

Long COVID & Post-Viral Syndromes ECHO

Dysautonomia: Excessive Sympathetic Tone & Stellate Ganglion Blocks



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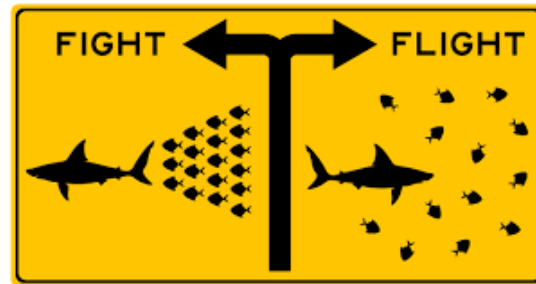
Bateman Horne Center
RESEARCH | CLINICAL CARE | EDUCATION

Patient cases are shared in this session for educational purposes. In some cases, the information does not relate to an individual, and instead represents a compilation of disease presentation.

In cases involving individual patient information, the patients have authorized the discussion of their case in this setting.

Sympathetic Nervous System Hyper-Reactivity: Symptoms (G90.9)

- Increased startle response
- Nightmares
- Panic attacks
- Emotional lability
- Muscle fasciculations (particularly after orthostatic or other physiological challenge)
- Insomnia (“wired-but-tired”), nightmares, frequent nighttime awakenings, Circadian rhythm disruption
- Medication Sensitivities (independent of the pharmacological action of the drugs)
- Sensory Sensitivities

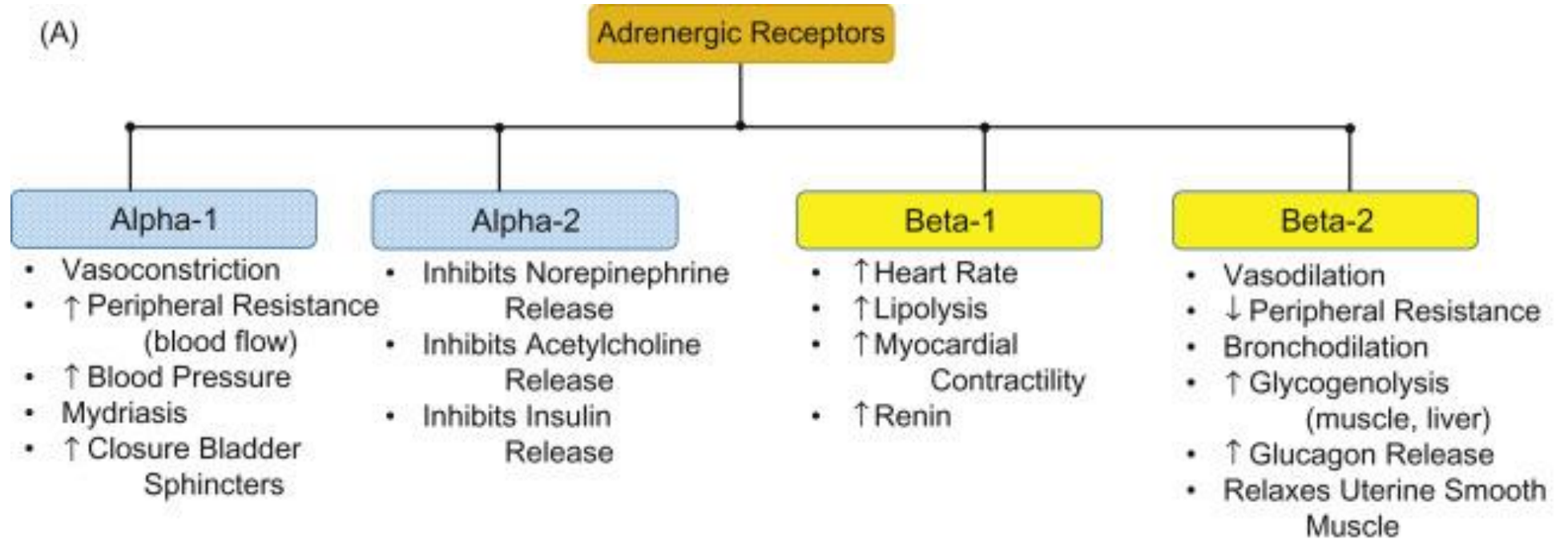


Treatments: Beta Blockers

- Propranolol (short and long-acting)
- Atenolol
- Metoprolol



- Ivabradine (Corlanor) has no direct effect on the sympathetic nervous system



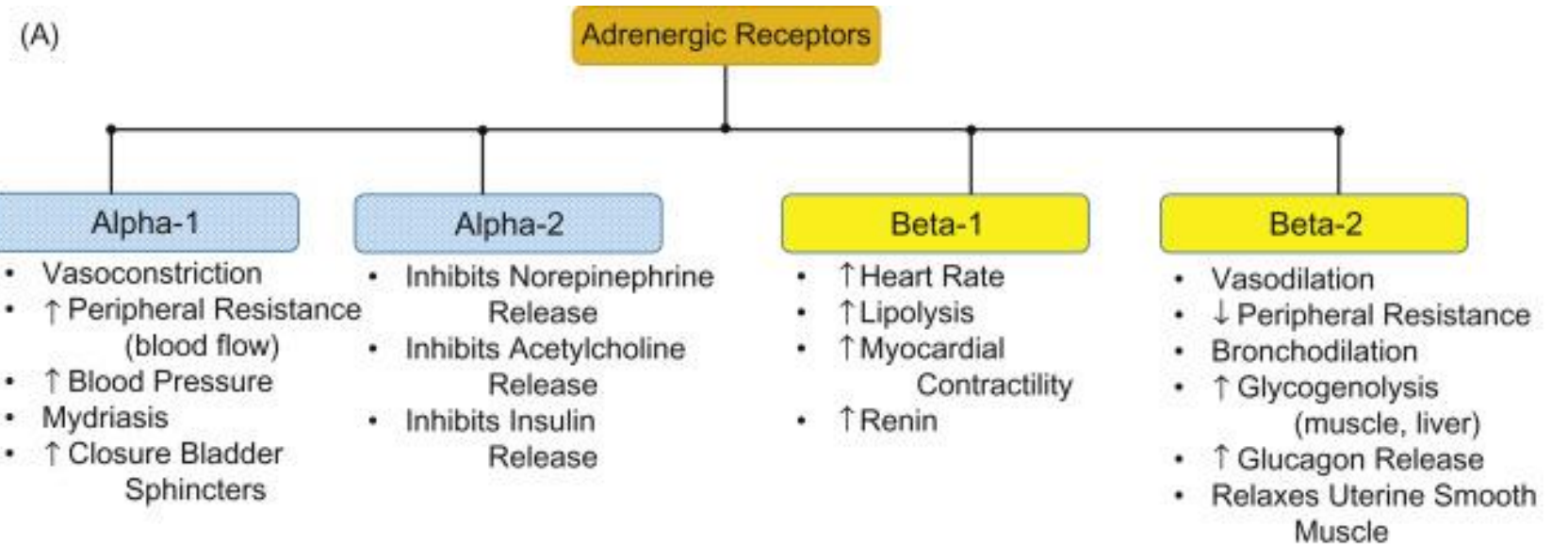
(B)

Alpha-1	Alpha-2	Beta-1	Beta-2
NE > E	E > NE	E = NE	E >> NE

NE = Norepinephrine; E = Epinephrine

Treatments: Alpha Blockers

- Clonidine (alpha 2a agonist → reduces peripheral sympathetic outflow)
- Guanfacine (selective alpha 2a agonist)
- Prazosin (alpha-1 blocker)



(B)

Alpha-1	Alpha-2	Beta-1	Beta-2
NE > E	E > NE	E = NE	E >> NE

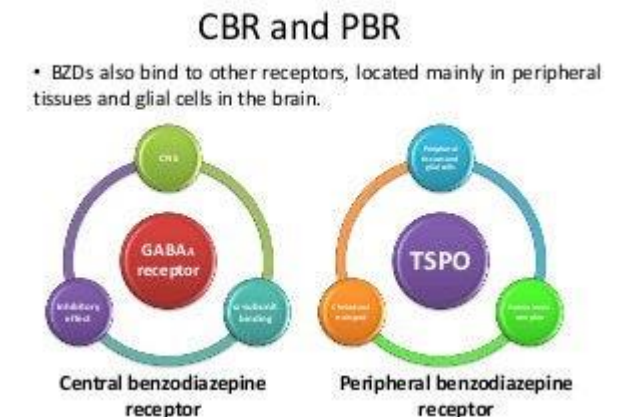
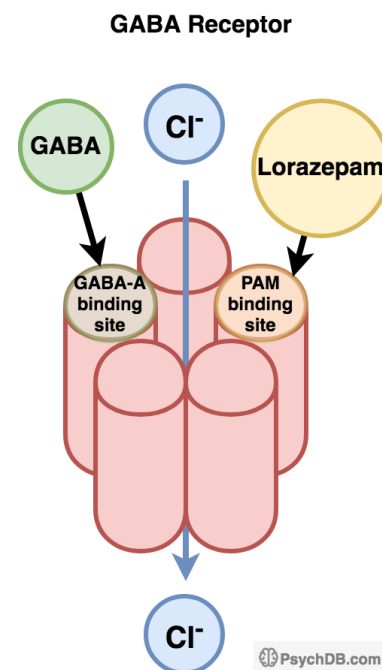
NE = Norepinephrine; E = Epinephrine

Treatments: Benzodiazepines

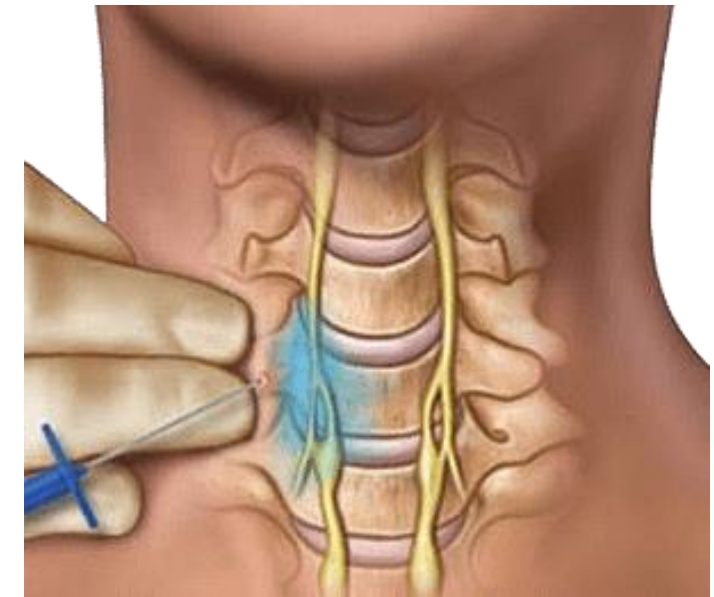
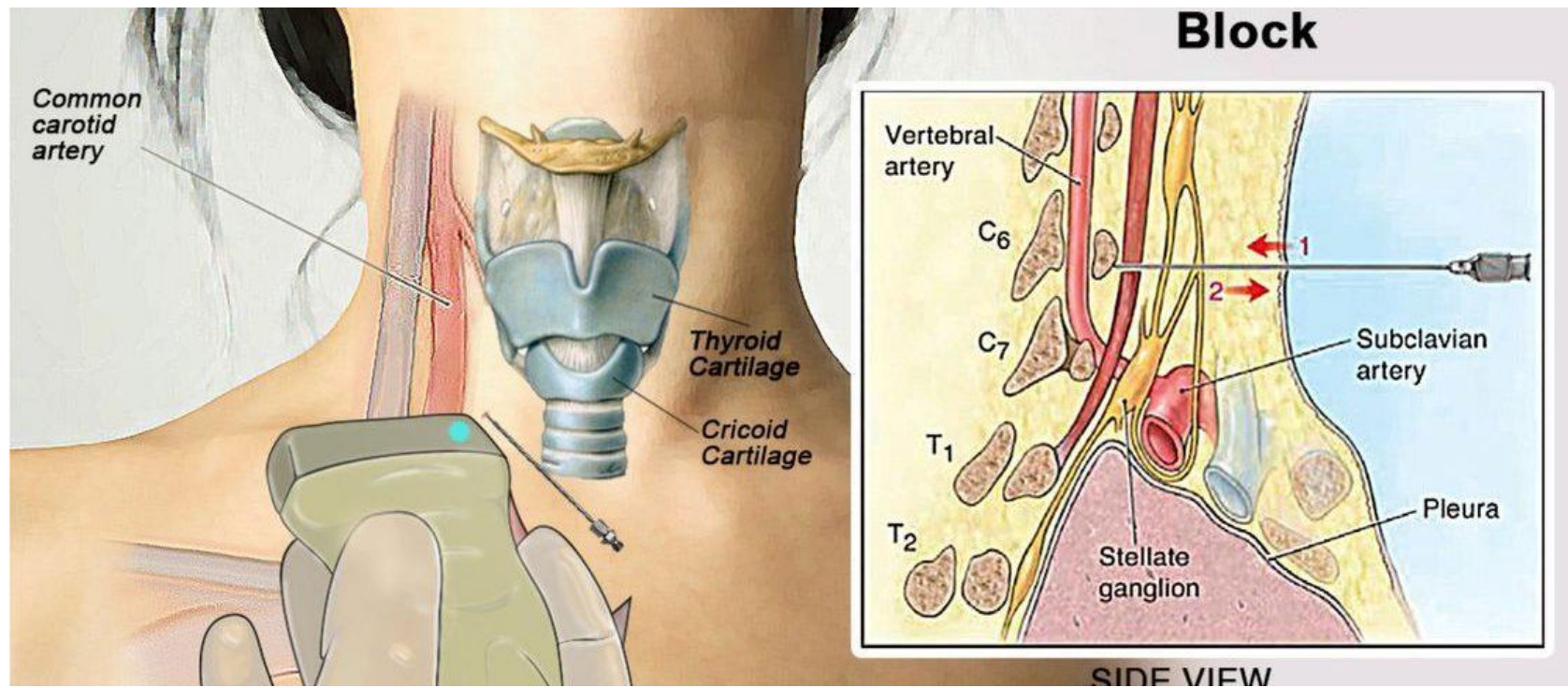
Bind to GABA_A receptors, potentiating GABA neurotransmission, increasing chloride influx into neurons and increasing the neuronal excitability threshold

- Diazepam (scheduled or prn)
- Clonazepam (scheduled)
- Lorazepam (prn)

- Importantly, there are many **peripheral** nervous system as well as **glial cell** benzodiazepine receptors
- These peripheral benzodiazepine receptors are present in particularly high concentrations **on immune cells, platelets, erythrocytes,** and cells within the **gastrointestinal tract**
- Some peripheral benzodiazepine receptors have also been implicated in regulation of **mitochondrial function**

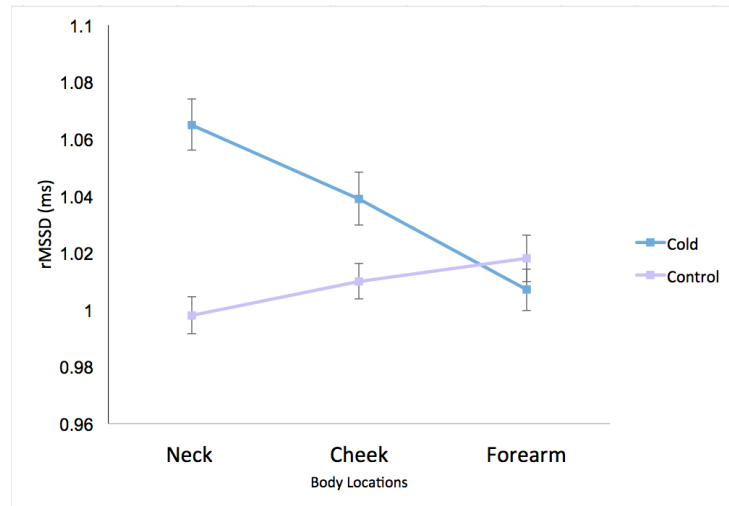


Stellate Ganglion Blocks



Treatments: Vagal Maneuvers

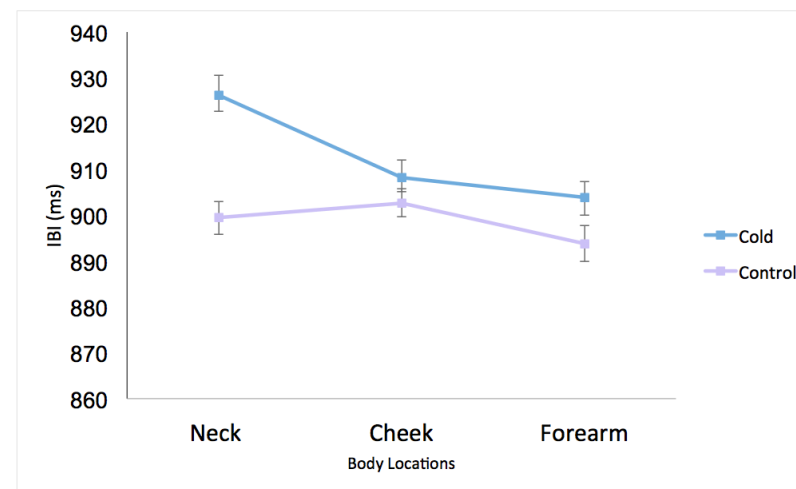
- Cranial nerves responsible for cardiac-vagal stimulation and that participate in trigeminal-brainstem-vagal pathways are located in the facial area, head, and neck regions
- Using cold to activate these nerves has been referred to as the “diving reflex,” which involves a pattern of respiratory, cardiac, and vascular responses thought to help control oxygen conservation and survival when diving



Normalized root mean square (rMSSD) of successive differences of body locations for cold stimulus – statistical measure of heart rate variability



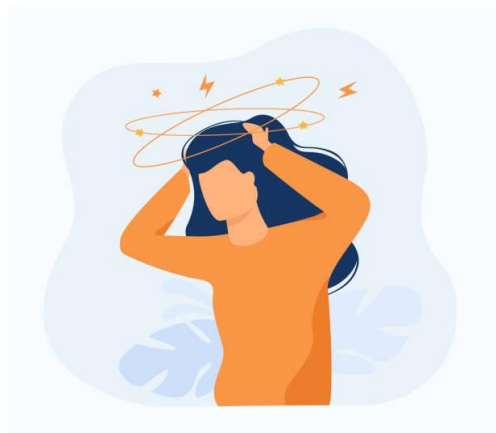
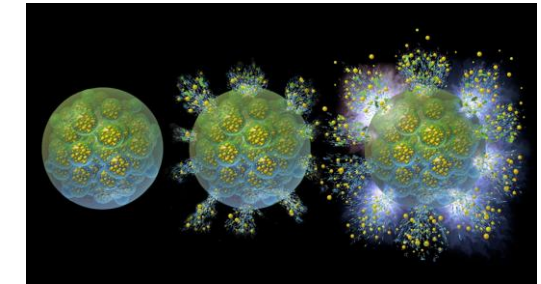
Mean interbeat intervals (IBI's) of all body locations for cold stimulus – statistical measure of heart rate responses



Treatments: Treat Co-morbidities



- Uncontrolled orthostatic intolerance can drive very significant exacerbations of sympathetic overdrive
- Mast cell activation exacerbations often significantly worsen sympathetic overdrive
- Neurological sensory sensitivities to light, sound, conversation, multiple sensory inputs can exacerbate
 - Consider aripiprazole, dextromethorphan
- Craniocervical instability/Atlanto-axial instability (CCI/AAI) may lead to irritation of sympathetic autonomic signaling at the level of the brainstem
- Sympathetic overdrive is usually worse during PEM → not much you can do to emerge from PEM other than to not make it worse



A Word on Stimulants...

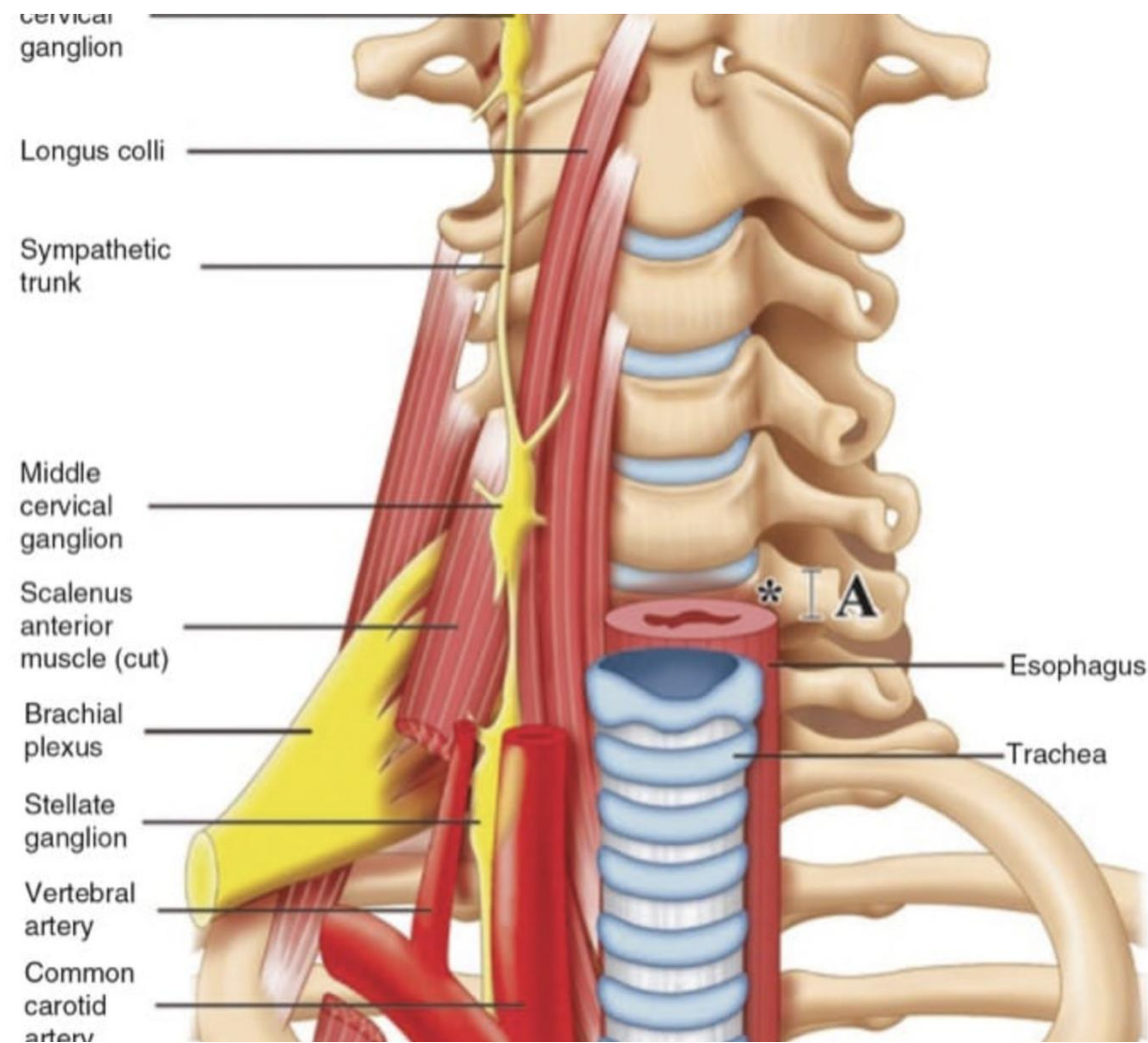
- Stimulant therapies (bupropion, modafinil, dextroamphetamine-amphetamine, methylphenidate, lisdexamphetamine) are often used to help improve brain fog, attention, and other cognitive complaints in PASC
- Remember that stimulants can significantly alter or worsen sympathetic overdrive or hypervigilance
- Generally best practice to implement these therapies only after making some clinical improvements in symptoms of sympathetic overdrive first



Invisible Pain: Novel use of the Stellate Ganglion Block to change lives

Gregory Condie DO
Interventional Spine and Pain

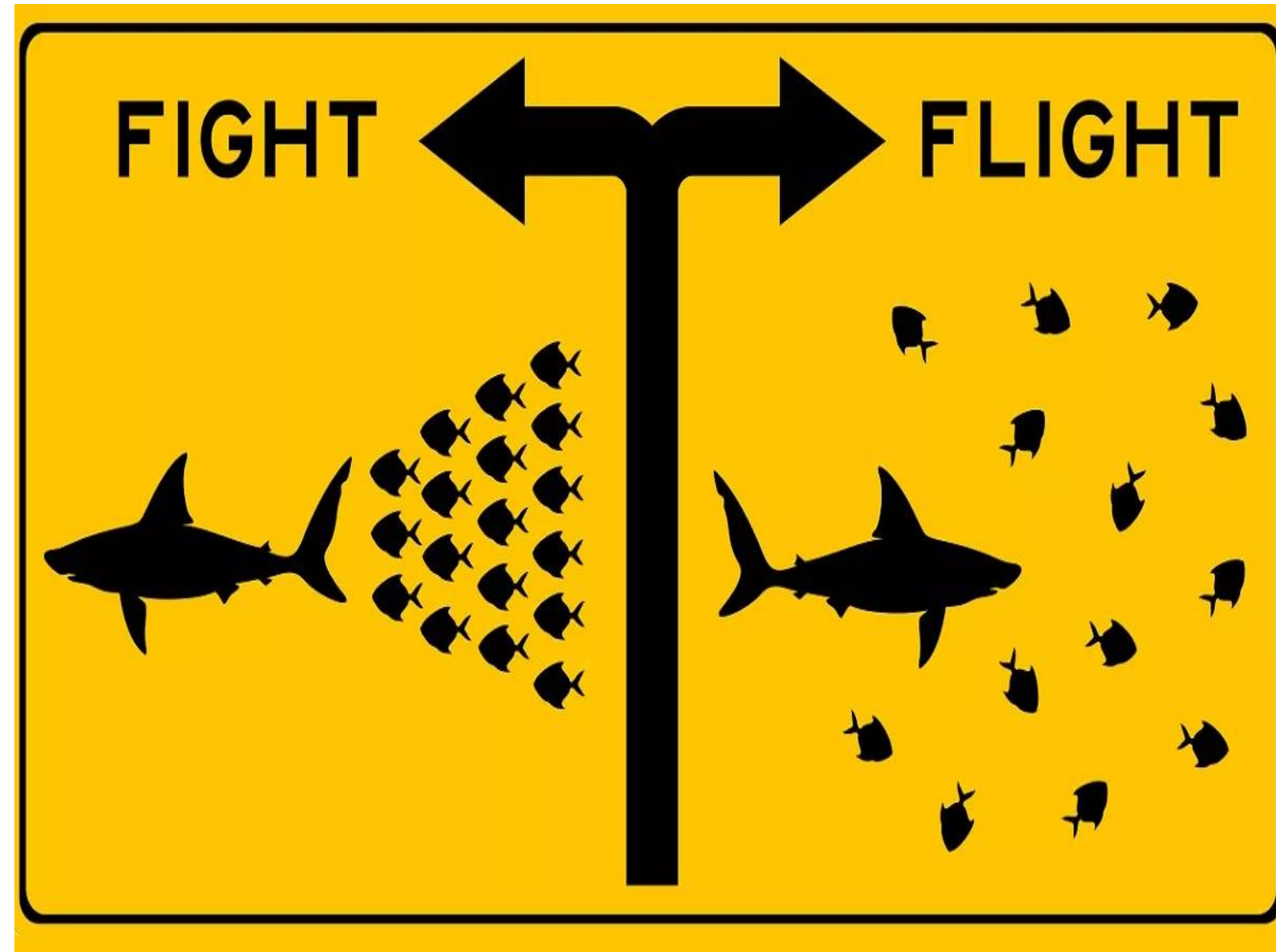
The Sympathetic Nervous System



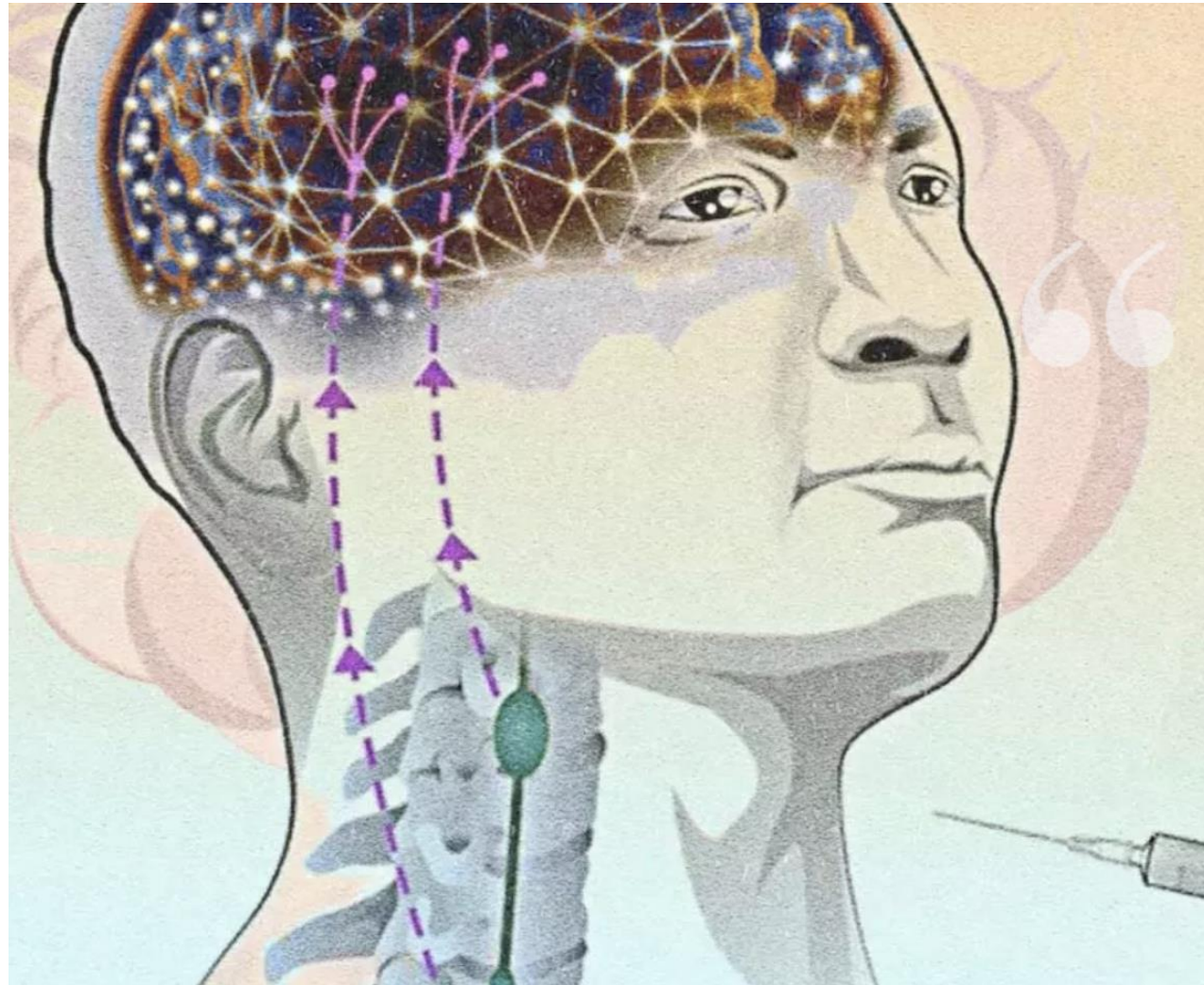
- Your sympathetic nervous system is a network of nerves that helps your body activate its “fight-or-flight” response. This system’s activity increases when you’re stressed, in danger or physically active. Its effects include increasing your heart rate and breathing ability, improving your eyesight and slowing down processes like digestion.

The Fight or Flight Response

- When you experience something traumatic, the brain shuts down all nonessential systems and moves into the “lower” brain systems. This activates the sympathetic nervous system and signals the release of stress hormones, preparing you for survival mode: fight, flight, or freeze.



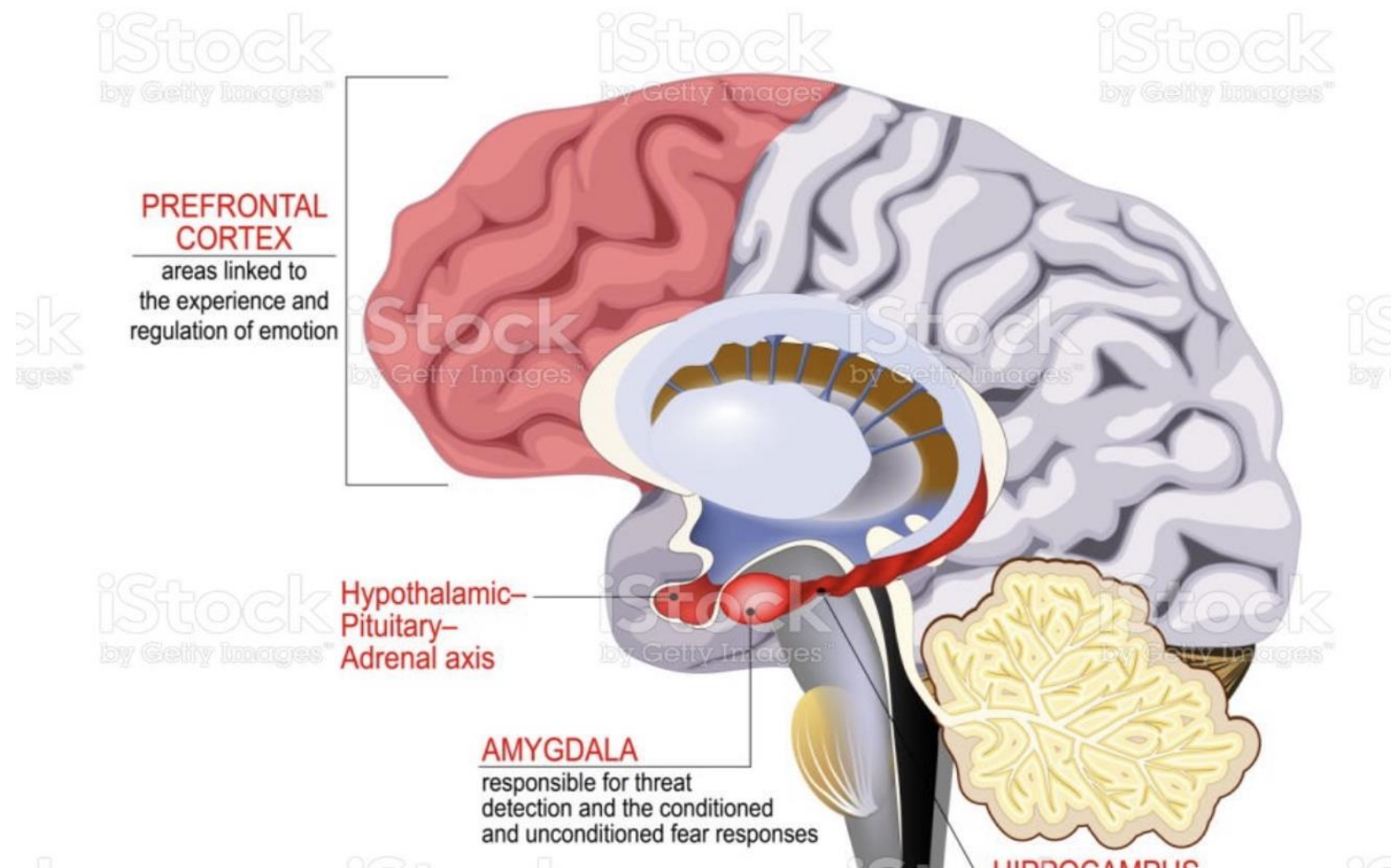
Why the Stellate Ganglion Block?



- One proposed mechanism of action is that SGB might inhibit connections between the peripheral sympathetic nerve system and regions of the cerebral cortex thought to be abnormally activated in PTSD.

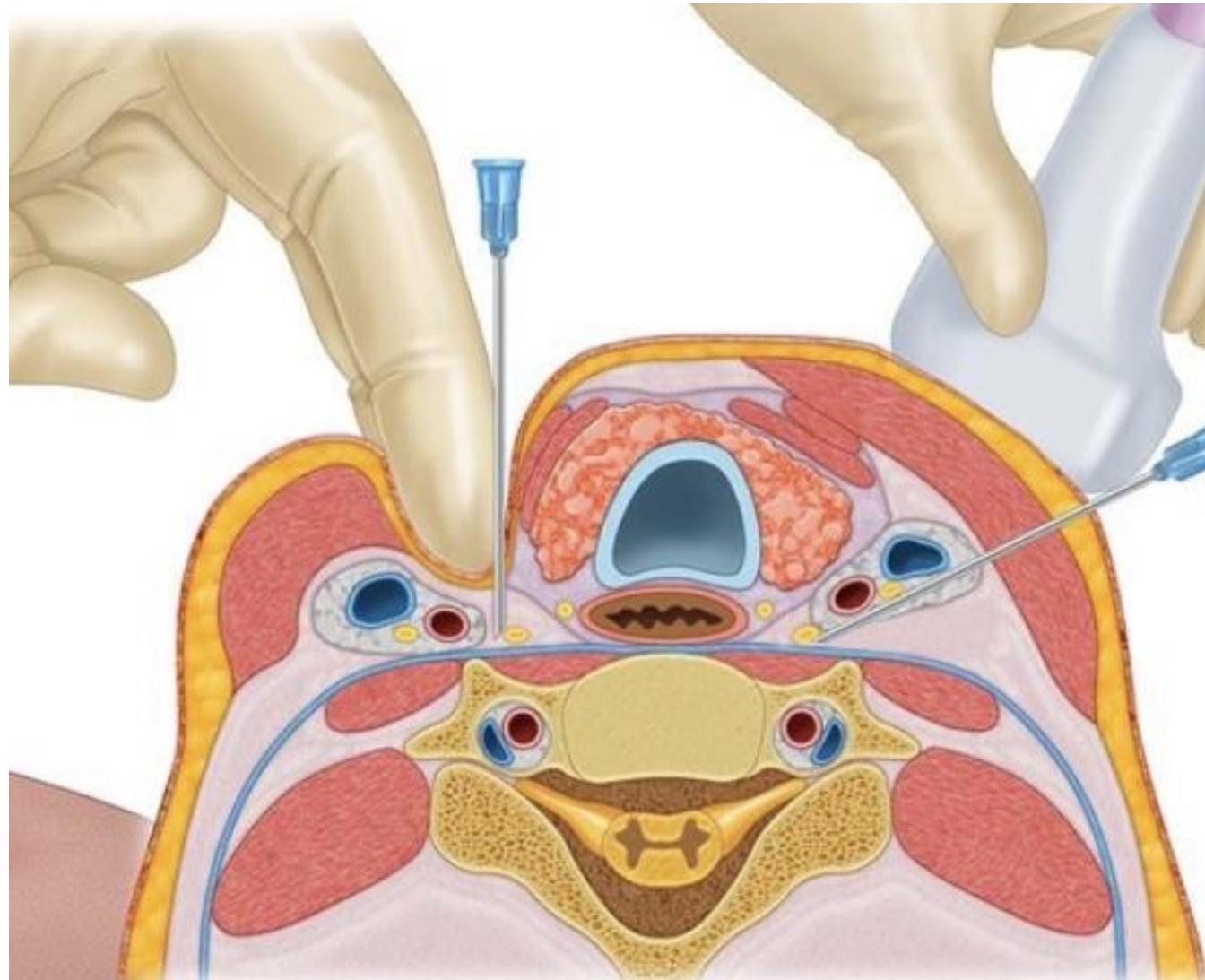
PTSD Affects on the Brain

Posttraumatic stress disorder



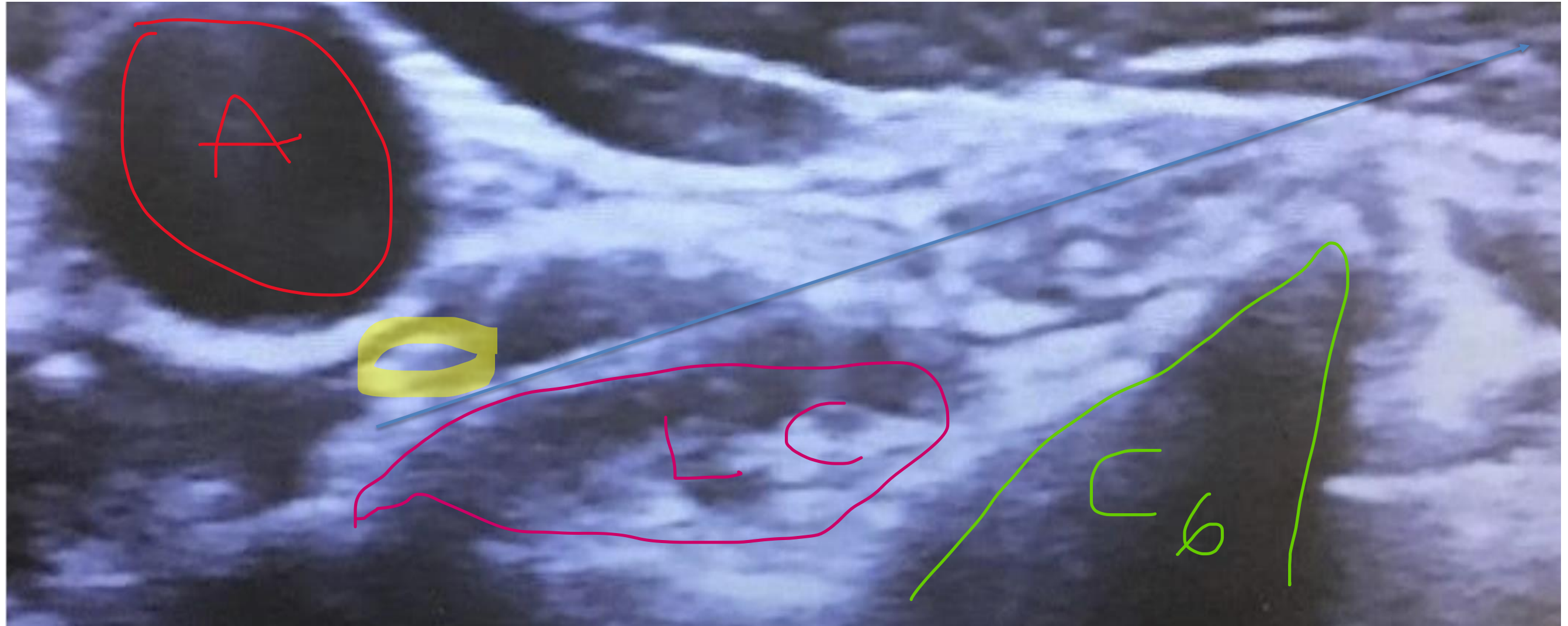
- Amygdala
- Hippocampus
- Prefrontal Cortex

Stellate Ganglion Block for PTSD



- Effect of Stellate Ganglion block treatment on PTSD. A randomized clinical trial.

It was a sham controlled randomized trial, 2 blocks, 2 weeks apart that were effective in reducing clinician administered scale score over 8 weeks.



The study showed improvement of sham by 50% in symptom severity score.





HORNERS

Canva photo

What else can the SGB do?

Conditions

Post-traumatic stress disorder

Anosmia

Long-COVID

Chronic fatigue syndrome

Hot flashes, vasomotor symptoms associated with menopause

Ventricular tachyarrhythmias

- Better sleep
- Better memory and concentration
- Decrease in anxiety, panic attacks and depression
- An ability to connect with others again
- Less jumpiness or nervousness
- Improved intimacy and sexual function

What about COVID?

- After recovering from COVID-19, a significant proportion of symptomatic and asymptomatic individuals develop Long COVID. Fatigue, orthostatic intolerance, brain fog, anosmia, and ageusia/dysgeusia in Long COVID resemble "sickness behavior," the autonomic nervous system response to pro-inflammatory cytokines (Dantzer et al., 2008).
- Aberrant network adaptation to sympathetic/parasympathetic imbalance is expected to produce long-standing dysautonomia. Cervical sympathetic chain activity can be blocked with local anesthetic, allowing the regional autonomic nervous system to "reboot."

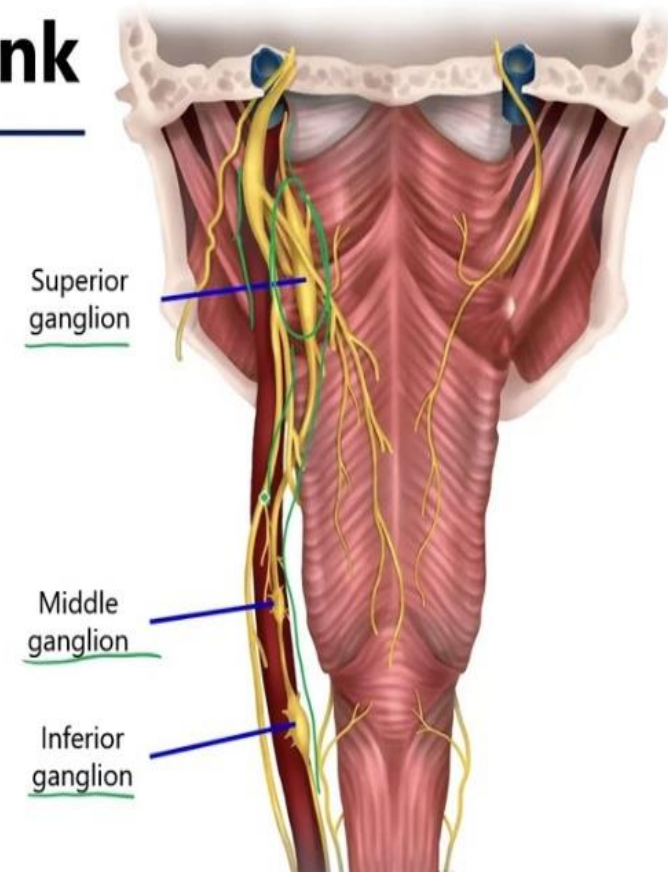


LONG COVID

- Sympathetic innervation to the head, neck, upper limbs, and upper thoracic region including the thymus, heart, lungs and the lacrimal, salivary, thyroid, and pineal glands is provided by the cervical sympathetic chain, which consists of the superior cervical ganglion, middle cervical ganglion, inferior cervical ganglion, and first thoracic ganglion.

Cervical Sympathetic Trunk

- Cervical sympathetic ganglia fuse
- **Superior cervical ganglion**
 - Fused C1-4
 - Sympathetics to head via perivascular plexuses
 - Vasomotor (constrictor) & Sudomotor (sweat gland) fibers to head via perivascular plexuses
 - Cardiac brs.
- Middle cervical ganglion
- Inferior cervical ganglion



Pilot Case Study: **Stellate Ganglion Block for the Treatment of COVID-19-Induced Olfactory Dysfunction: A Prospective Pilot Study**

- COVID 19 more than 12 months ago with persistent Olfactory dysfunction
- bilateral SGB
- 1 month follow up
- Clinical Global Impression-Improvement Scale for smell loss.

Case continued...

- 20 subjects, mean age 46 and mean OD 5 months
- After 1 month,
 - 10 (50%) participants experienced at least slight subjective improvement in their OD,
 - 11 (55%) attained a clinically meaningful improvement in smell identification using the UPSIT
 - 7 (35%) achieved a clinically meaningful improvement in olfactory-specific quality of life (QoL) measured by the ODOR.
 - Clinically significant difference

Conclusion

- Sequential SGBs for COVID-19-associated OD were safe and associated with modest improvements in subjective olfaction, odor identification, and olfactory-specific QoL.
- A placebo-controlled trial is warranted to determine the efficacy of SGBs for COVID-19-associated OD.

Stellate ganglion block reduces symptoms of Long COVID: A case series.

- Two Long COVID patients using stellate ganglion block
- Dysautonomia implications
- Case series suggesting that a regional sympathetically mediated process is involved in the maintenance of their Long COVID symptoms.
- Pathophysiology of Long COVID/PASC patients.
- The autonomic nervous system has feedback loops

COVID and POTS

- Cerebral blood flow (CBF) connection to the cervical sympathetic chain.
- The connection between Long COVID and myalgic encephalitis/chronic fatigue syndrome (ME/CFS) as well as postural orthostatic tachycardia syndrome (POTS).

Continued...

- Compared to healthy controls, ME/CFS patients ubiquitously display reduced CBF and impaired cognitive function during orthostatic testing ([van Campen et al., 2020a](#); [van Campen et al., 2020b](#); [Medow et al., 2014](#));
- a impairment of CBF restoration is linearly related to disease severity ([van Campen et al., 2021](#)).
- After strenuous mental tasks, CBF fails to recover normally in regions involved in memory, goal-oriented attention, and visual function ([Staud et al., 2018](#)).
- Similarly, impaired CBF and cognitive dysfunction are observed in POTS patients with orthostatic challenge and with a prolonged cognitive stress test ([Wells et al., 2020](#)).

Continued...

- SGB causes “luxury perfusion” that should alleviate symptoms associated with impaired CBF.
- Improvement in anosmia after SGB has been reported previously, although the mechanism is unknown ([Moon et al., 2007](#); [Park et al., 2013](#); [Moon et al., 2013](#))

Continued...

- CBF affects on taste and smell
- Affects last longer than the usual duration of lidocaine.
- Possibilities may include:
 - local recalibration of regional sympathetic influence,
 - central integration of the effects of increased CBF,
 - rebalancing of the interaction between the nervous and immune systems.

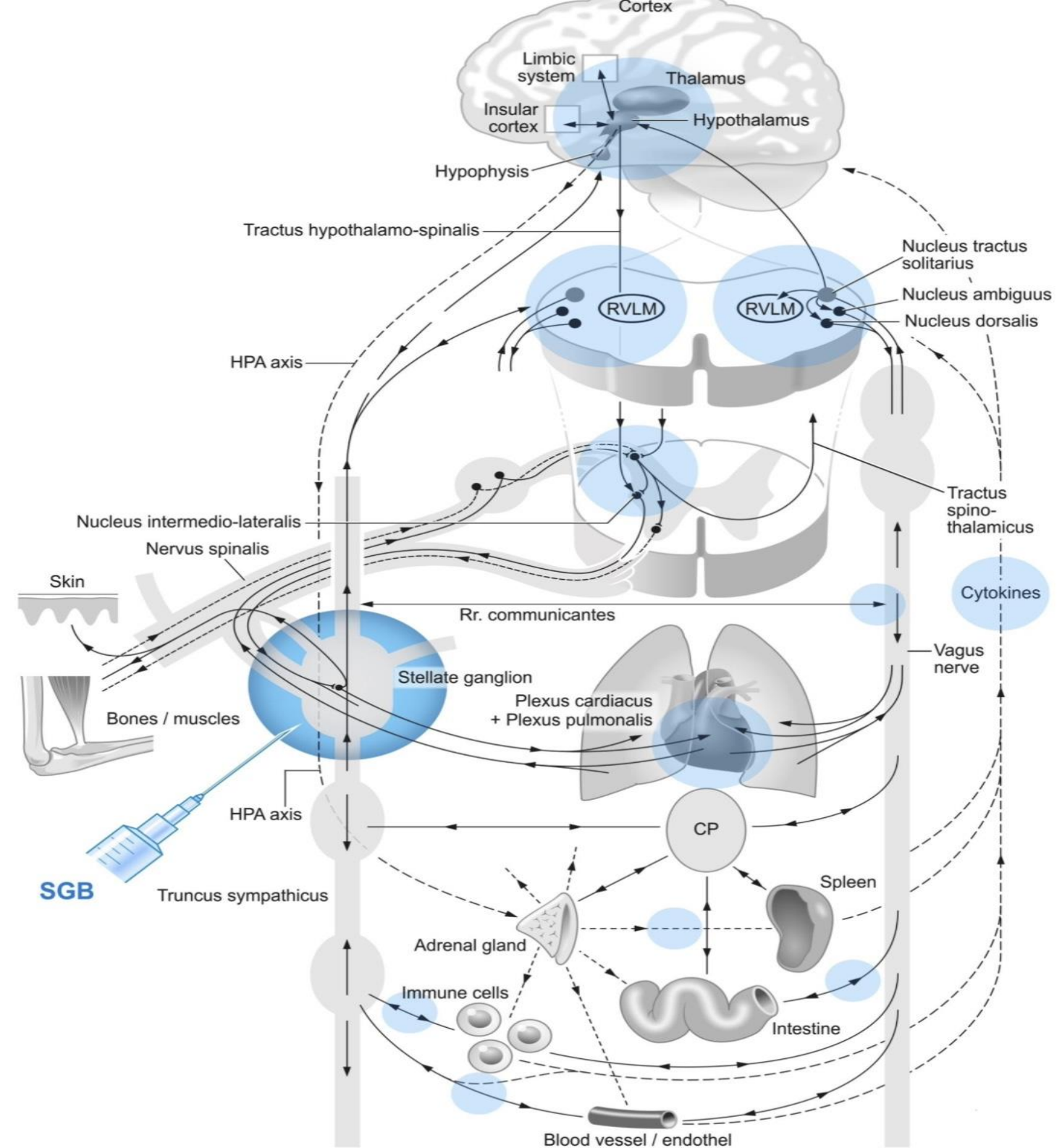
Connection between the ANS and immune system

- The nervous and the immune system were traditionally thought to be involved in separate functions, it has become clear since the works of Elenkov et al. in 2000 and Tracey in 2002 that the ANS and the immune system (and thereby inflammatory cascades) are in fact inseparable.

Continued...

- The immune and inflammatory processes are – also in the case of a [virus](#) infection – controlled by the autonomic nervous system (ANS)
- the nerve-immune-inflammation cascade
- SGB reset can affect all 3 parts of the cascade due to the Interdependent positive feedback loops.

The Complex Role of the ANS and SGB



Regulation of acute refractory hyperinflammation in viral and other diseases by means of stellate ganglion block. A conceptual view with a focus on Covid-19
 November 09, 2021 DOI:<https://doi.org/10.1016/j.autneu.2021.102903>

THANK YOU!