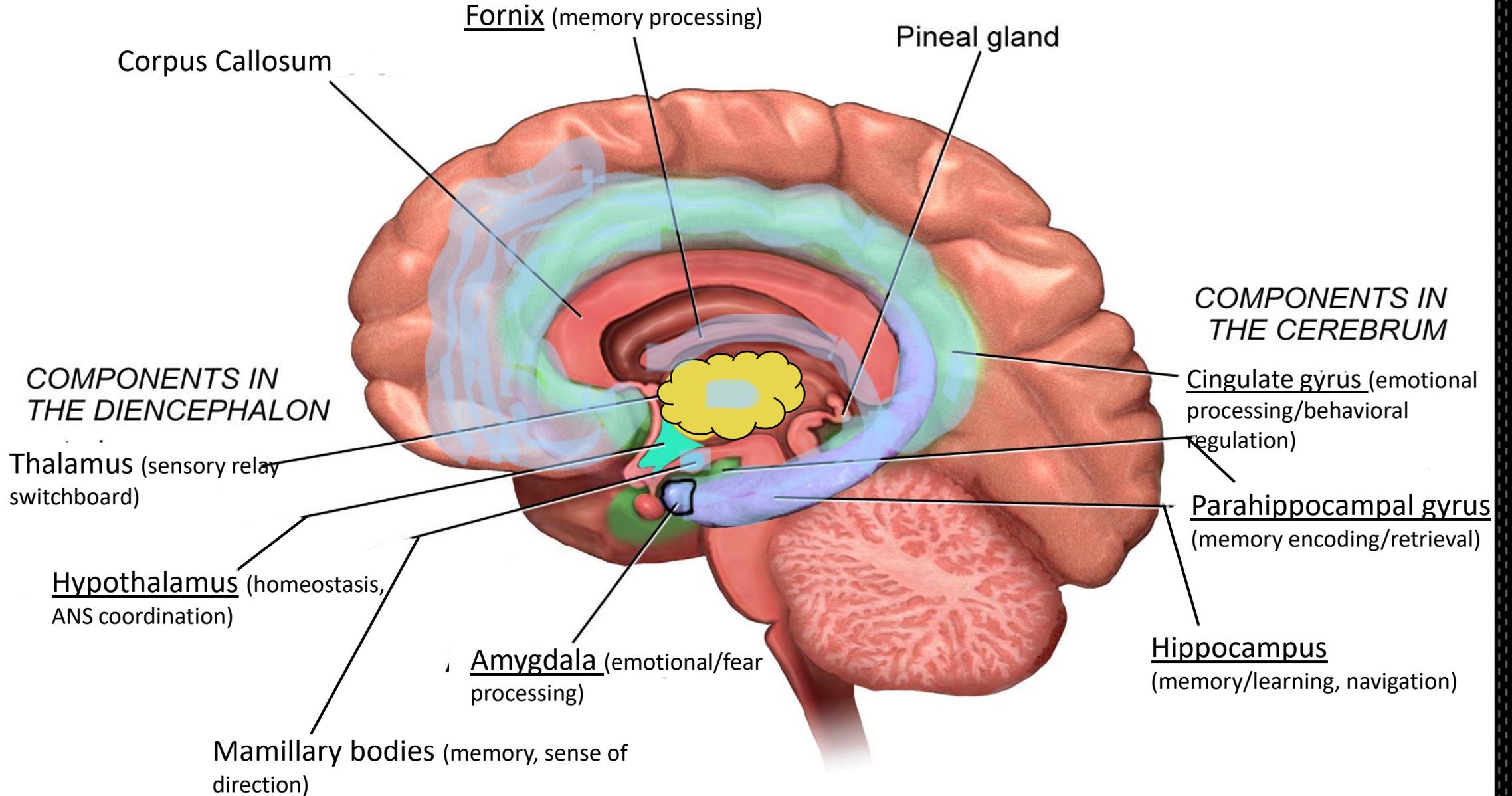
Stress and Structural Plasticity in the Brain

- Restraint-induced stress in tree shrews:
 - Neuroplastic changes in dendritic branching within 3 weeks
 - Increased glucocorticoids and excitatory AAs (glutamate), NMDA receptor activation and Ca^{++} influx result in neuron death
 - Persisting stress (> 1 mo) reduction in atrophy of hippocampus and medial prefrontal cortex (reversible), and hypertrophy of the amygdala (permanent).
- Humans with MDD were seen to have the same hippocampal atrophy. When MDD was treated, atrophy was reversible. ⁽¹⁰⁾

PTSD vs. MDD

- MDD is primarily mediated via the HPA (high cortisol) and autonomous of NE influence
- PTSD has a strong central sensitivity to GCs, and robust negative feedback inhibition (low levels of cortisol), appears to have greater input mediation from SNS (catecholamines)
- fMRI studies suggest that PTSD circuitry involves decreased ability of the ventromedial PFC to inhibit the amygdala resulting in a heightened physiologic fear response. (11)

The Limbic System



PTSD (DSM-V)

- ✘ Criterion A: Direct exposure, First person witness, Learning about a loved-one's exposure, or repeated indirect exposure to death, serious injury, or sexual violence, or threat of one of the above.
- ✘ Criterion B: Event is persistently re-experienced as: unwanted memories, nightmares, flashbacks, emotional distress or physical reactivity
- ✘ Criterion C: Avoidance of trauma-related thoughts or reminders
- ✘ Criterion D (2): Inability to recall key features of the trauma, overly negative thought about oneself/the world, exaggerated blame or self/others for the trauma, negative affect, anhedonia, feeling isolated
- ✘ Criterion E (2): Arousal and reactivity that occurs after the trauma as follows: irritability/aggression, risky/destructive behavior, hyper vigilance, heightened startle response, difficulty concentrating, difficulty sleeping
- ✘ Criterion F: Symptoms for longer than 1 month
- ✘ Criterion G: Symptoms caused distress or functional impairment
- ✘ Criterion H: Symptoms are not due to medication, substance abuse, or other illness

Complex PTSD/DESNOS

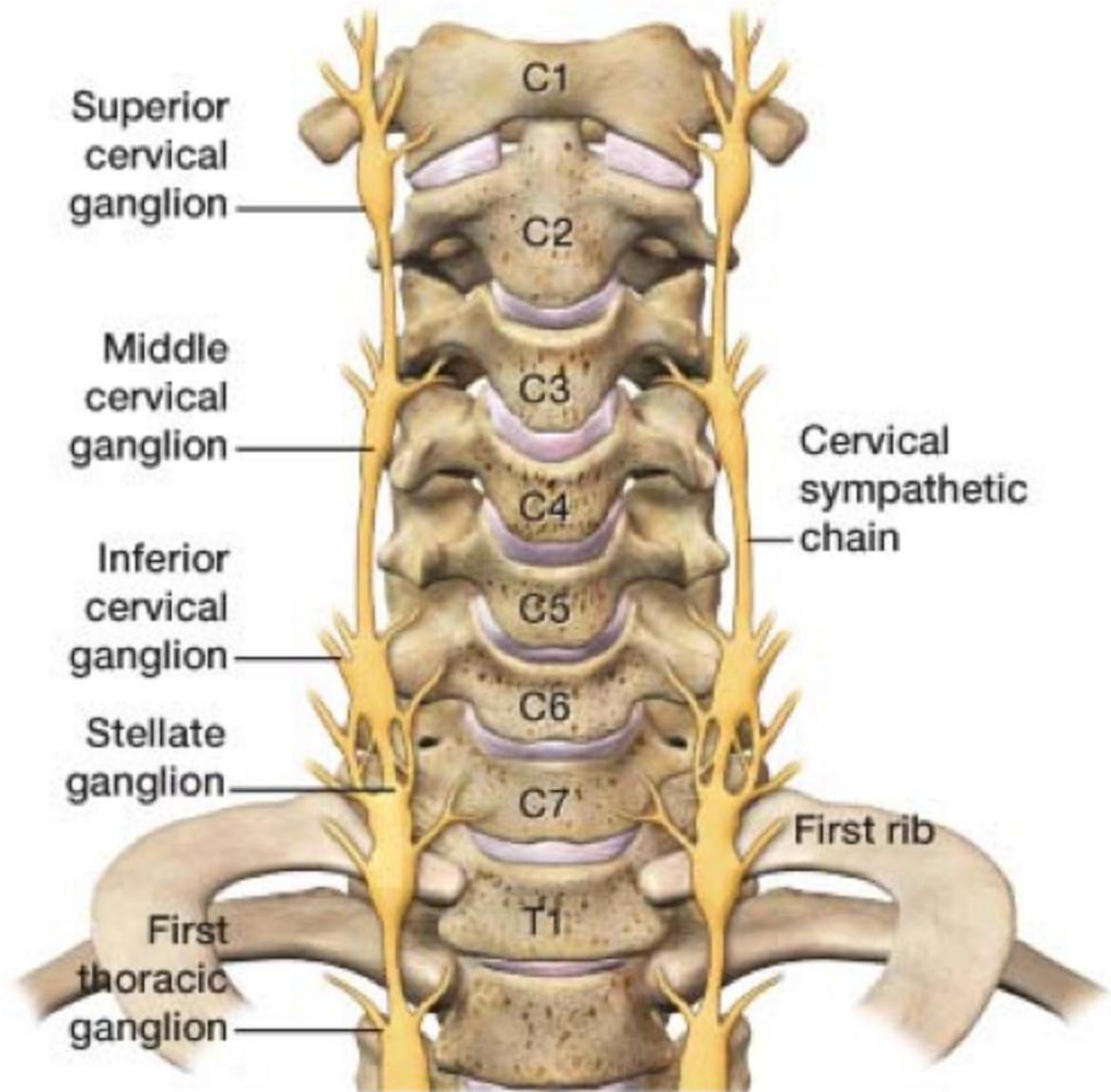
- Not included in DSM IV, V given argument that there was sufficient overlap with (regular) PTSD
- DSM-5 does include diagnostic criteria designed to address the added severity of cPTSD/DESNOS (disorders of extreme stress NOS)
 - Impulsivity, Anger, Emotional difficulties, PTSD Dissociative subtype
- WHO in ICD-11 differentiates cPTSD from PTSD by expanding on the diagnosis of PTSD to include:
 - Affect dysregulation
 - Negative self-concept
 - Disturbed relationships ⁽¹²⁾

Recommended Treatments

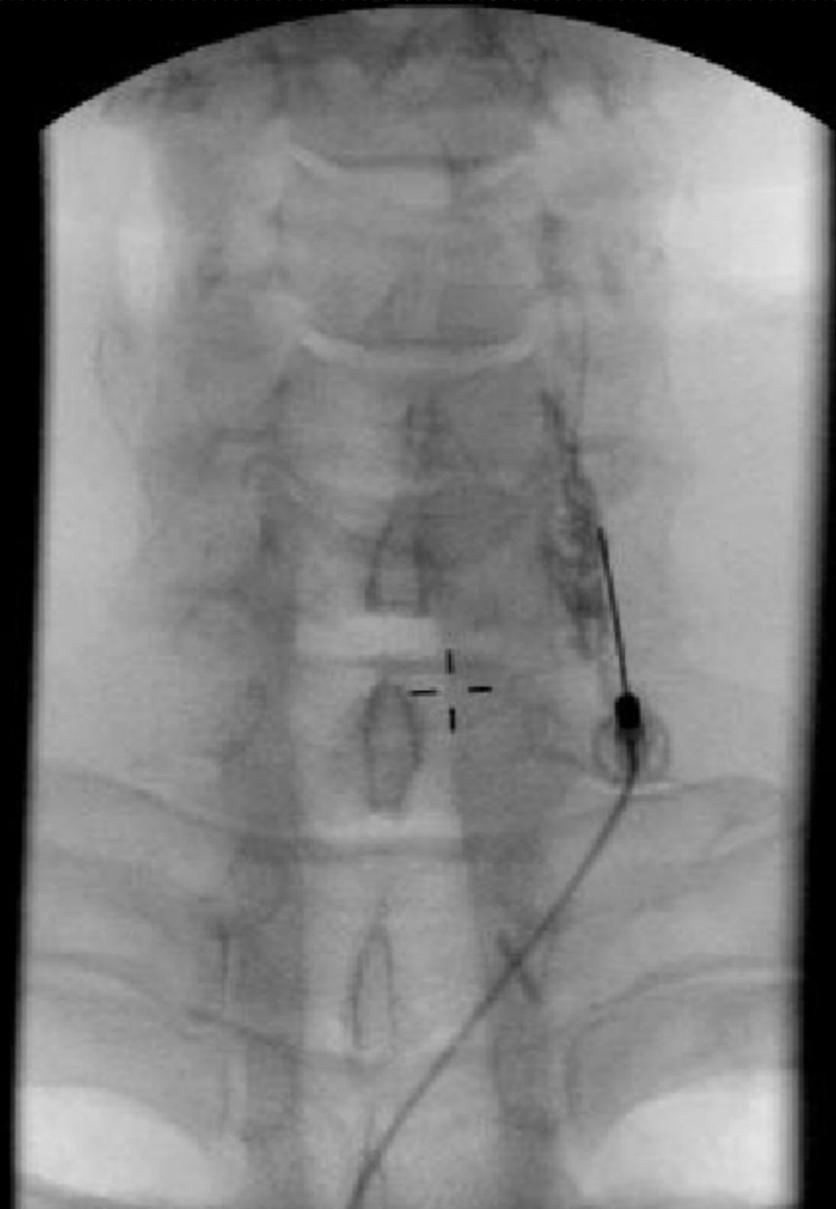
- Evidence-based psychotherapies
 - Cognitive Processing Therapy (CPT)
 - Prolonged Exposure
- VA recognizes that those with cPTSD may not benefit or may have higher drop-out rates than those with PTSD⁽¹¹⁾
 - “Talk therapy” is less effective in PTSD as it discussing the traumatic events “triggers” or re-activates the circuit of memory→emotion (fear)→SNS/ physiologic response (fight or flight)→deactivation of the pre-frontal cortex/logical reasoning, only serving to reinforce a negative response to the memory
- Eye Movement Desensitization and Reprocessing
- Emotional Freedom Technique

Stellate Ganglion

- Located anterior to C7 vertebral body
- Union of Inferior cervical ganglion and the superior thoracic sympathetic ganglia.
- Four cortical regions (insular, infralimbic (amygdala), ventromedial temporal, and ventral hippocampal) are linked via multi-synaptic connections to three sympathetic targets—the stellate ganglion, adrenal gland, and celiac ganglion. ⁽¹³⁾
- Regulates sympathetic tone for the head and upper extremities.



kVp



SGB: Mechanism of Action

- Anesthetic block of the sympathetically-oriented stellate ganglion is thought to decouple the emotional/physiological response to the triggering memory, allowing the sufferer to retrieve/process the memories and feelings without the corresponding physical effects.
- For PTSD/chronic PTSD, this is most effective with adjunctive trauma therapy
- By attenuating the sympathetic hypertonia, allostatic load is decreased and the cumulative effects of chronic sympathetic upregulation are eased. This in turn can decrease the risk of chronic disease. (14)

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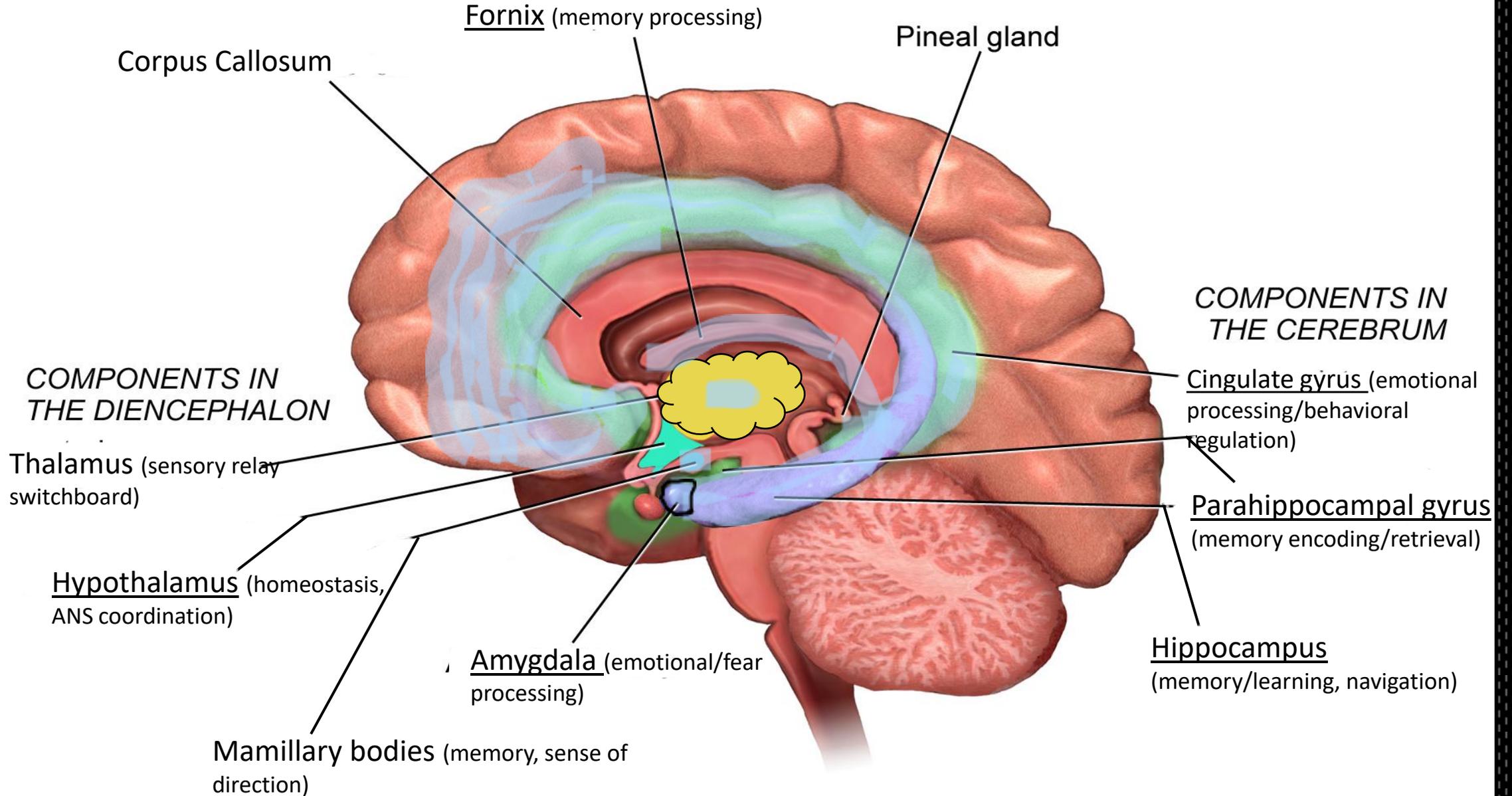
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The Limbic System



Stellate Ganglion Block

- In a series of 166 combat veterans, over 70% of patients treated with SGB had a clinically significant improvement which persisted beyond 3 months. ⁽¹⁵⁾
- Behavioral Health Clinicians Survey results
 - 96% noted 'Arousal/Reactivity' as the symptom most improved by SGB,
 - 0% described SGB as 'Harmful' or 'Not Helpful'
 - Of all psychological interventions in the 2017 APA CPG for Treatment of PTSD, SGB was perceived to be at least as useful as the highest rated standard interventions. ⁽¹⁶⁾

Stellate Ganglion Block

Clinical Indications for Stellate Ganglion Block

- CRPS
- Hyperhidrosis
- Raynauds
- Neck pain
- Radiculopathy
- Headaches/Migraines
- ACES systemic sequelae
- Herpes Zoster
- Cancer Pain
- Postherpetic neuralgia
- Phantom Limb pain
- Frost bite
- Radiation neuritis

“The good physician treats the disease;
the great physician treats the patient
who has the disease.”

--Sir William Osler

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Bonus

- https://embed.ted.com/talks/nadine_burke_harris_how_childhood_trauma_affects_health_across_a_lifetime