The Role of The Vagus Nerve In Circadian Biology

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ACA-CDID Conference

Savannah GA 2025

Faculty Disclosure Information

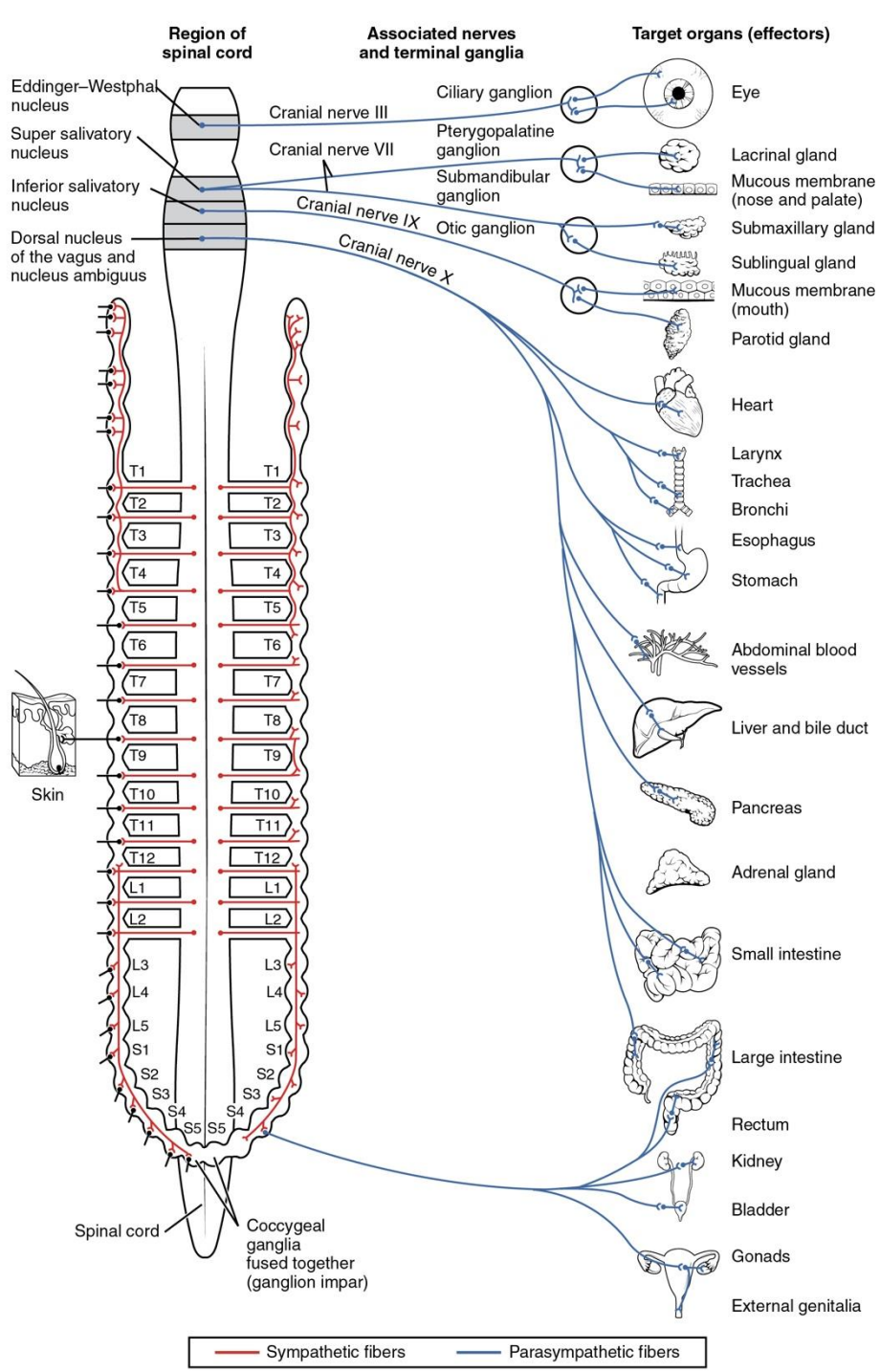
- Faculty Name: Navaz Habib

- Relationships with Commercial Interests:
  - Speaking and Consulting – ElectroCore Inc. (Truvaga)
  - Speaking – Berkeley Life Professional
  - Speaking – Rupa Health

A Little About Me

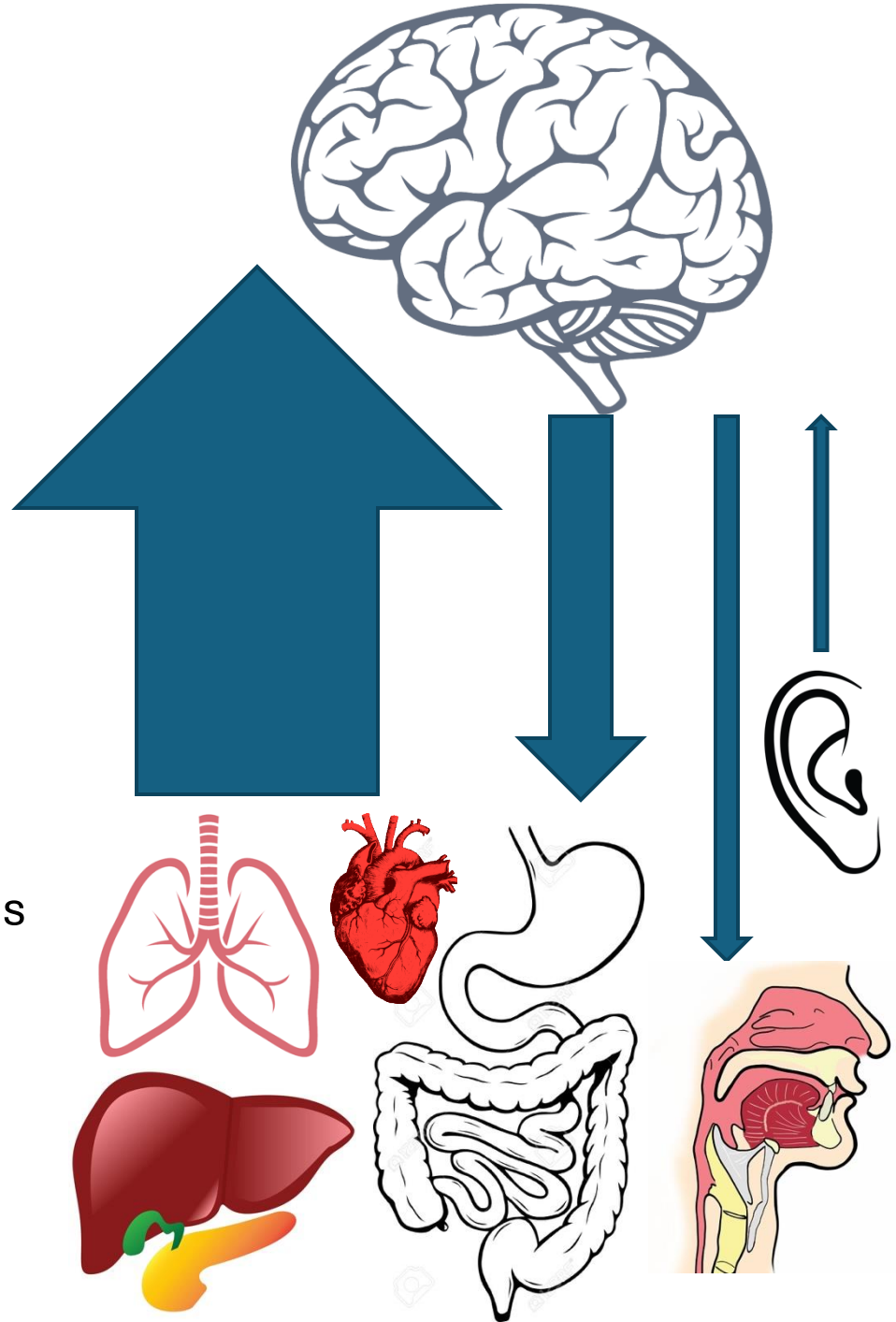
- Canadian Memorial Chiropractic College
  - Class of 2010 Valedictorian
- Certified Acupuncture provider
- Certified Functional Medicine Practitioner
- Husband and father to 2 amazing daughters
- Founder of Health Upgraded, online health consulting and education resource

Why the Vagus Nerve?


Region of spinal cord
Associated nerves and terminal ganglia
Target organs (effectors)
Eddinger–Westphal nucleus
Super salivatory nucleus
Inferior salivatory nucleus
Dorsal nucleus of the vagus and nucleus ambiguus
Cranial nerve III
Cranial nerve VII
Cranial nerve IX
Cranial nerve X
Ciliary ganglion
Pterygopalatine ganglion
Submandibular ganglion
Otic ganglion
Eye
Lacrinal gland
Mucous membrane (nose and palate)
Submaxillary gland
Sublingual gland
Mucous membrane (mouth)
Parotid gland
Heart
Larynx
Trachea
Bronchi
Esophagus
Stomach
Abdominal blood vessels
Liver and bile duct
Pancreas
Adrenal gland
Small intestine
Large intestine
Rectum
Kidney
Bladder
Gonads
External genitalia
Skin
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
T11
T12
L1
L2
L3
L4
L5
S1
S2
S3
S4
S5
Spinal cord
Coccygeal ganglia fused together (ganglion impar)
Sympathetic fibers
Parasympathetic fibers

Vagus Nerve Signaling

- 80% Parasympathetic Afferent
  - Information from Organs to the Brain
- 15% Parasympathetic Efferent
  - Rest and Digest information from Brain to Organs
- 4% Motor
  - To the muscles of the airway, throat and vocal cords
- 1% Sensory
  - From the skin of the ear



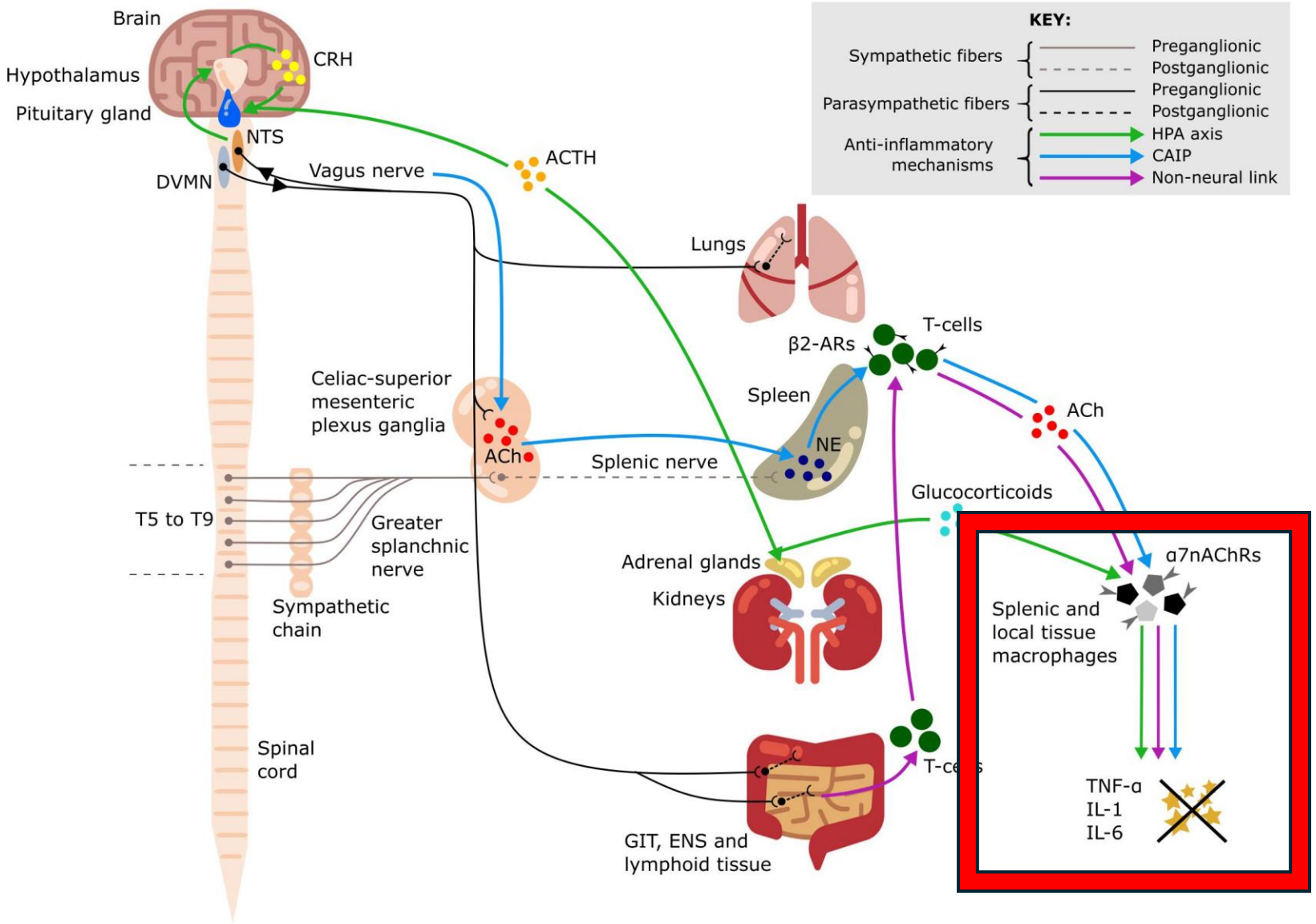
Systems Managed by Vagus Nerve

- **The Cholinergic Anti-Inflammatory Pathway**
  - Macrophage and Microglial activity are modulated by Acetylcholine, regulated by Vagus nerve signaling centrally and peripherally
- Microbiome–Gut–Brain Axis
  - Stomach acid production, satiety signaling, intestinal peristalsis, microbiome management, maintenance of intestinal permeability etc.
- Interoception
  - Awareness of visceral organ function, dysfunction and inflammation

Other Systems Managed by Vagus Nerve

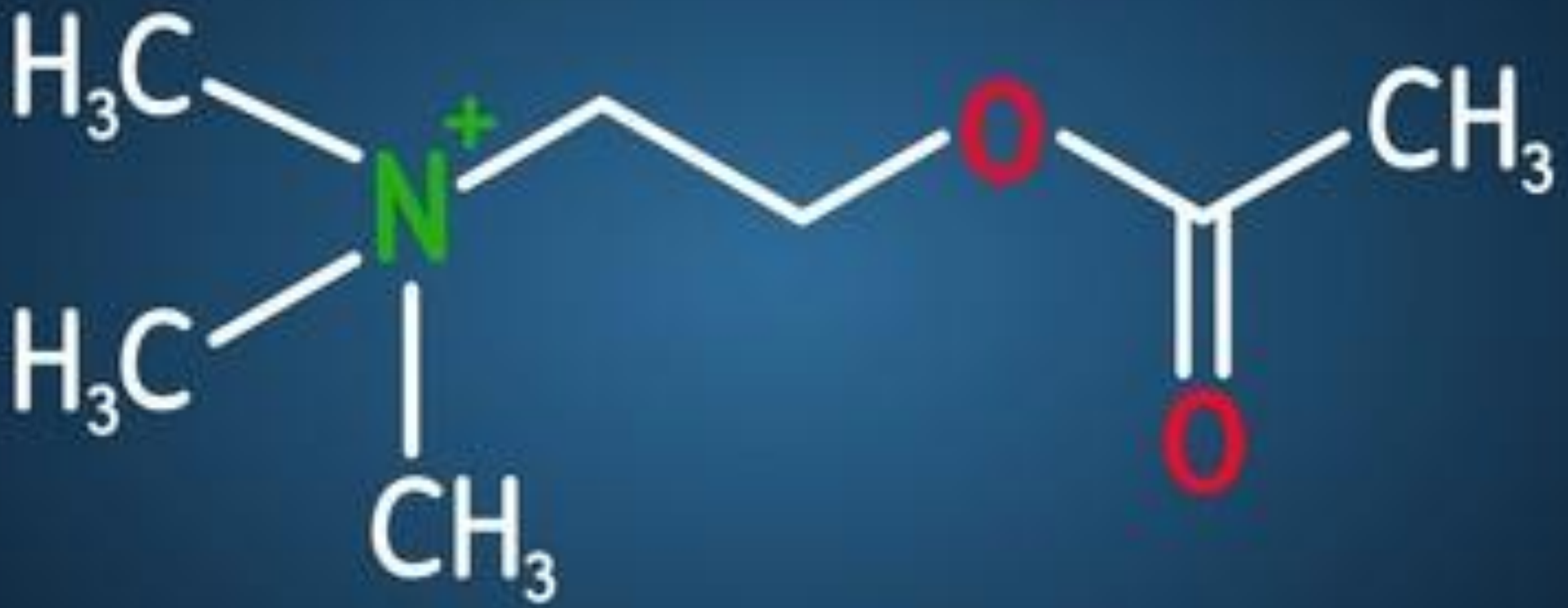
- Hepatic metabolic function and detoxification
- Management of Renal hemodynamics and blood pressure
- Secretion of Pancreatic digestive enzymes
- Lowering of Heart Rate and elevation of Heart Rate Variability
- Maintenance of Homeostatic balance and recovery

The Cholinergic Anti-Inflammatory Pathway



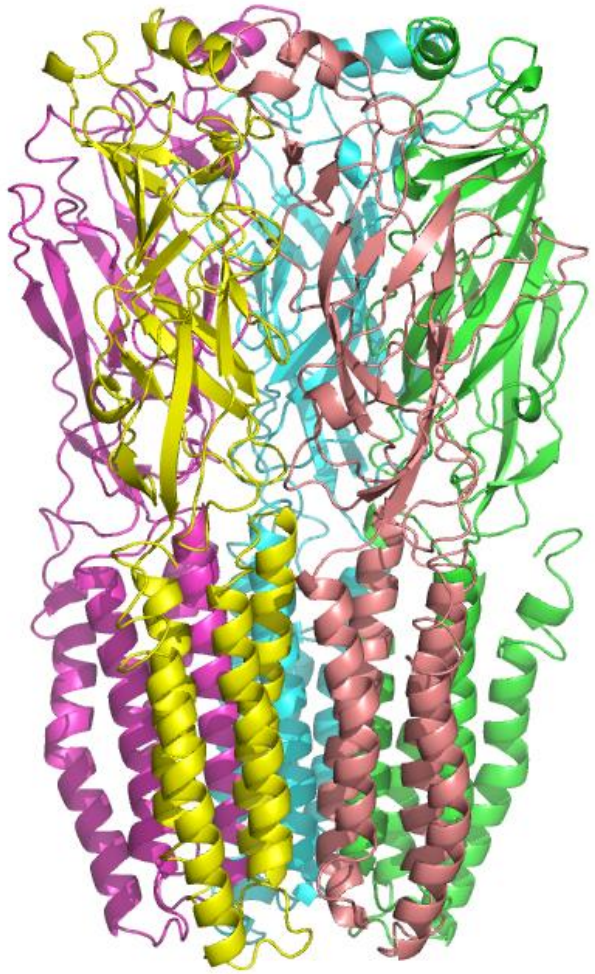
Acetylcholine

Is The Tool



α7nAChR

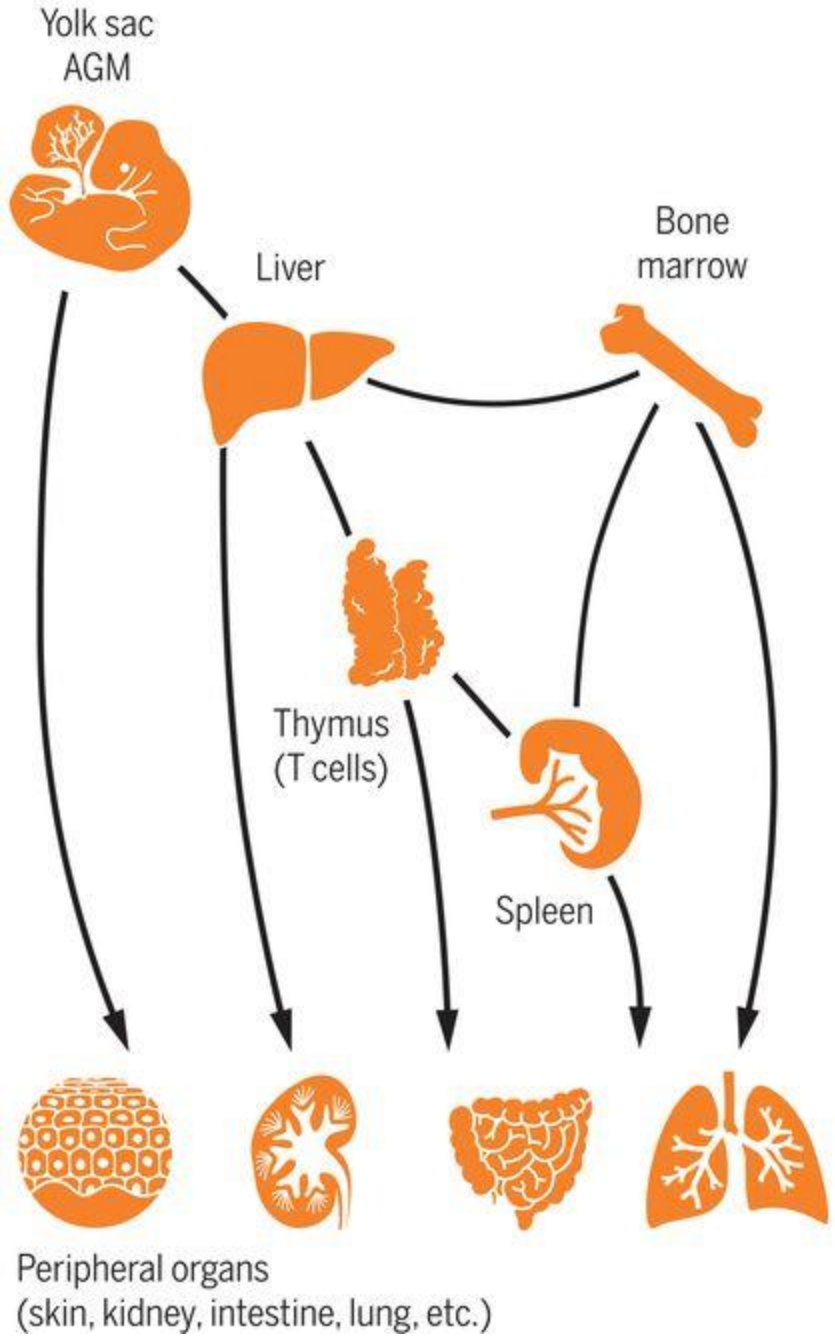
is the Target Receptor

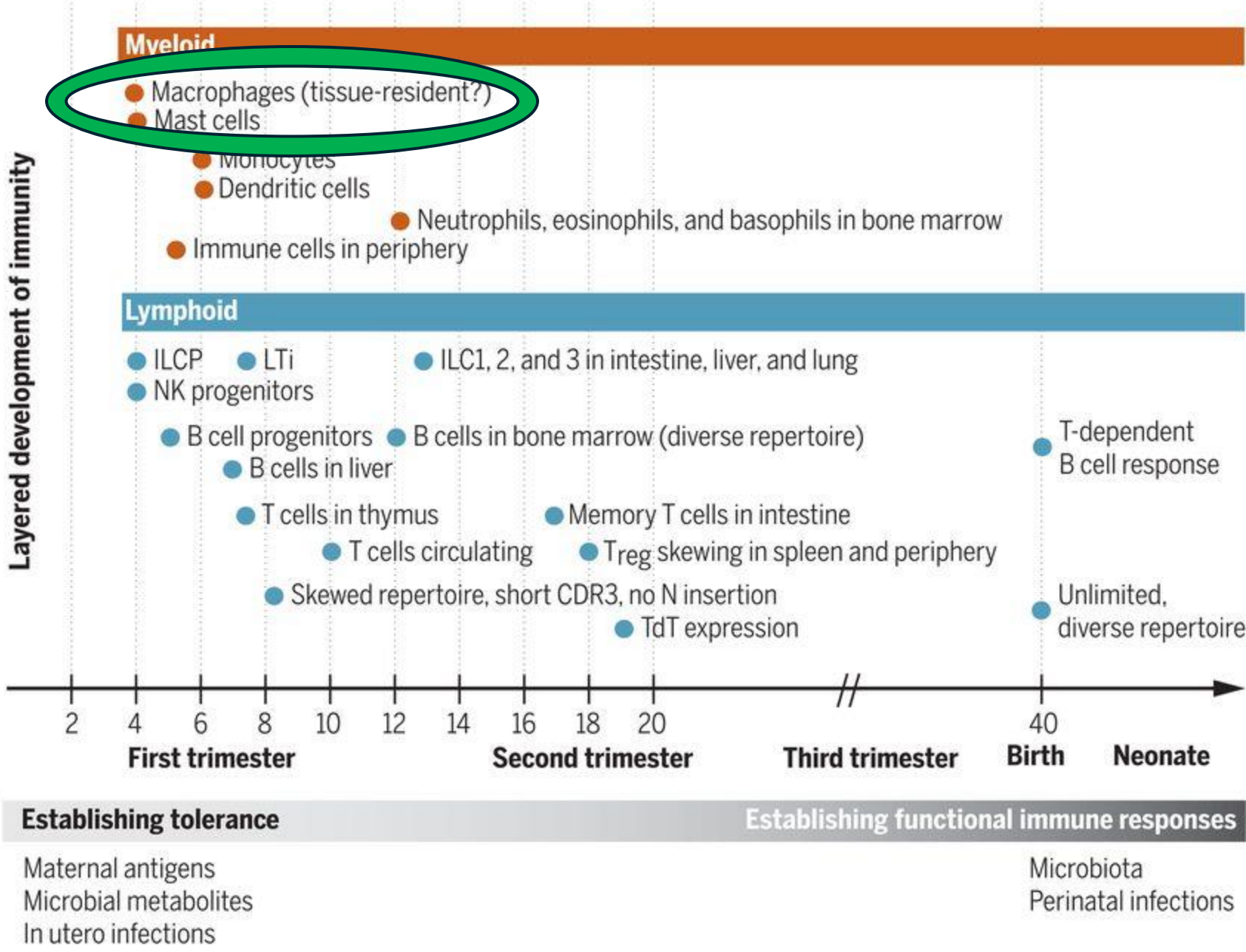


The Macrophage

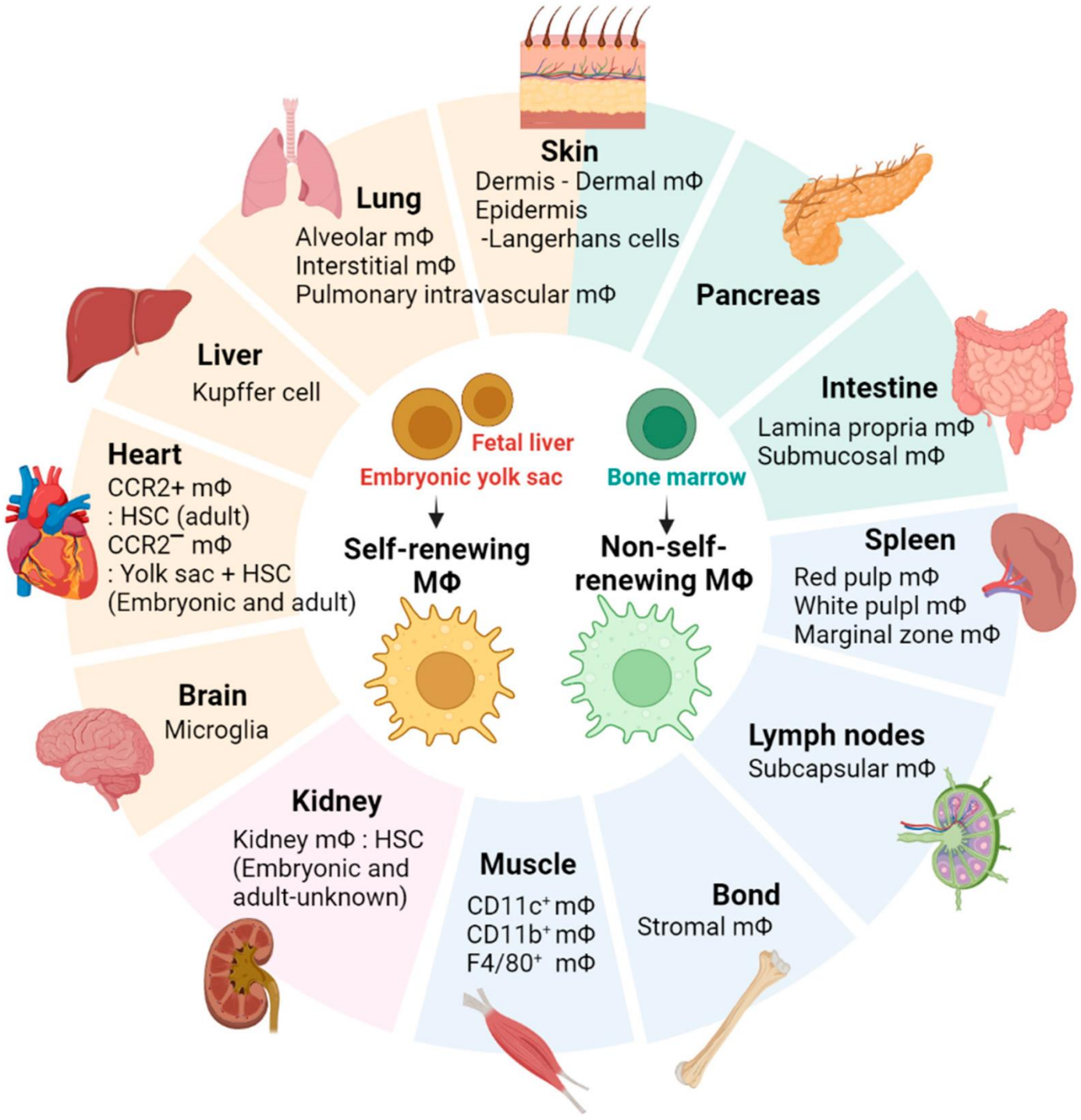
Is The Target Cell

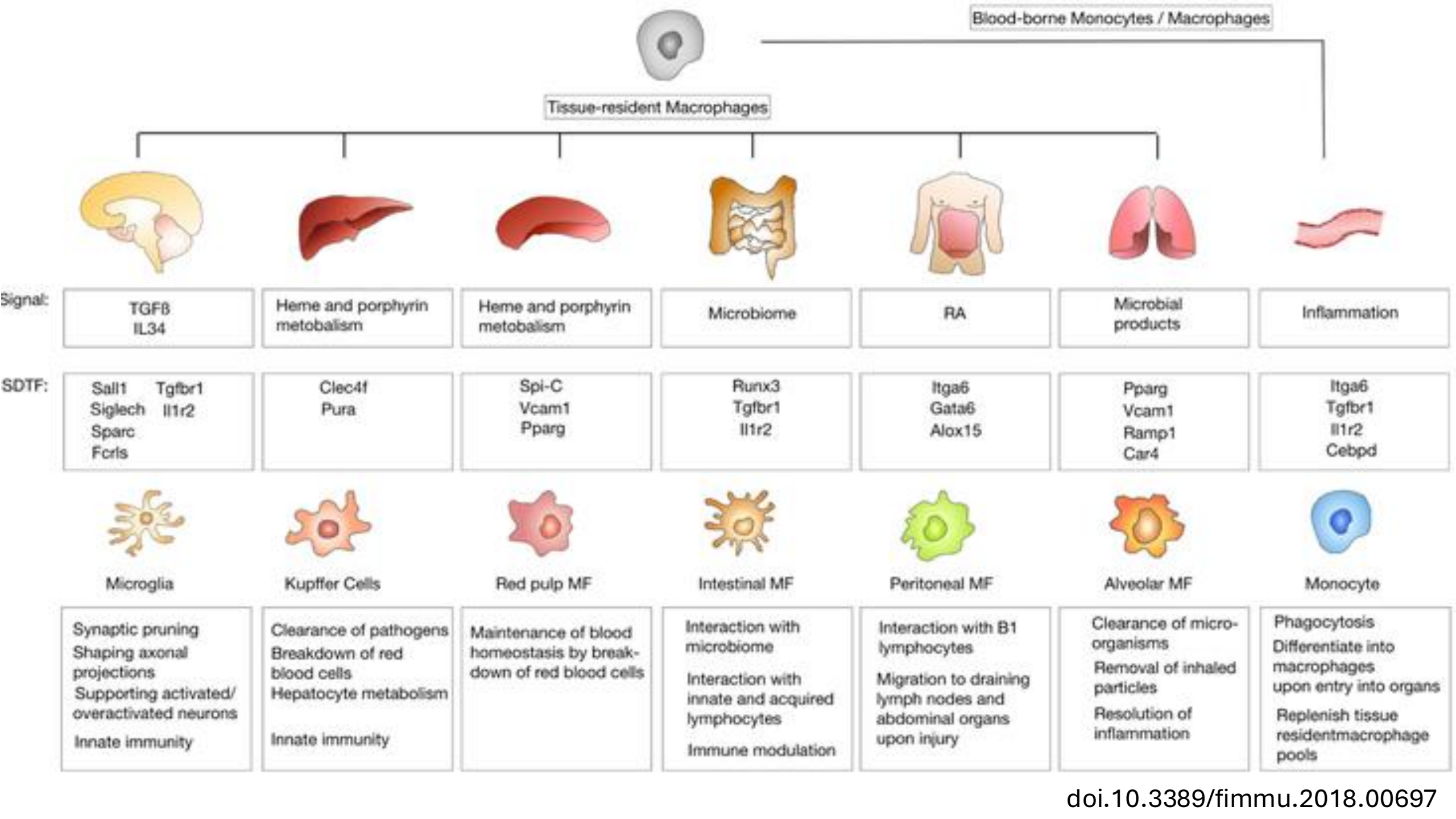
Developmental timeline of the human immune system



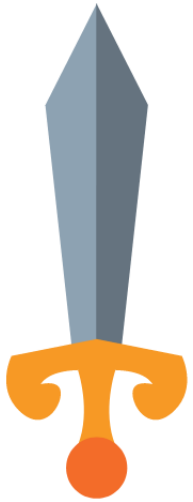


Tissue Resident Macrophages

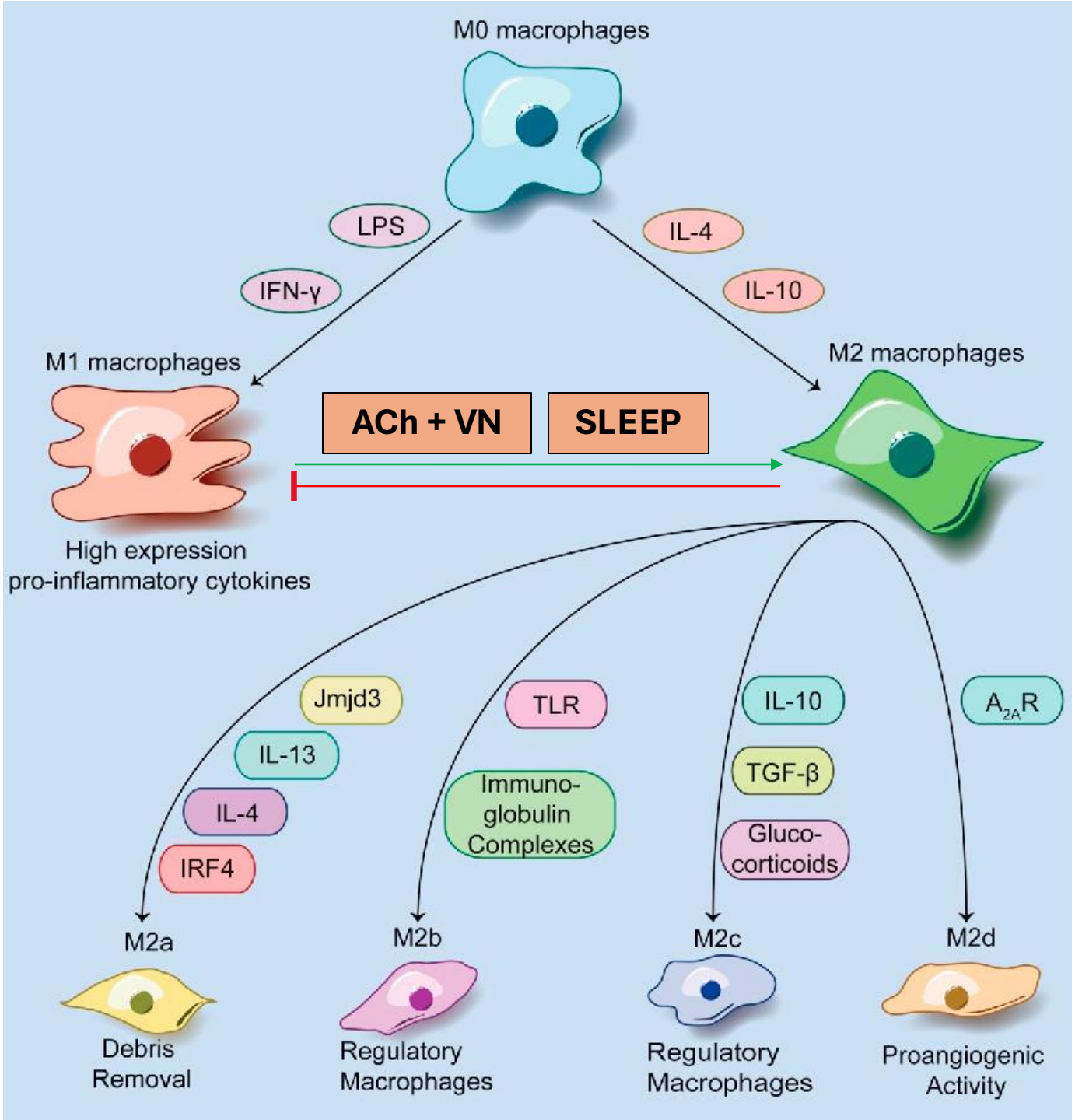


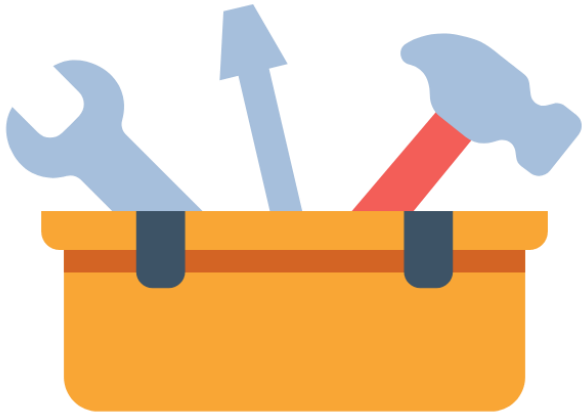


doi.10.3389/fimmu.2018.00697



FIGHT

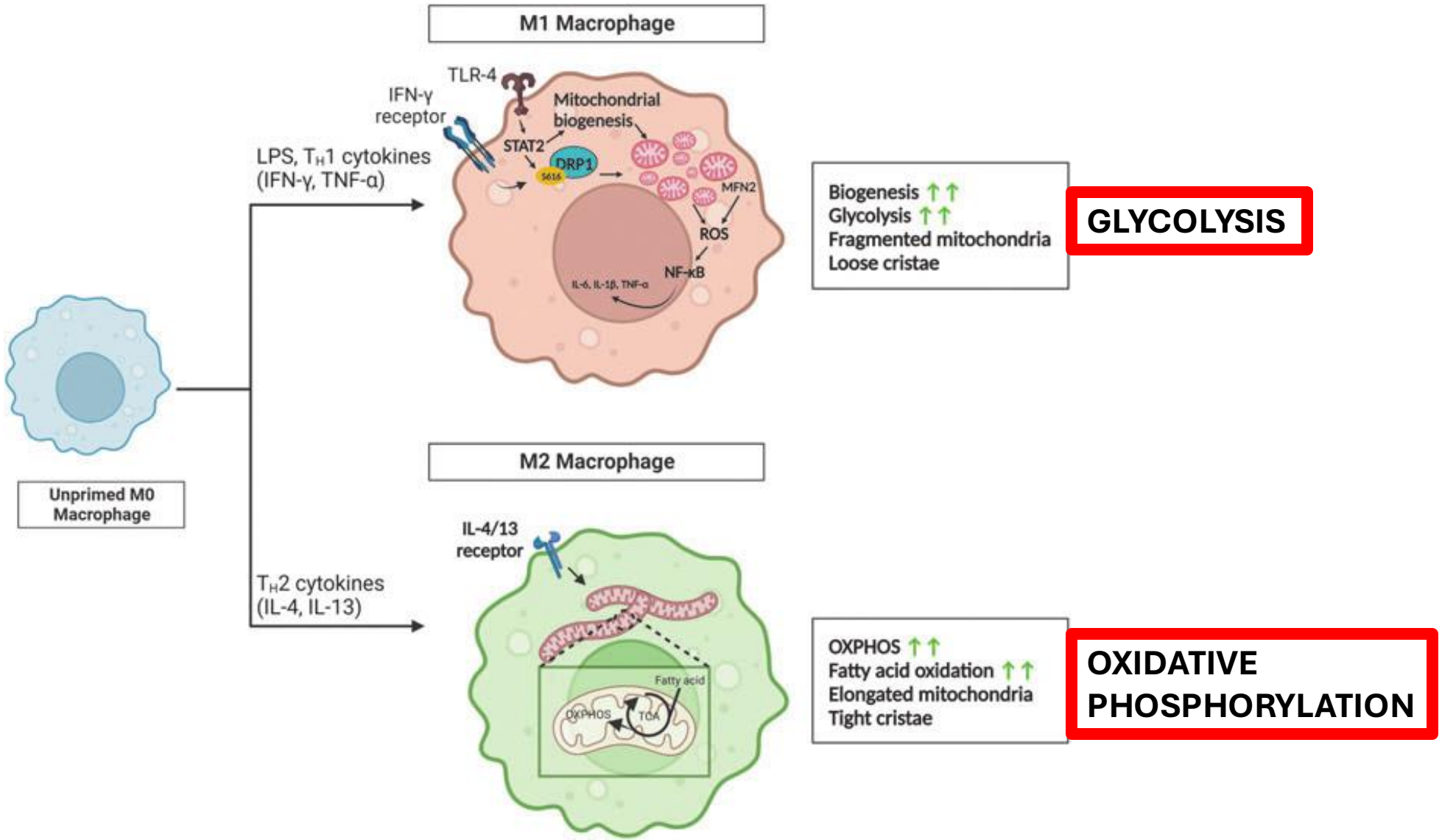




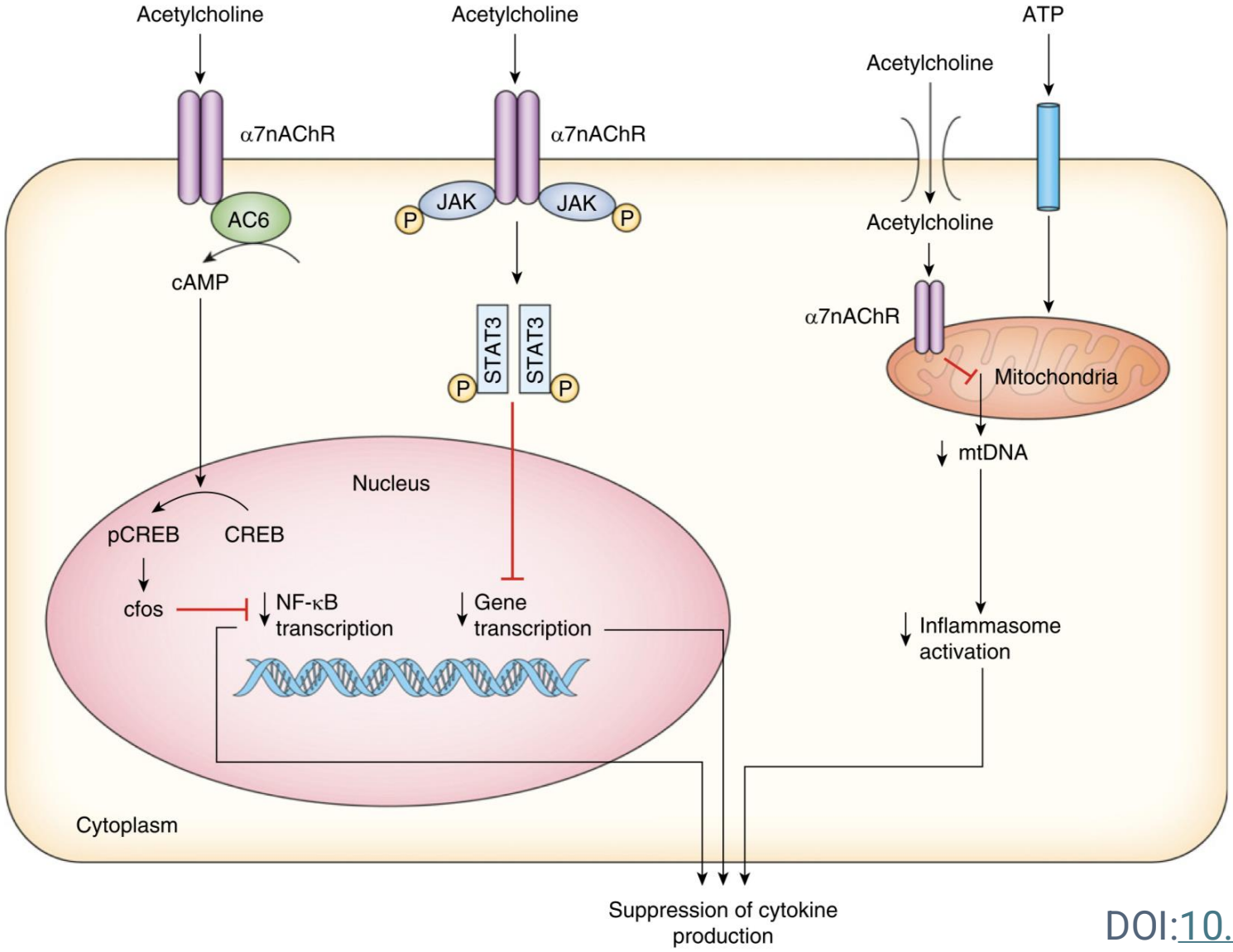
FIX

Adapted from:
doi: 10.1016/j.intimp.2019.02.050

Macrophages are driven by Mitochondria

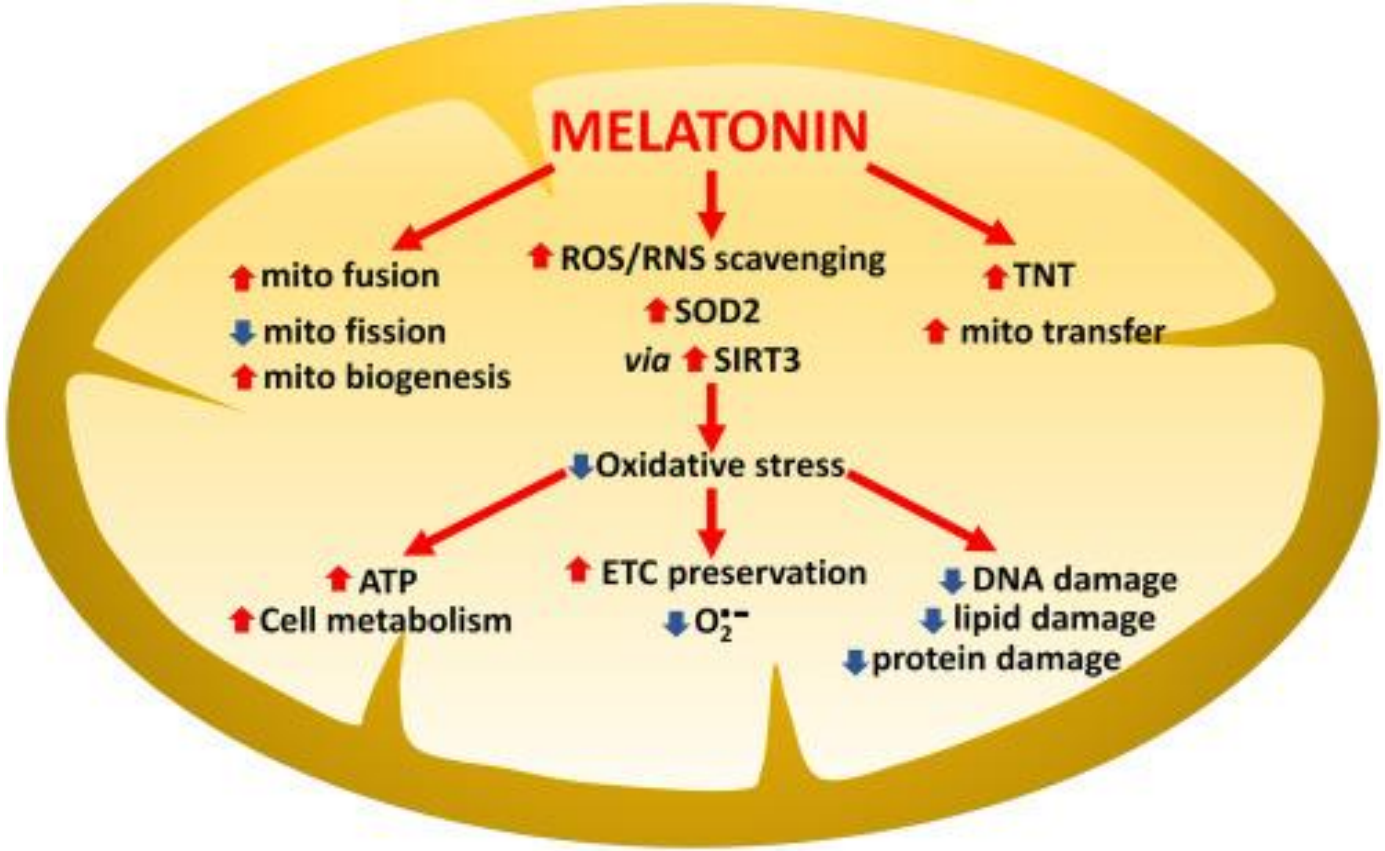


Acetylcholine Protects Mitochondria



DOI:10.4049/jimmunol.1601613

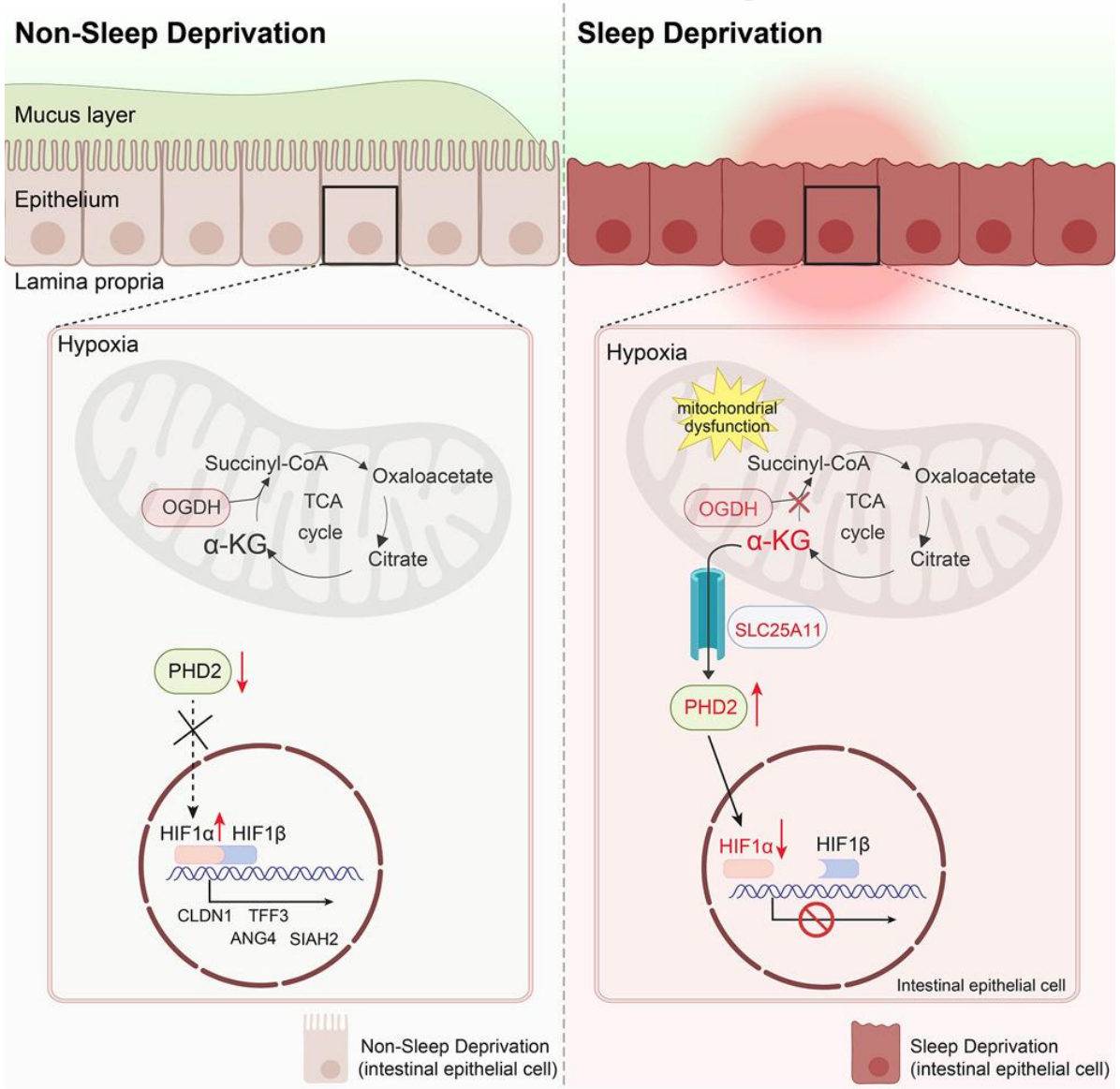
Melatonin Protects Mitochondria



- Antioxidant activity inhibits
  - Mitochondrial Fission
  - Oxidative Stress
  - DNA damage
  - Lipid damage
  - Protein damage
- Improves ATP and cell metabolism as well as Mitochondrial Biogenesis

https://doi.org/10.1016/j.lfs.2022.120612

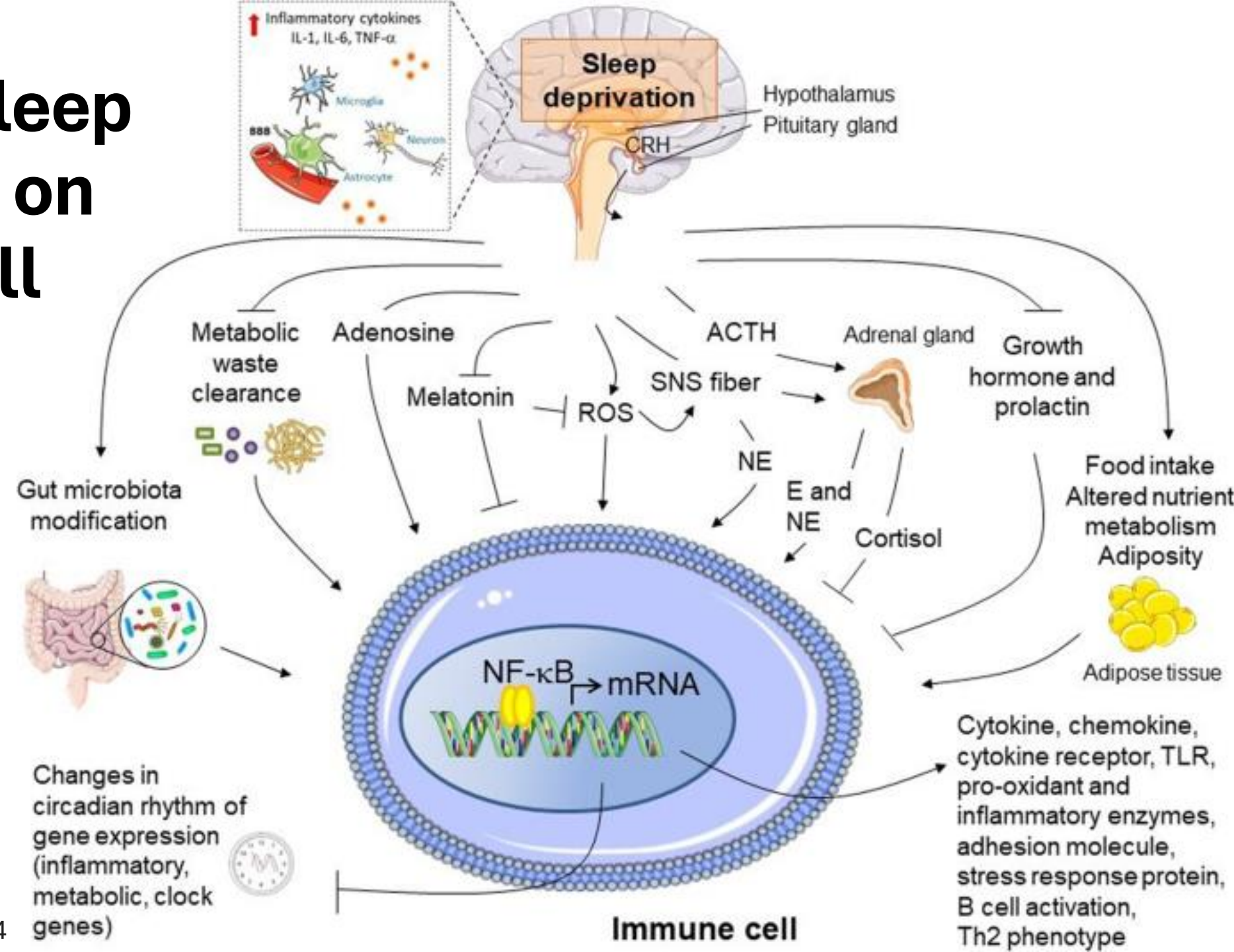
Mitochondrial Dysfunction in Sleep Deprivation



- Sleep deprivation leads to mitochondrial dysfunction, and is linked to intestinal epithelial cell dysfunction (driver of intestinal hyperpermeability)

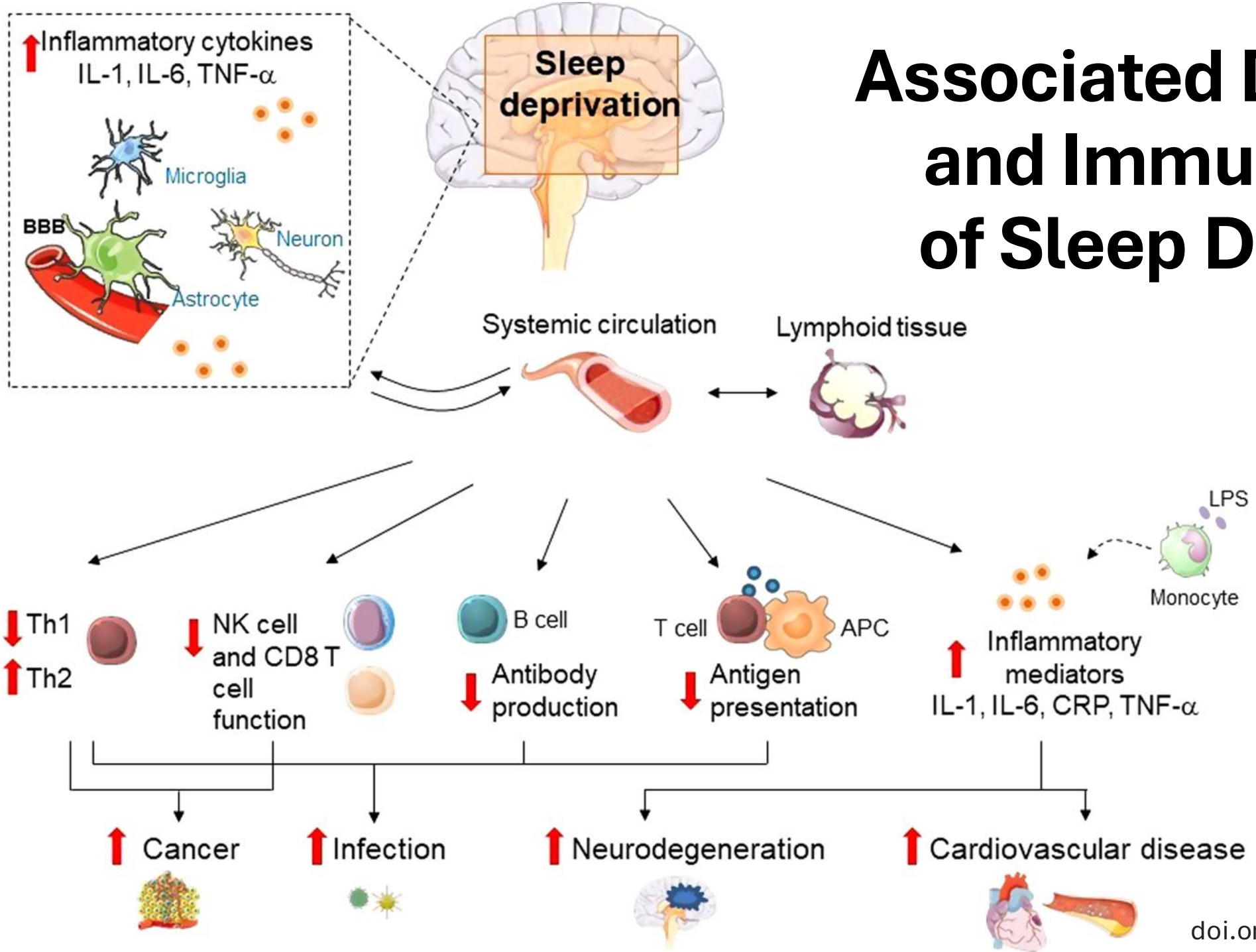
https://doi.org/10.1016/j.celrep.2024.114915

Effects of Sleep Deprivation on Immune Cell Function



doi.org/10.1038/s42003-021-02825-4

Associated Diagnoses and Immune Effects of Sleep Deprivation



doi.org/10.1038/s42003-021-02825-4

What Does Vagus Nerve have to do with the Circadian Rhythm?

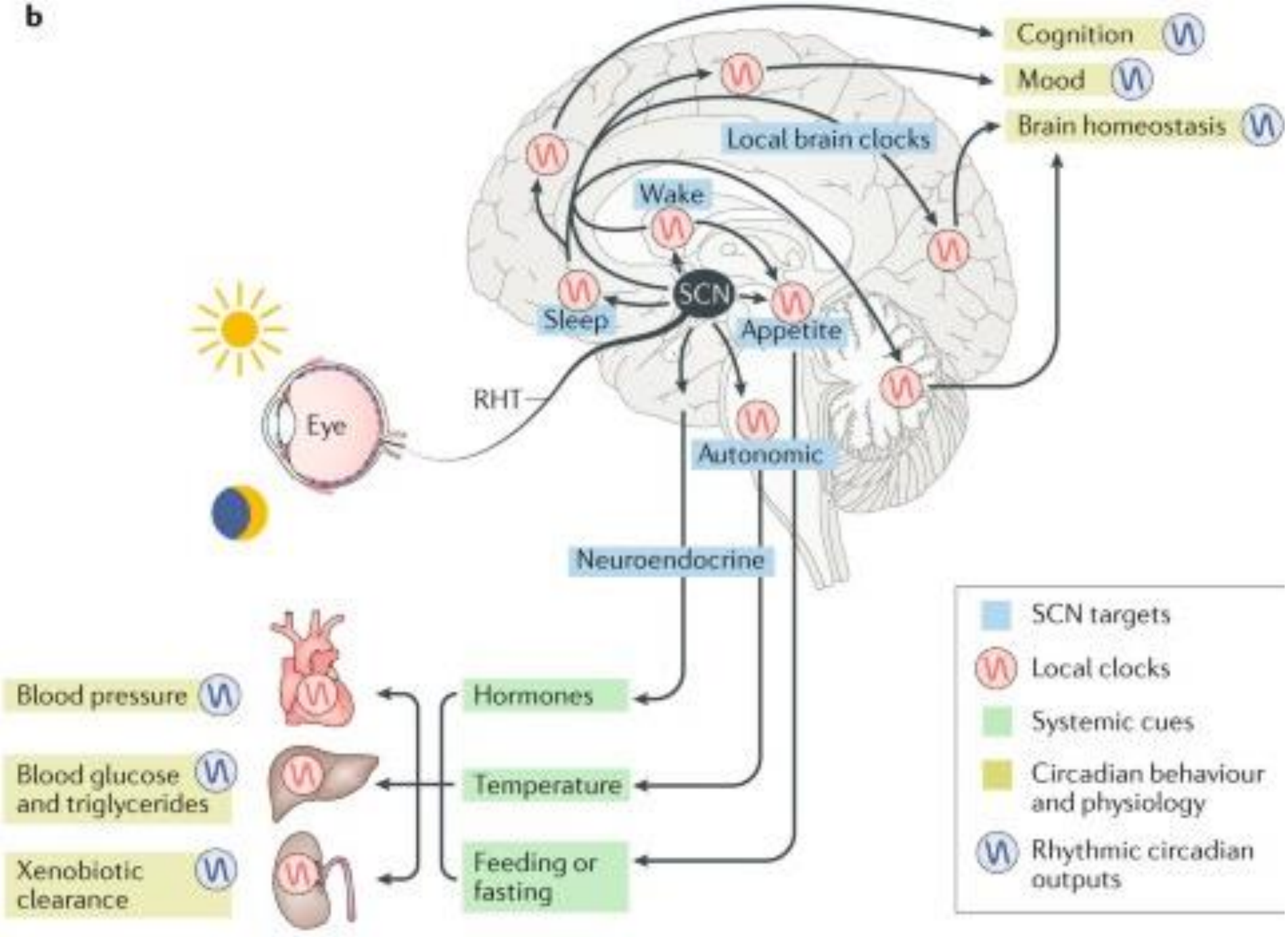
What does light have to do with Vagus nerve?

- Vagus nerve signals regulate many physiological functions – breath rate, heart rate, immune cell function, digestion and others

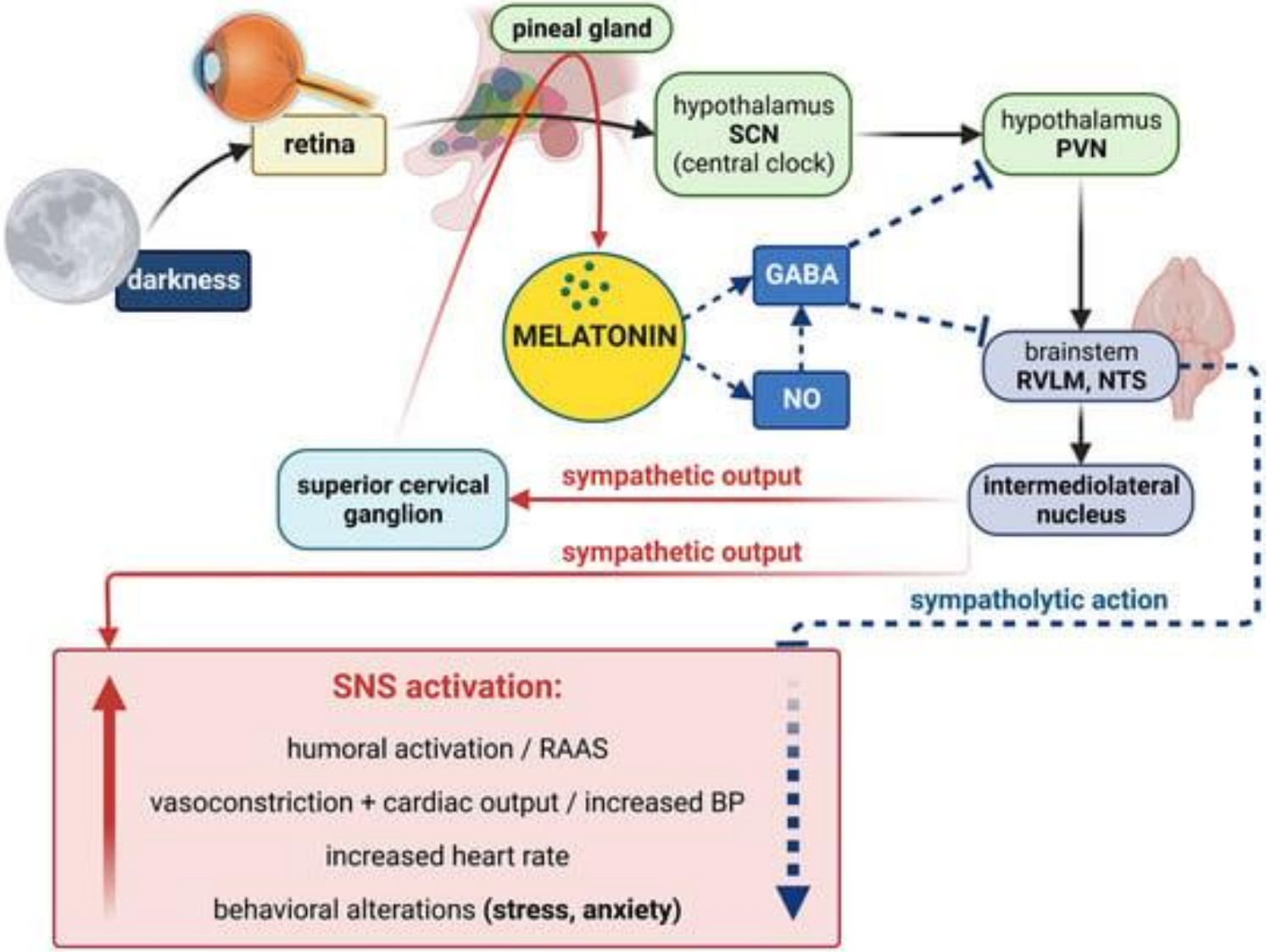
- These functions are turned on or off, based on our sleep-wake cycle, which ideally follows the CIRCADIAN RHYTHM

- The Circadian Rhythm is an (approximately) 24-hour cycle, triggered by light inputs through our eyes that work to turn on some functions and turn off other functions
  - Light is the key signal telling us if it is day or night

Light Wavelength Changes Through The Day


b
Cognition
Mood
Brain homeostasis
Local brain clocks
Wake
SCN
Sleep
Appetite
RHT
Eye
Autonomic
Neuroendocrine
Blood pressure
Blood glucose and triglycerides
Xenobiotic clearance
Hormones
Temperature
Feeding or fasting
SCN targets
Local clocks
Systemic cues
Circadian behaviour and physiology
Rhythmic circadian outputs

Melatonin – Autonomic N.S. Interaction



Melatonin blocks SNS activity via NO and GABA release

- Blocks activity in the SNS:
  - Humoral Activation / Renin-Angiotensin System (RAAS)
  - Vasoconstriction
  - Blood Pressure
  - Heart Rate

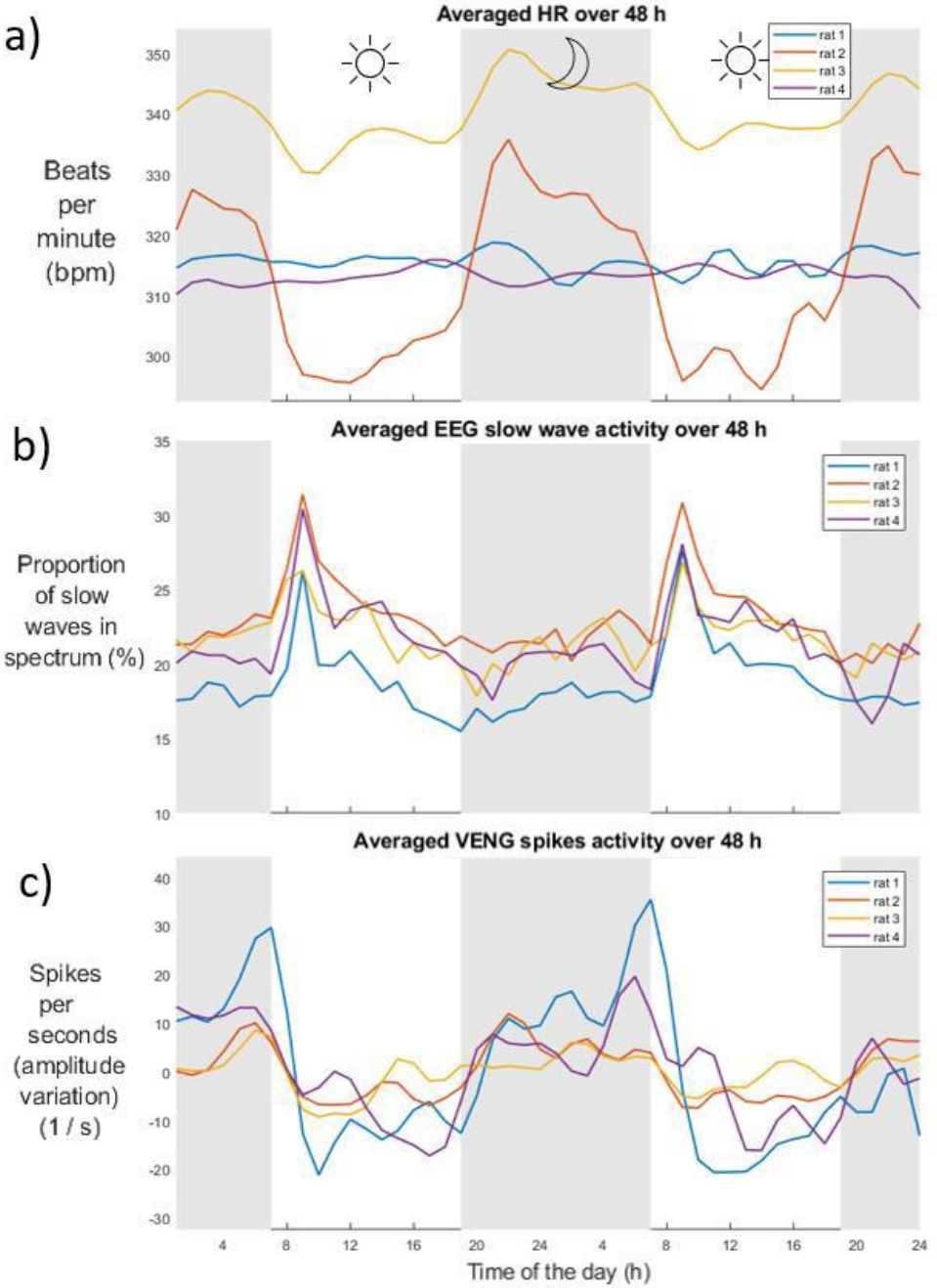
- Enables PNS/Vagus to work unhindered by SNS activity

Chronic recording of the vagus nerve to analyze modulations by the light-dark cycle

Hugo Smets[1], Lars Stumpp[2], Javier Chavez[1], Joaquin Cury[1], Louis Vande Perre[1], Pascal Doguet[3], Anne Vanhoestenberghe[4], Jean Delbeke[2], Riëm El Tahry[2], Antoine Nonclercq[1]

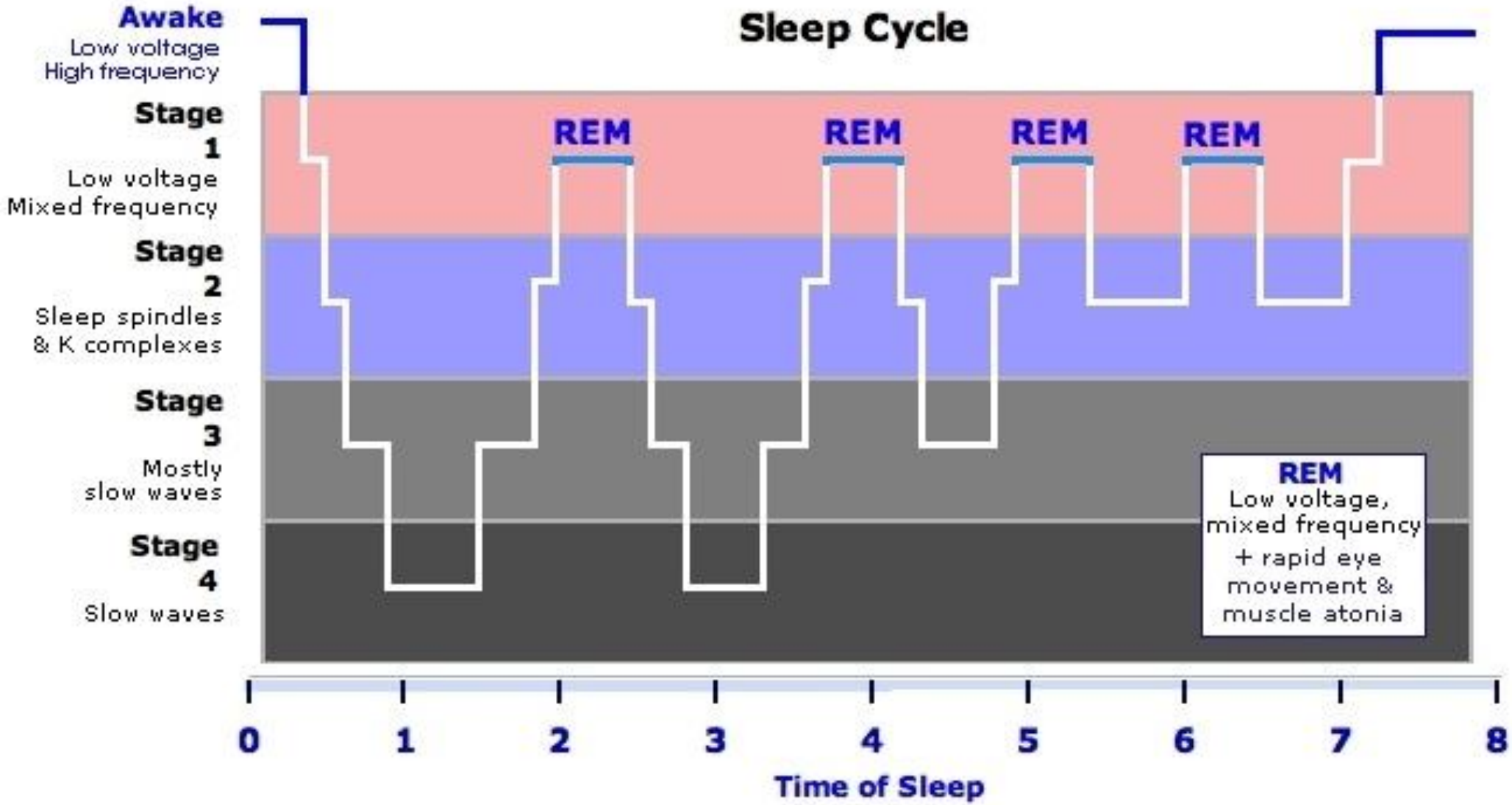
4.2. CONTRIBUTION TO LIGHT-DARK CYCLES

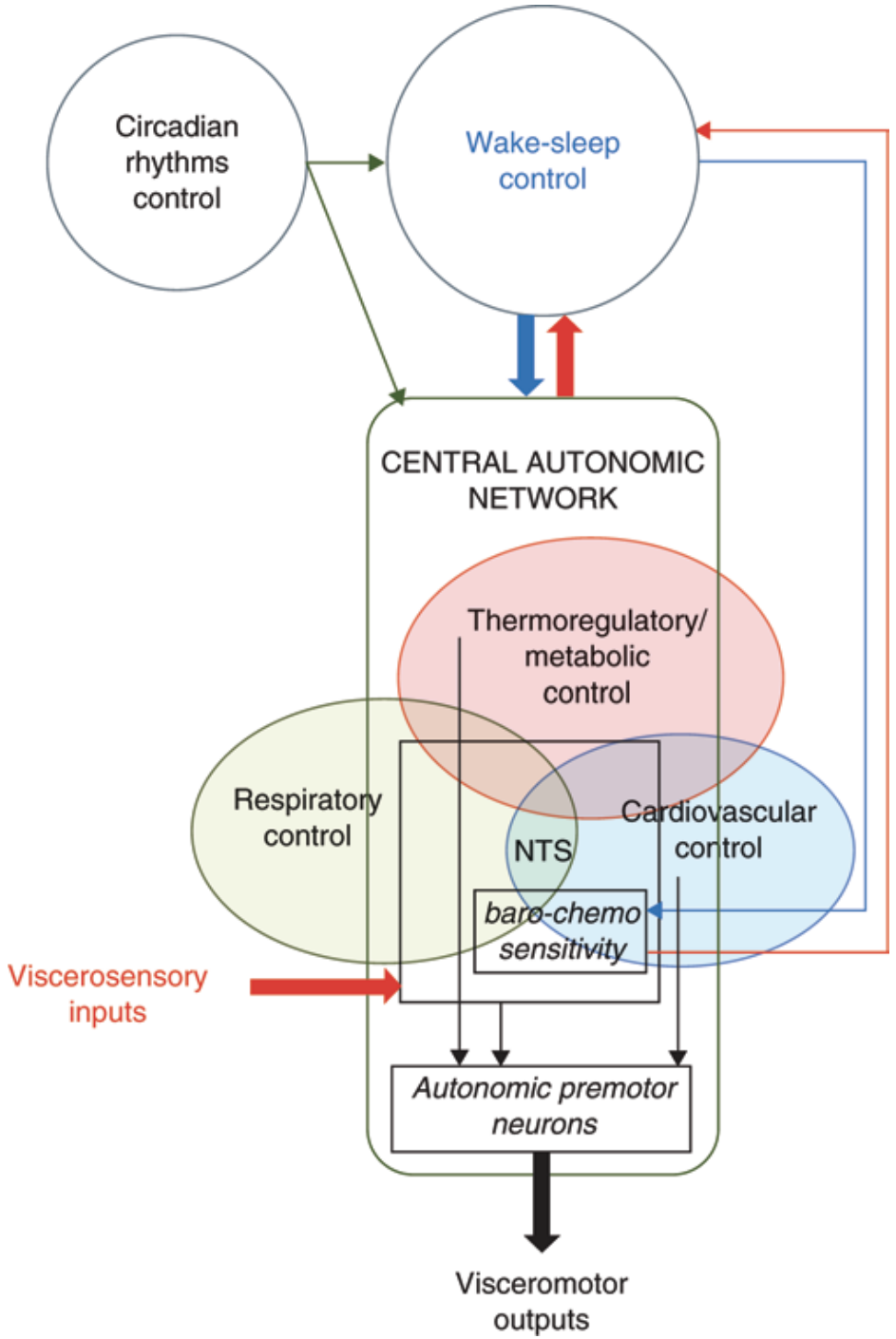
This is the first study showing the light-dark cycles of the vagus nerve spike activity by direct means. We presented a methodological approach to chronically record directly continuous vagus nerve activities in rats. During preliminary trials, we were able to show for the first time the light-dark cycles of the vagus nerve spike activity. As a major outcome of this study, vagus nerve recordings hold the promise to help understand intricate functions such as the circadian regulation. The vagus nerve is indeed well known to be involved in respiratory regulation [32], BP, immune control [38], thermoregulation [39], and many other essential functions. In acute recordings, vagus nerve activity has been shown to correlate with physiological parameters such as respiration cycles [40] and baroreceptive fibers [41]. Since the vagus nerve activity is linked to physiological parameters driven by circadian modulations, it can be expected that the vagus nerve activity will exhibit a circadian pattern as well. This is also expected since the vagus nerve is a well-known major control pathway from the SCN to body functions [9].



doi: 10.1088/1741-2552/ac7c8f. PMID: 35764074

Optimal Sleep Cycles

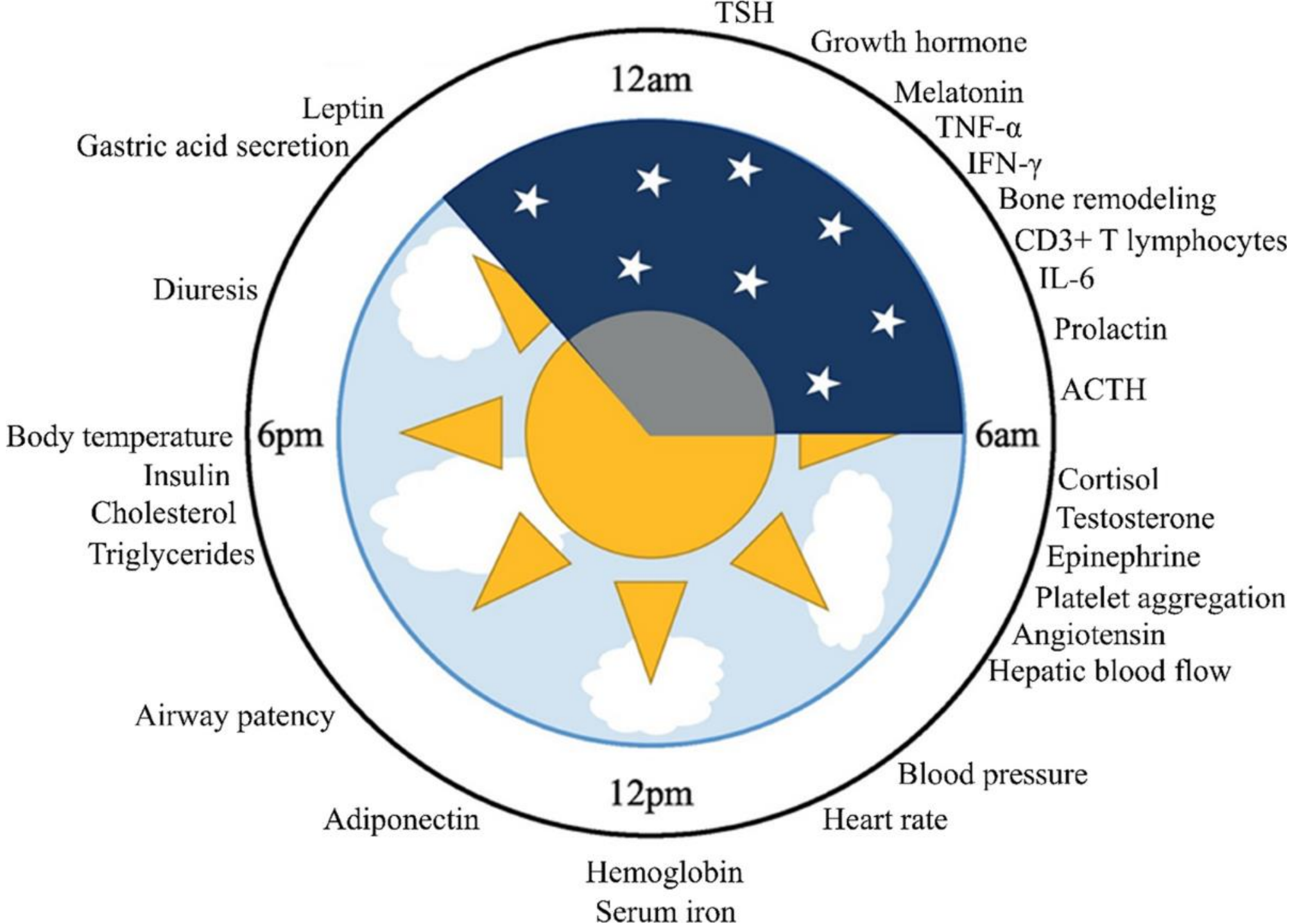




Circadian Regulation of Autonomic Nervous System

- Wakefulness:
  - SNS dominates PNS
- REM Sleep (Stage 1)
  - SNS and PNS both active in a phasic alternating pattern
  - Thermoregulation is impaired due to this alternating SNS-PNS balance
- Non-REM Sleep (Stage 3+4)
  - PNS dominates SNS

https://doi.org/10.1007/978-3-030-62263-3_5


TSH
Growth hormone
12am
Melatonin
TNF-α
IFN-γ
Leptin
Gastric acid secretion
Bone remodeling
CD3+ T lymphocytes
IL-6
Diuresis
Prolactin
ACTH
Body temperature
6pm
6am
Insulin
Cortisol
Cholesterol
Testosterone
Triglycerides
Epinephrine
Platelet aggregation
Angiotensin
Hepatic blood flow
Airway patency
Blood pressure
12pm
Adiponectin
Heart rate
Hemoglobin
Serum iron

How do the Vagus Nerve and Circadian Rhythm Become Dysregulated?

Physical Stress / Trauma

Whiplash, Concussion, Surgical trauma, Vascular, Meningeal Injury

brain sciences

Article

Autonomic Dysfunction after Mild Traumatic Brain Injury

Dmitry Esterov [1,*] and Brian D. Greenwald [2,*]

5. Conclusions

There is evidence of ANS dysfunction after a mild TBI, studied through various mechanisms, including changes in heart rate variability, arterial pulse wave analysis, graded exercise testing, and pupillary dynamics. Though studies have shown changes to autonomic function in the post-acute stage after a concussion [19], further prospective studies are needed to understand the long term effects of mild TBI on the autonomic nervous system, and the possible systemic effects of ANS dysfunction in mild TBI. Larger prospective studies are needed to determine whether graded exercise testing and submaximal exercise in patients with persistent symptoms will be a standard of care in management of concussions. Given the studies showing persistence of autonomic dysfunction after

PMID: 28800081

Physical Stress

Dysfunctional Breathing and Sleep Apnea

Heart rate variability during wakefulness as a marker of obstructive sleep apnea severity

Hua Qin[1,†], Brendan T. Keenan[2,†,*], Diego R. Mazzotti[3],

Conclusion

Measures of HRV during wakefulness were significantly associated with increased OSA severity, with a decrease in the overall HRV and less complex HRV measures among more severe patients after controlling for relevant covariates. These observed differences are consistent with worse cardiovascular abnormalities in the most severe OSA group. Thus, the HRV measures

PMID: 33506267

Biochemical Stress - Dietary Stress

Both high fat and high carbohydrate diets impair vagus nerve signaling of satiety

Hailley Loper[1,2], Monique Leinen[1,2], Logan Bassoff[1,2], Jack Sample[3,4], Mario Romero-Ortega[5], Kenneth J. Gustafson[3,6], Dawn M. Taylor[3,6,7] & Matthew A. Schiefer[1,3,6]✉

Conclusions

This study found that the change in vagal tone was depressed significantly in animals fed either a chronic high fat or high carbohydrate diet when compared to animals fed a standard diet. If a minimum degree of or increase in vagal tone is required to feel satiated, then the reduction observed in this study would be expected to drive both groups to consume more and gain more weight, the latter of which was shown to be true. These results suggest VNS systems to reduce obesity will need to increase the change in vagal tone by approximately 4× in order to convey stomach distension. Further studies are needed to determine stimulation parameters required for this fourfold increase in neural signaling.

PMID: 34001925

Biochemical Stress - Dysbiosis

Bacteria, Viruses, Yeast, Parasites and Worms

frontiers in Neuroscience

MINI REVIEW
published: 07 February 2018
doi: 10.3389/fnins.2018.00049

The Vagus Nerve at the Interface of the Microbiota-Gut-Brain Axis

Bruno Bonaz[1,2*], *Thomas Bazin*[3,4] *and Sonia Pellissier*[5]

composed of 80% afferent and 20% efferent fibers. The VN, because of its role in interoceptive awareness, is able to sense the microbiota metabolites through its afferents, to transfer this gut information to the central nervous system where it is integrated in the central autonomic network, and then to generate an adapted or inappropriate response. A cholinergic anti-inflammatory pathway has been described through VN's

a dysbiosis. A low vagal tone has been described in IBD and IBS patients thus favoring peripheral inflammation. Targeting the VN, for example through VN stimulation which has anti-inflammatory properties, would be of interest to restore homeostasis in the microbiota-gut-brain axis.

PMID: 29467611

Biochemical Stress - Poor Detoxification

Vagus nerve cholinergic circuitry to the liver and the gastrointestinal tract in the neuroimmune communicatome

Christine N. Metz[1,2] and Valentin A. Pavlov[1,2]

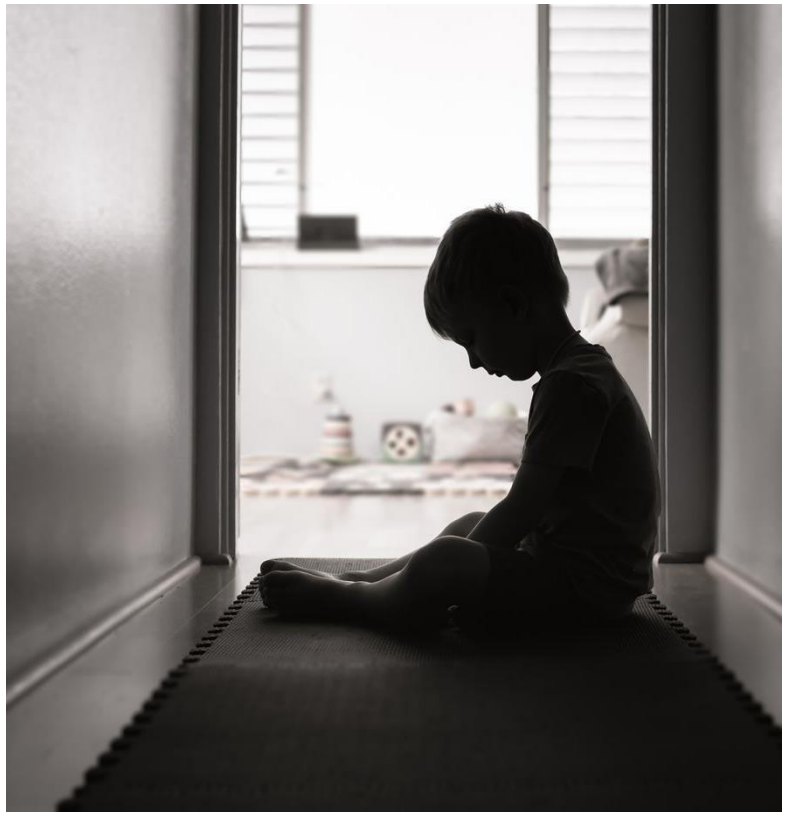
DMN (54). The hepatic branch of the vagus nerve is supplied mainly through the anterior trunk, which is an extension of the left vagus nerve under the diaphragm. Efferent vagus nerve signaling to the liver regulates hepatic metabolic function, such as the control of hepatic glucose production (gluconeogenesis) (29, 49–51). Interactions between the DMN, NTS, thalamus, hypothalamus, amygdala, cortex areas, and other brain regions mediate forebrain regulation of the autonomic control of GI and hepatic function, and its coordination with behavioral, cognitive, and endocrine regulation (49).

VAGUS NERVE CHOLINERGIC REGULATION OF HEPATIC IMMUNE RESPONSES AND INFLAMMATION

Abundant experimental evidence indicates that in addition to controlling "classical" physiological processes, efferent vagus nerve cholinergic signaling regulates immunity and inflammation. Cholinergic modulation of liver inflammation by the vagus nerve was first reported by Tracey and colleagues (11) almost 20 years ago. They demonstrated that electrical stimu-

PMID: 30001146

Psychological Stress / Trauma / ACEs



Childhood adversity and vagal regulation: A systematic review and meta-analysis

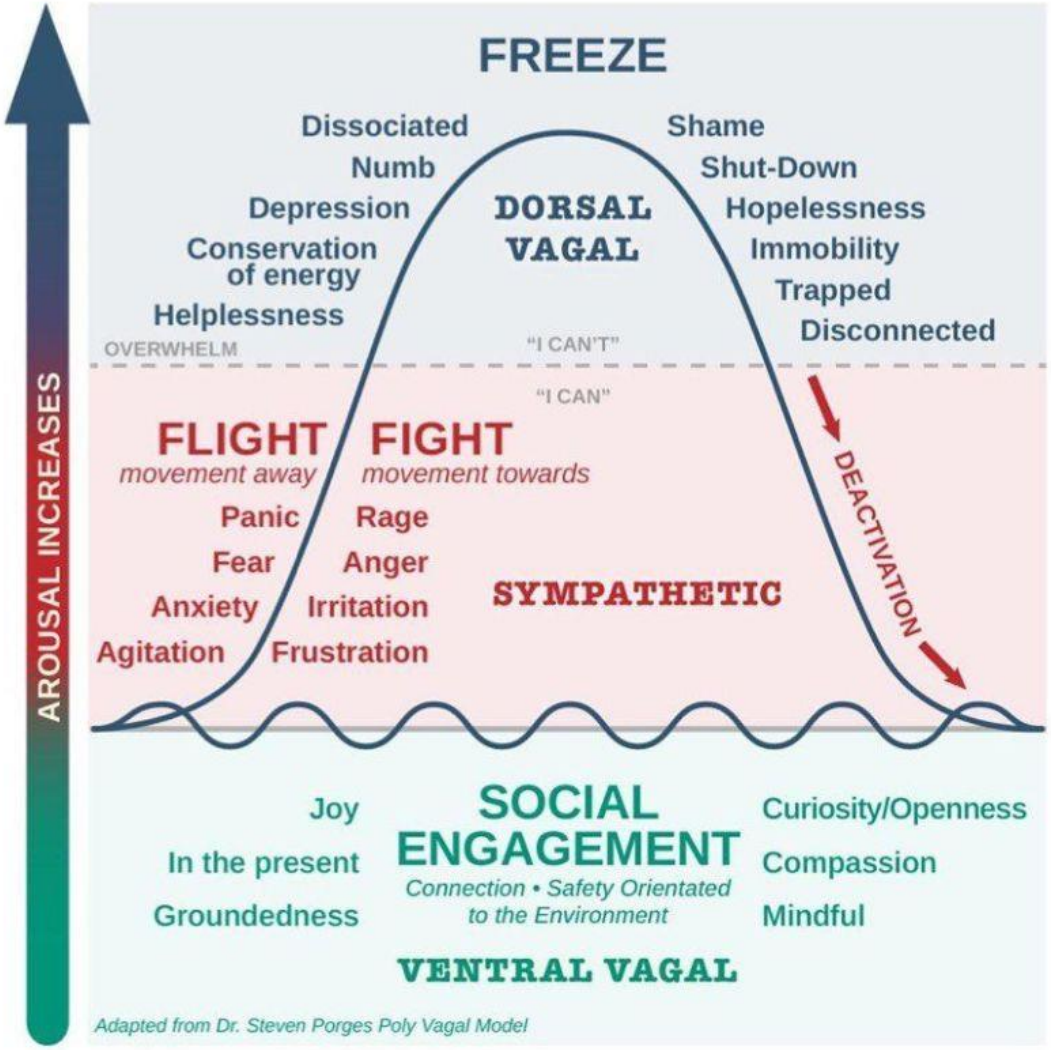
Christiane Wesarg [a,b,*], Alithe L. Van den Akker [a,c], Nicole Y.L. Oei [a,b,d], Reinout W. Wiers [a,b,d,e], Janneke Staaks [f], Julian F. Thayer [g], DeWayne P. Williams [g], Machteld Hoeve [a,c]

- History of ACEs exhibited lower vagal tone, as measured by HRV, compared to those without ACEs
  - Childhood adversity may have long-lasting effects on the autonomic nervous system, particularly vagus nerve function
- Noted reduced HRV during stress tasks, indicating impaired vagal withdrawal in response to stressors
  - Difficulties in emotion regulation and stress management in individuals with a history of childhood adversity

doi.org/10.1016/j.neubiorev.2022.104920

Psychological Stress

Polyvagal Theory and the Feeling of Safety



The Complex Construct of Wellbeing and the Role of Vagal Function

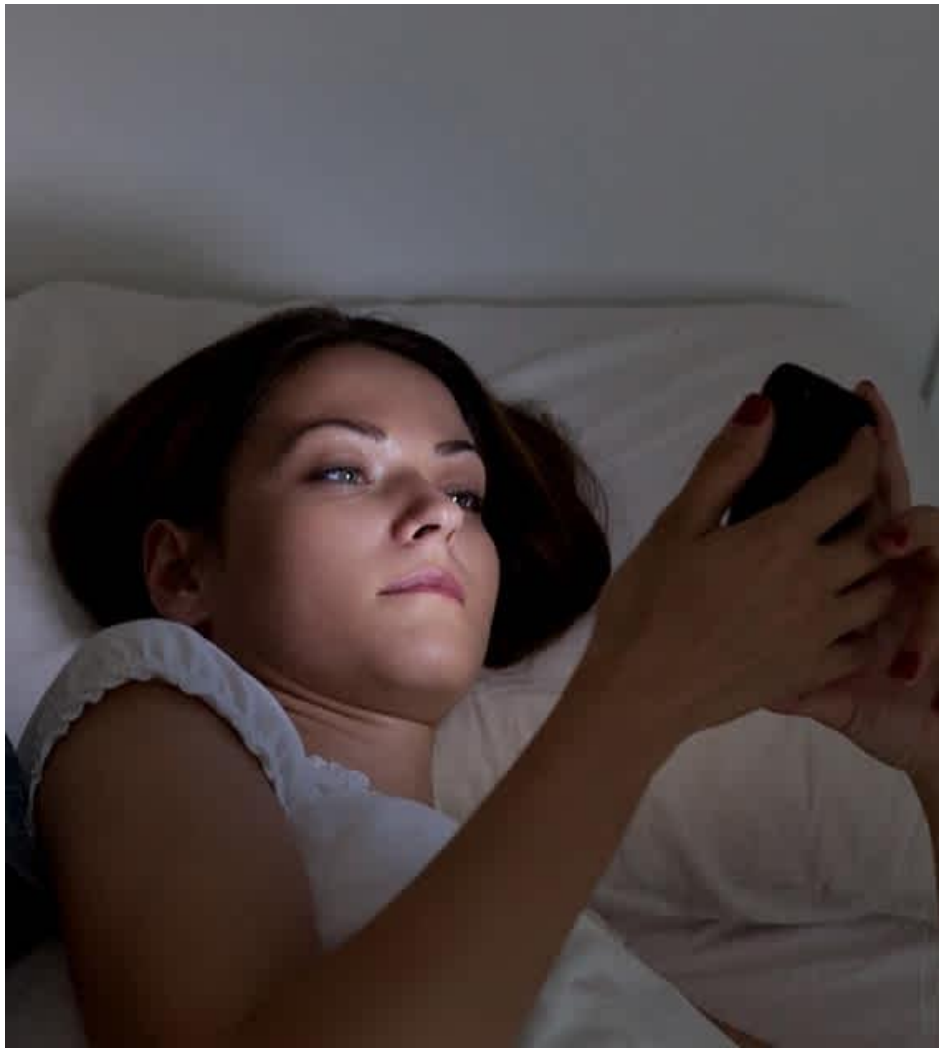
*Lowri Wilkie [1,2], Zoe Fisher [2,3] and Andrew H. Kemp [1,2]**

- Higher levels of vagally-mediated HRV facilitate the **experience of safety** and increase capacity for connection and wellbeing
- Conversely, lower HRV and reduced vagal tone are associated with a **lack of perceived safety** and diminished wellbeing.

doi: 10.3389/fnint.2022.925664

Circadian Misalignment

Light Inputs During Nighttime



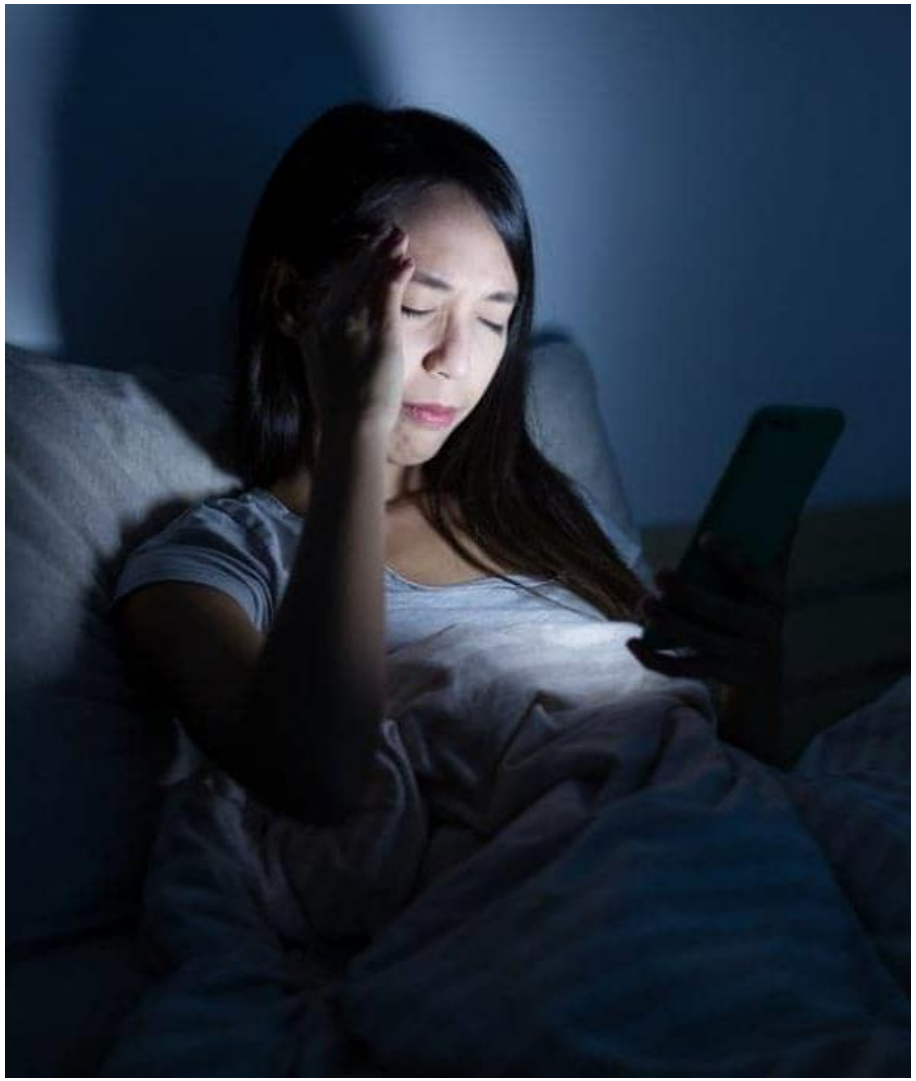
Light exposure during sleep impairs cardiometabolic function

Ivy C. Mason[a,b,c,1], Daniela Grimaldi[a,1], Kathryn J. Reid[a], Chloe D. Warlick[a], Roneil G. Malkani[a], Sabra M. Abbott[a], and Phyllis C. Zee[a,2]

similar in both conditions. In the room light condition, participants spent proportionately more time in stage N2 and less in slow wave and rapid eye movement sleep. Heart rate was higher and heart rate variability lower (higher sympathovagal balance) during sleep in the room light versus the dim light condition. Importantly, the higher sympathovagal balance during sleep was associated with higher 30-min insulin AUC, consistent with increased insulin resistance the following morning. These results demonstrate that a single night of exposure to room light during sleep can impair glucose homeostasis, potentially via increased SNS activation. Attention to avoiding exposure to light at night during sleep may be beneficial for cardiometabolic health.

doi.org/10.1073/pnas.2113290119

Effects of OLED Light on Vagus Nerve



Suppression of vagal cardiac modulation by blue light in healthy subjects

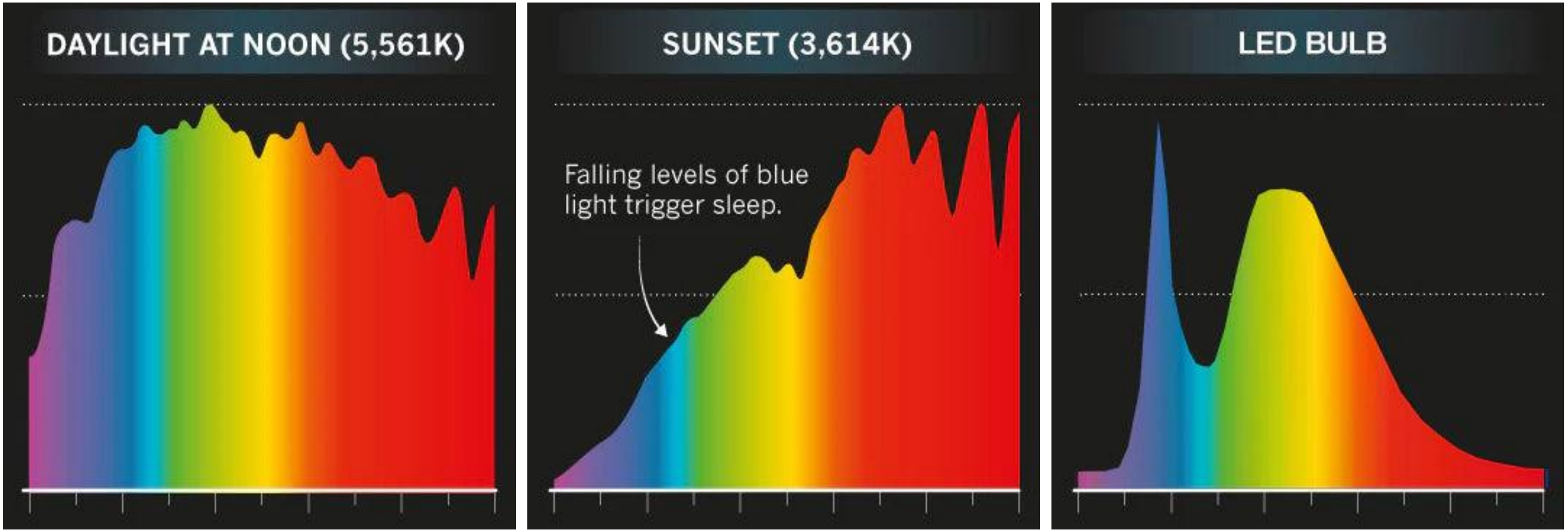
Emi Yuda, Hiroki Ogasawara, Yutaka Yoshida and Junichiro Hayano*

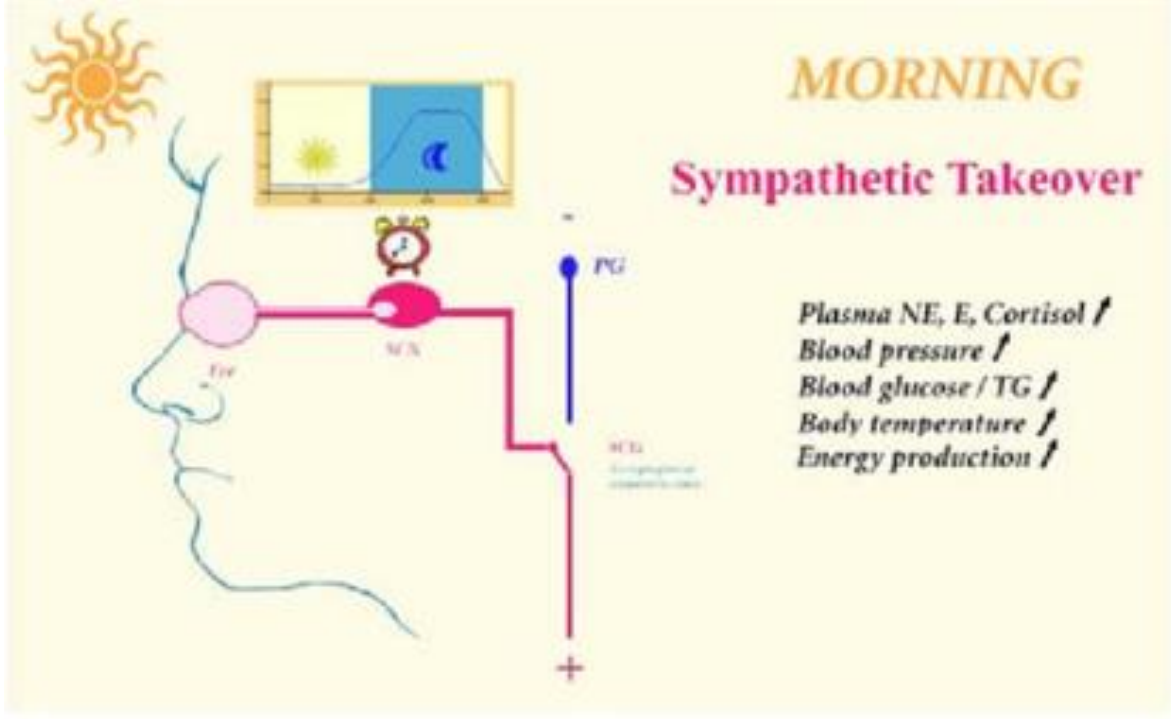
Conclusions

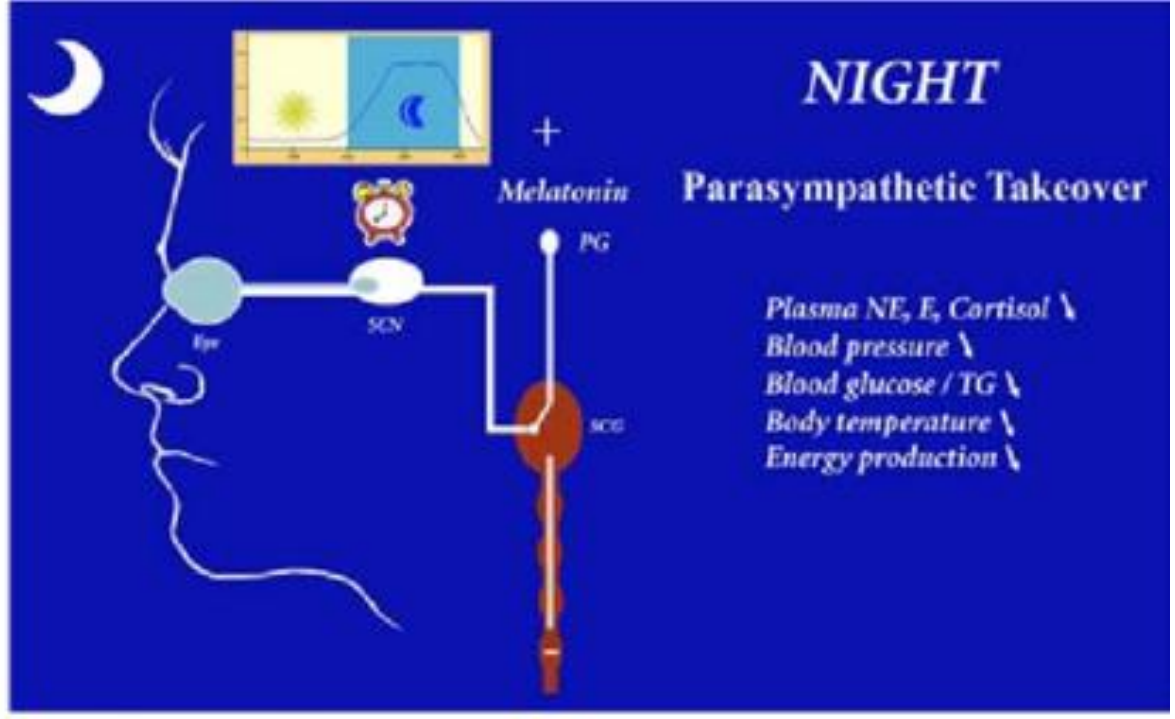
We examined the impact of OLED colored lights on HRV in healthy young subjects under paced breathing. Our observations indicate that vagal cardiac modulation is suppressed by OLED illumination as a direct response not mediated by respiratory frequency. Also, this response may be more sensitive to blue light than to red and green OLED lights and may last even after the exposure. This study suggests that on the use of colored OLED lighting in a variety of environments, we need to consider the difference in physiological effects with the color of illuminations.

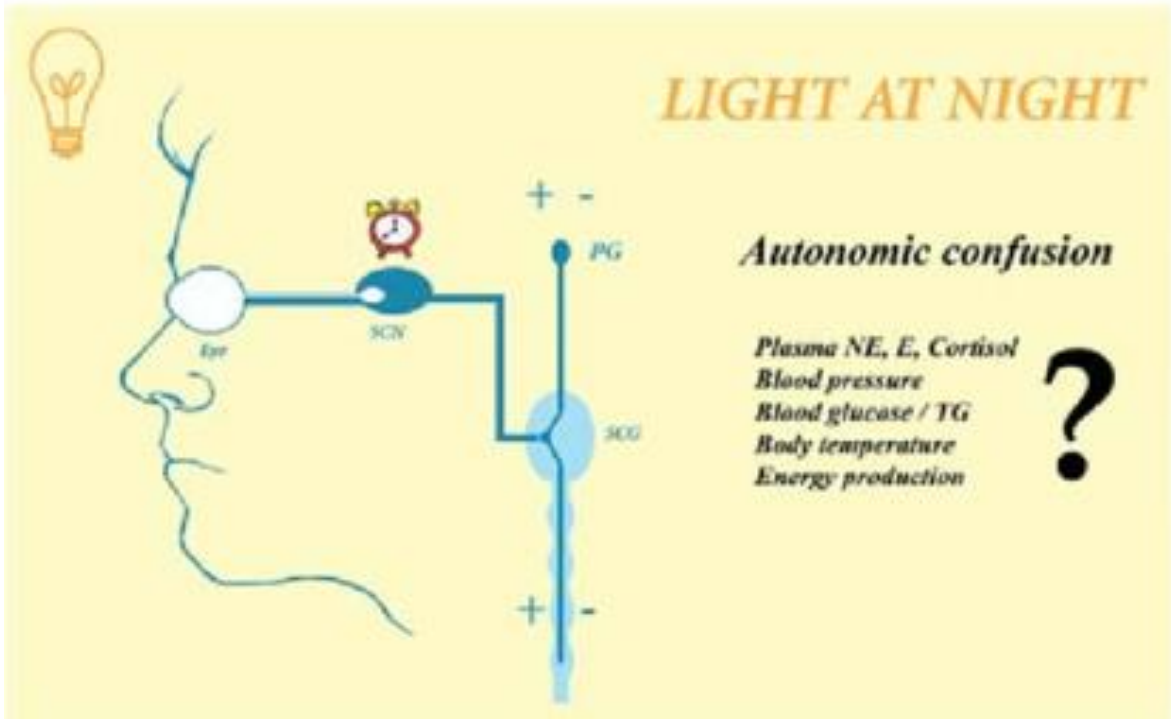
DOI 10.1186/s40101-016-0110-x

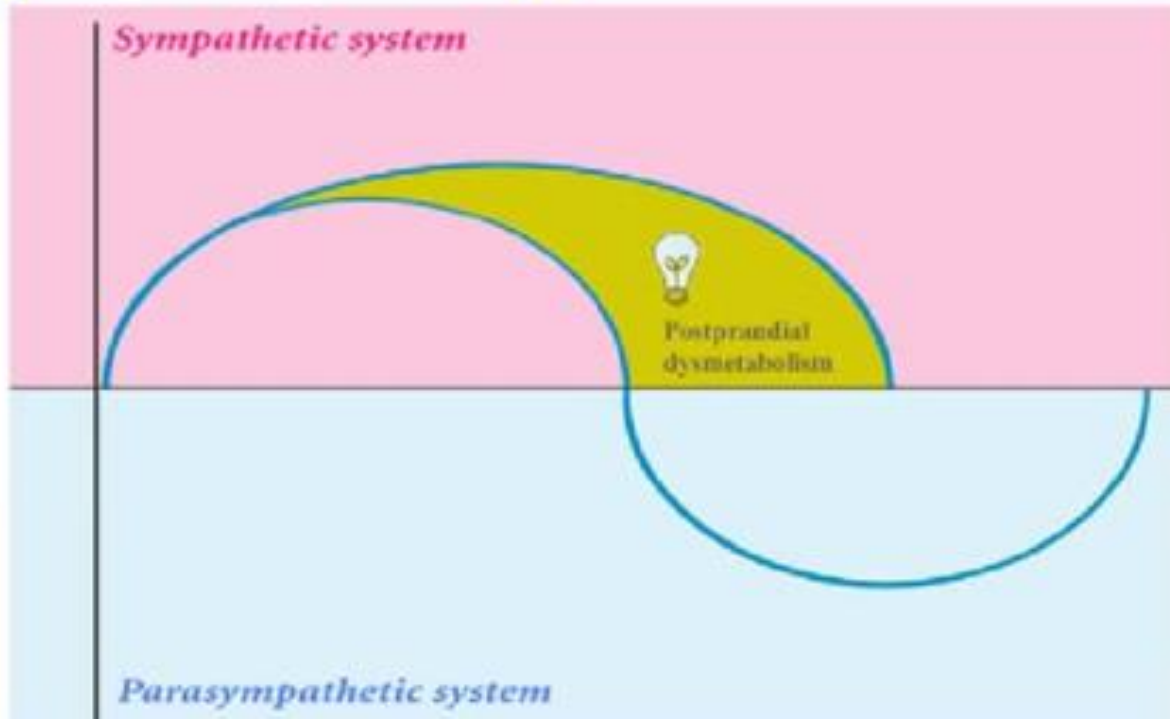
Sunlight vs. Junk Light




MORNING
Sympathetic Takeover
PG
Eye
SCN
SCG
Plasma NE, E, Cortisol ↑
Blood pressure ↑
Blood glucose / TG ↑
Body temperature ↑
Energy production ↑


NIGHT
Melatonin
Parasympathetic Takeover
PG
Eye
SCN
SCG
Plasma NE, E, Cortisol ↓
Blood pressure ↓
Blood glucose / TG ↓
Body temperature ↓
Energy production ↓


LIGHT AT NIGHT
PG
Eye
SCN
SCG
Autonomic confusion
Plasma NE, E, Cortisol
Blood pressure
Blood glucose / TG
Body temperature
Energy production
?


Sympathetic system
Postprandial dysmetabolism
Parasympathetic system

Circadian Misalignment

Food consumption too close to bedtime

Late-Night Eating-Induced Physiological Dysregulation and Circadian Misalignment Are Accompanied by Microbial Dysbiosis

*Yinhua Ni, Lianxin Wu, Jinlu Jiang, Tianqi Yang, Ze Wang, Lingyan Ma, Liujie Zheng, Xin Yang, Zeming Wu, and Zhengwei Fu**

In summary, the present study mimicked the most common lifestyle in human by changing to a 16 h/8 h light/dark cycle and setting patterns with different meal time, and our data revealed that the late-night eating caused an increase of body weight gain and a decrease of physical activity, and these results were associated with hepatic lipid accumulation and systemic inflammation in peripheral tissues. The impact of late-night eating on these physiological functions might be partly induced by the dyssynchrony of peripheral clock and master clock, which was an overall 4 h phase delay in the late-night eating rats. Moreover, late-night eating also resulted in a significant alternation in the compositions and functions of gut microbiota, and thereby further contributing to the development of metabolic disorder.

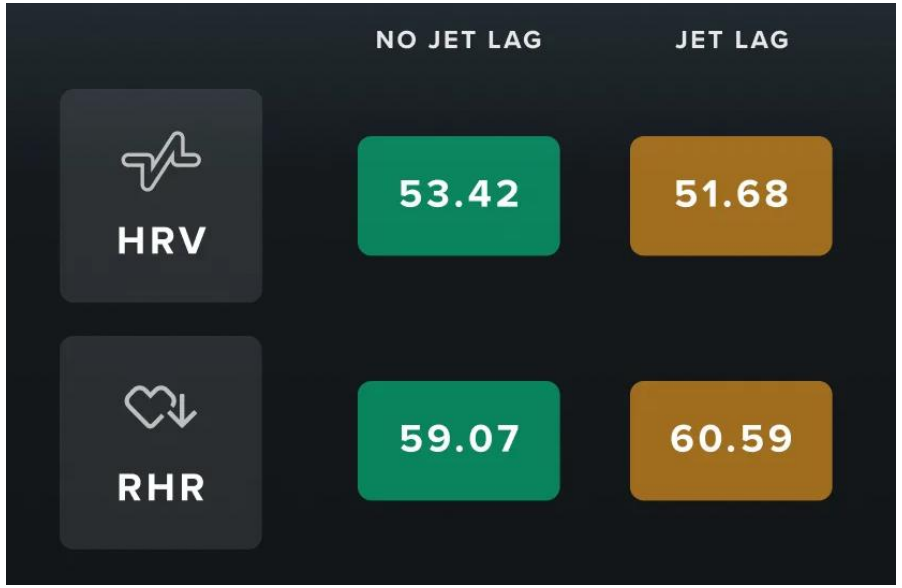
DOI: 10.1002/mnfr.201900867

Circadian Misalignment

Trans-Meridien Travel (Jet Lag)

A New Study by WHOOP and CLEAR Uncovers The Impact of Travel on Sleep and Stress

For every hour of travel, there's evidence that both heart rate variability and resting heart rate are negatively impacted, so practicing good habits in flight may help support better post-flight recovery. Recycled air on planes can be dehydrating, and alcohol has been shown to reduce blood oxygen saturation and increase heart rate.



Reminder
We are losing an hour of sleep TONIGHT

Questions to Ask Your Patients…

- Do you feel safe in your home/bedroom/bed?

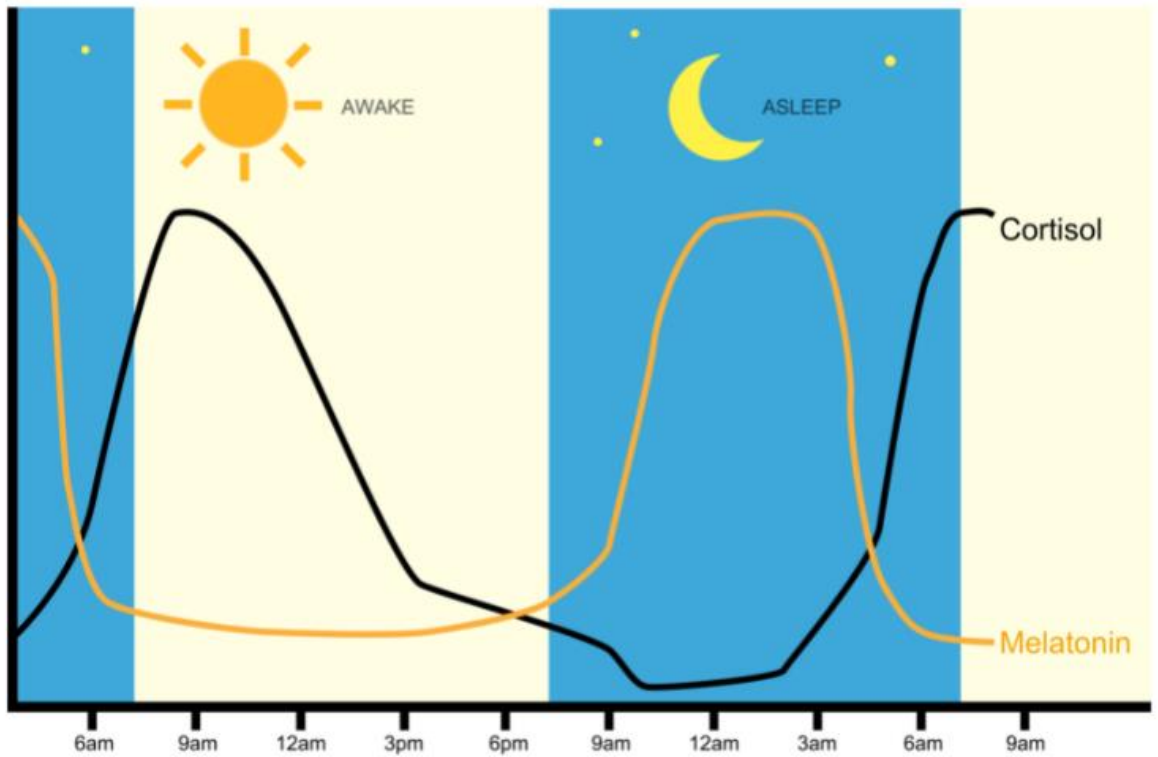
- Do you have…
  - Difficulty falling asleep?
  - Staying asleep?
  - Multiple wakings at night?
  - Difficulty waking in the morning?
  - Good energy upon waking?
  - A wind-down practice?

- What is your…
  - Routine for 2 hours before bed?
  - Routine for first hour upon waking?
  - Work schedule like?
  - Exercise timing?
  - Supplement timing?

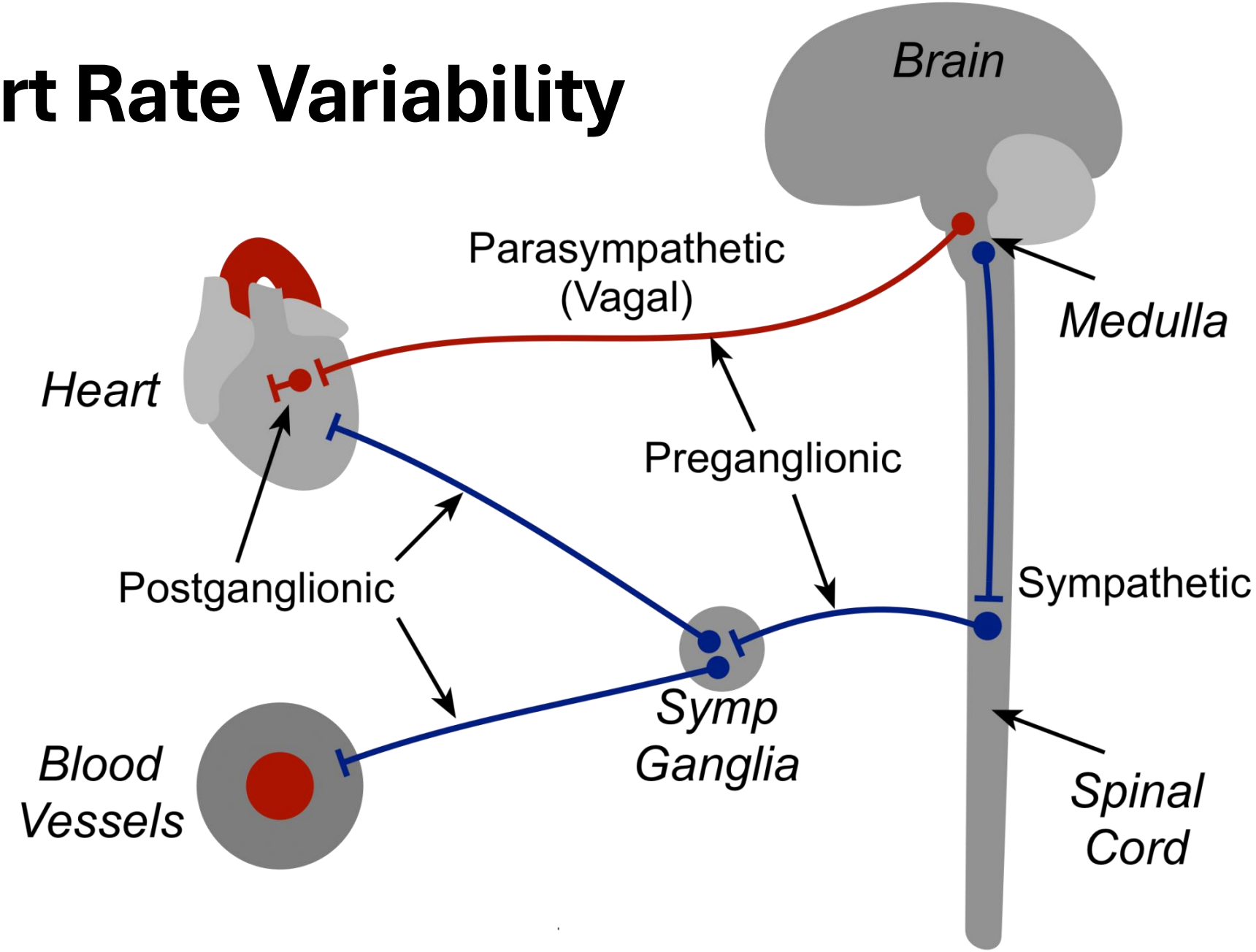
- Are you able to go outdoors during the day?

How do we Measure the Function of Vagus Nerve and Sleep?

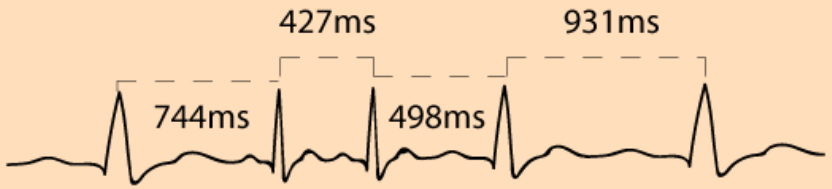
Wearable Devices and Hormone Testing



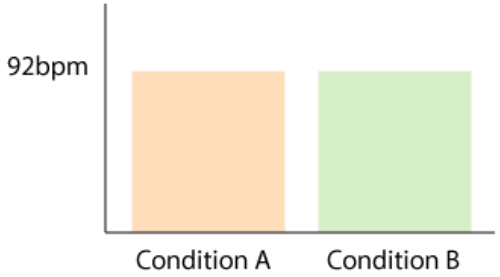
Heart Rate Variability



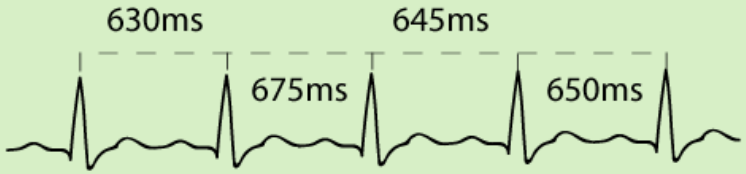
Heart Rate vs. Heart Rate Variability



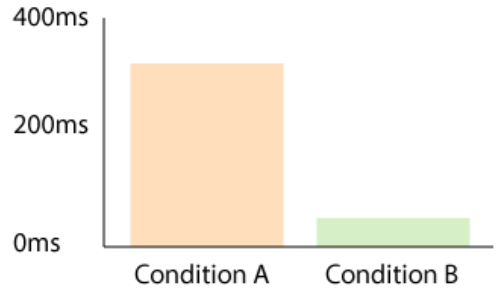
Average RR interval = 650ms / 92bpm
mean RMSSD = 313ms



No difference discernible when compared across beats per minute (bpm), or RR interval.

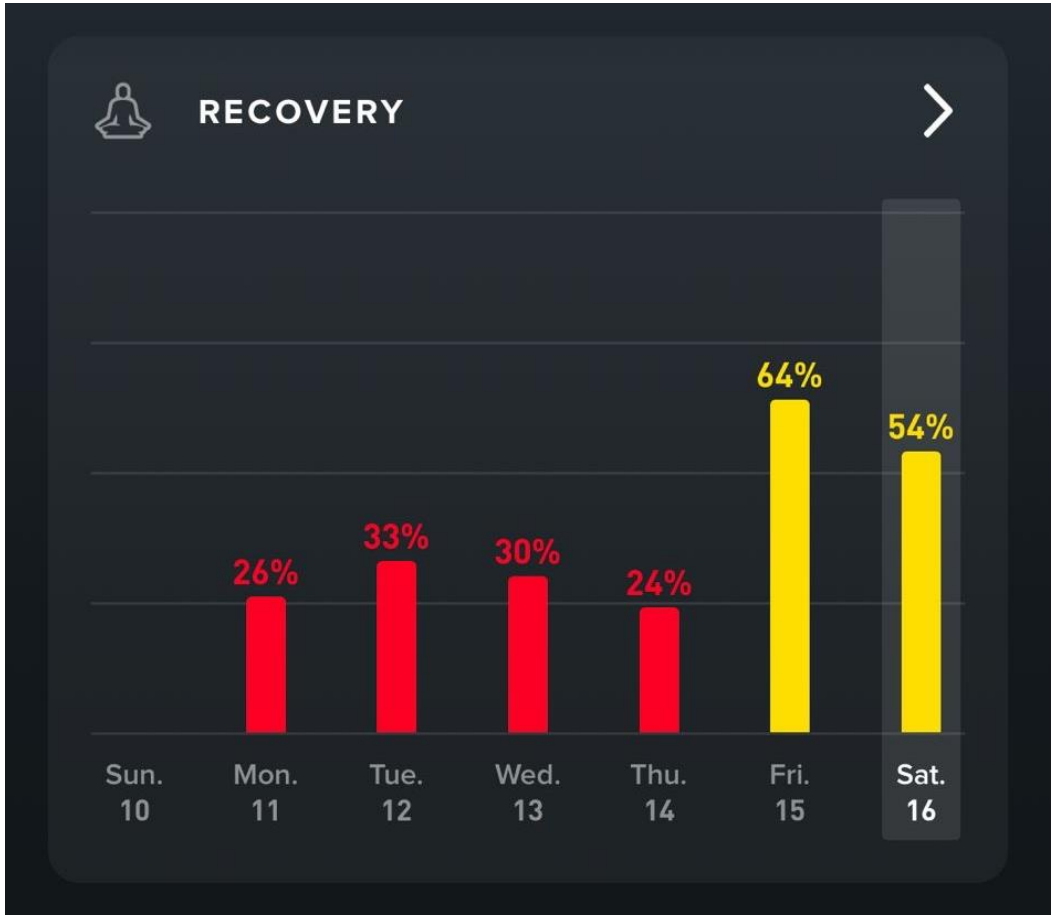


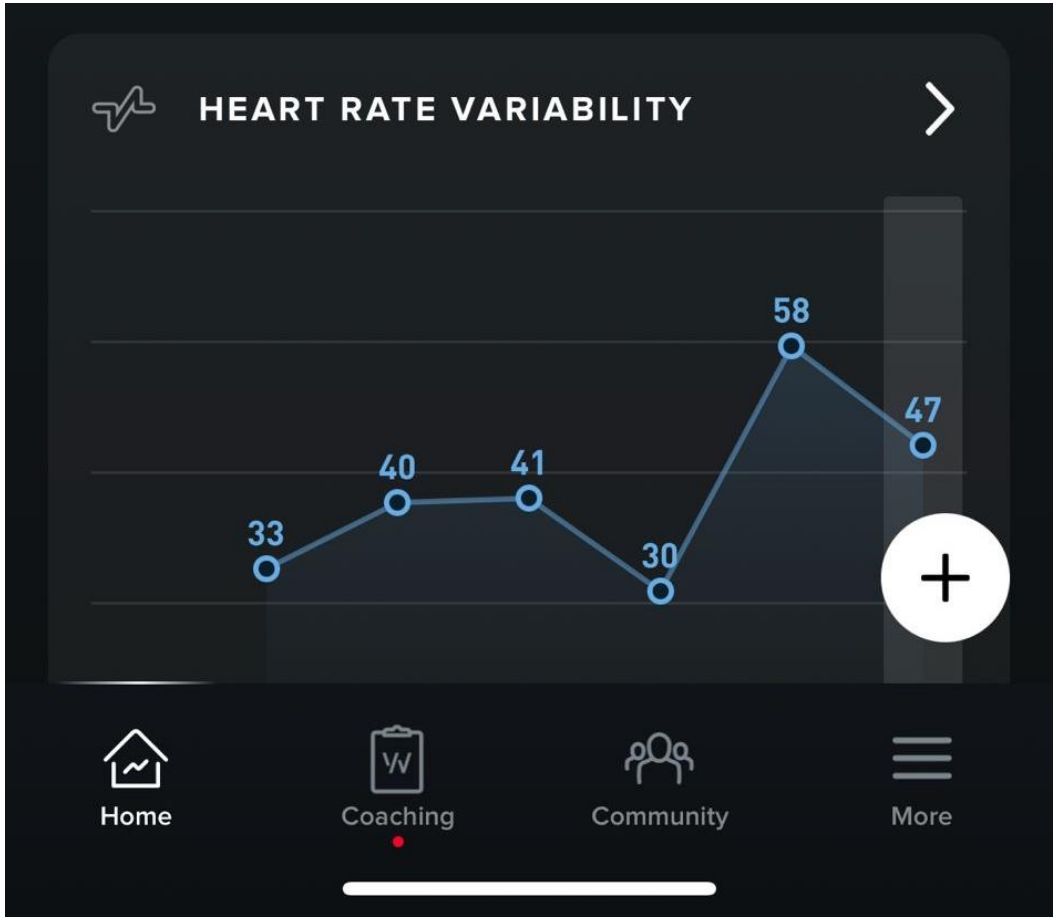
Average RR interval = 650ms / 92bpm
mean RMSSD = 31ms



The RMSSD values suggest that **condition B is more physiologically arousing than condition A** (lower HRV associated with increased physiological arousal).

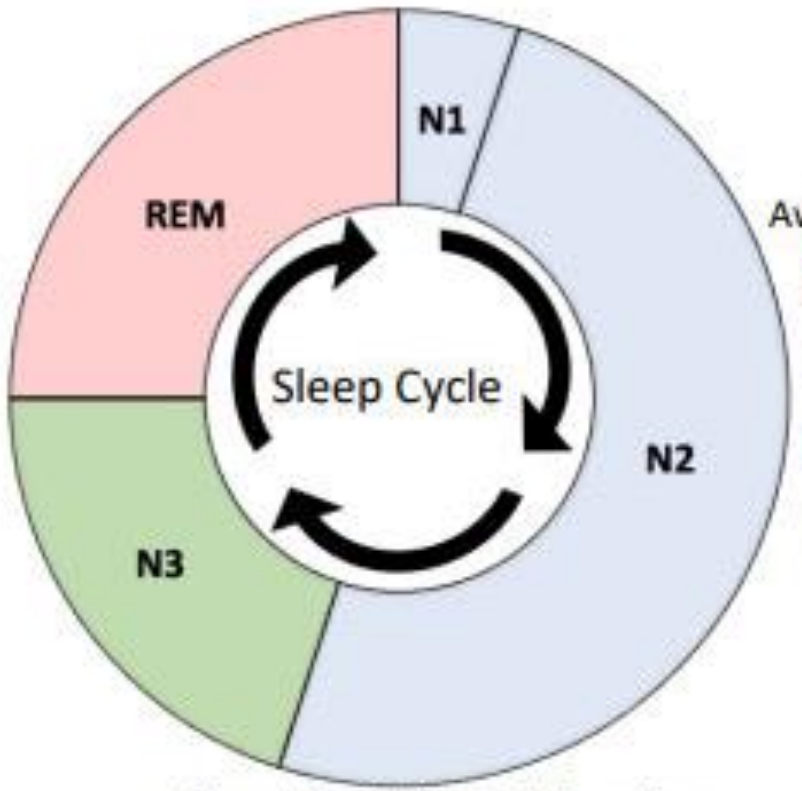
Recovery is directly linked to HRV

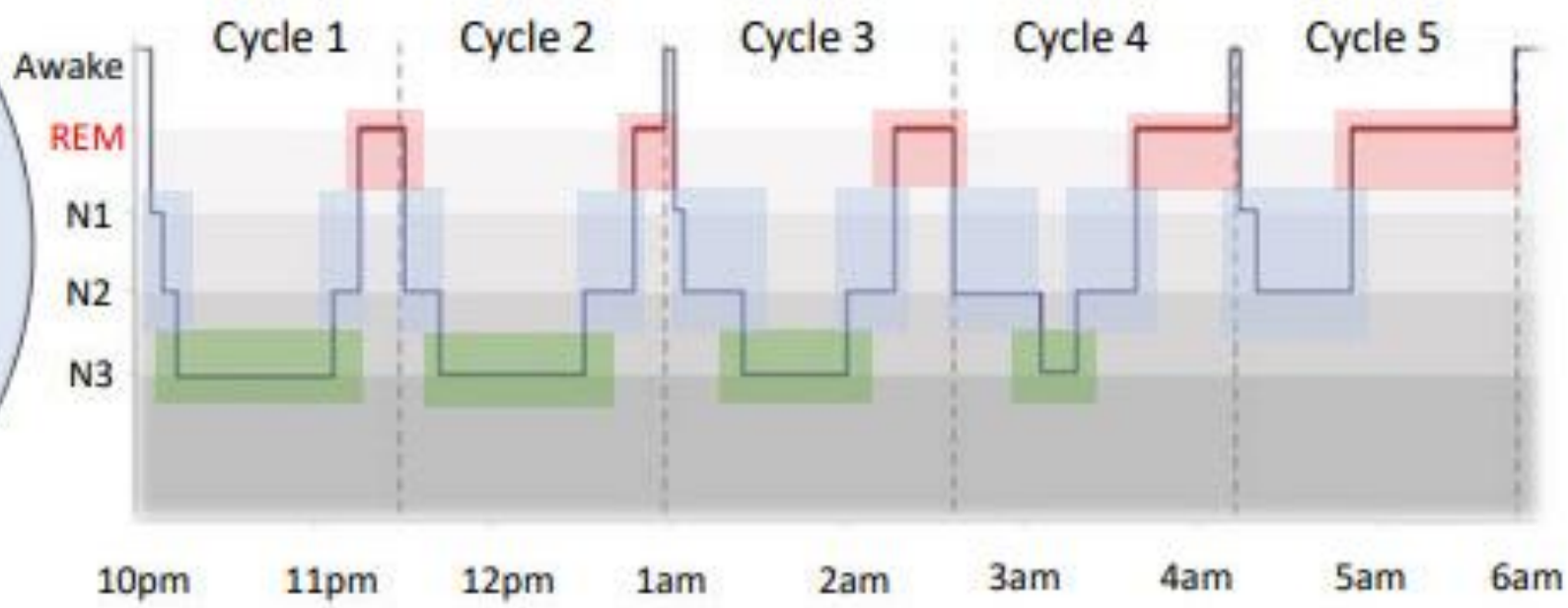




Measuring HRV and Recovery Index

Optimal Sleep Architecture





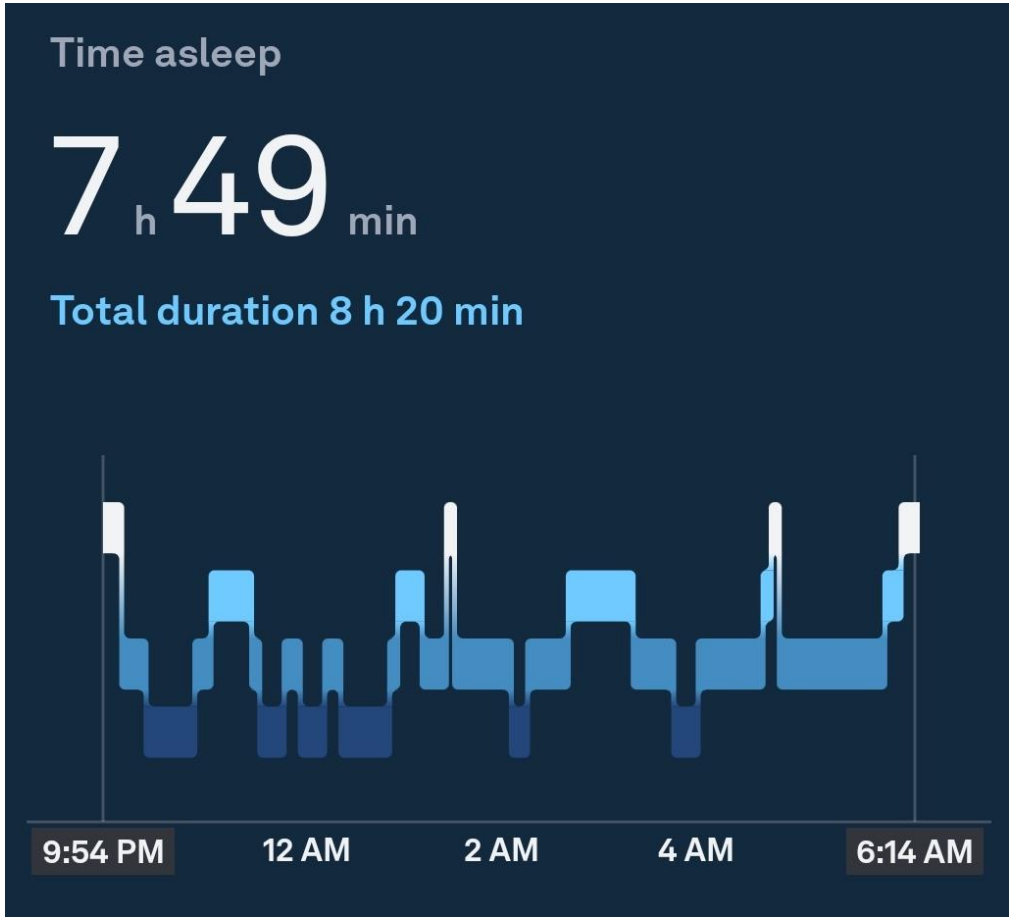
NREM

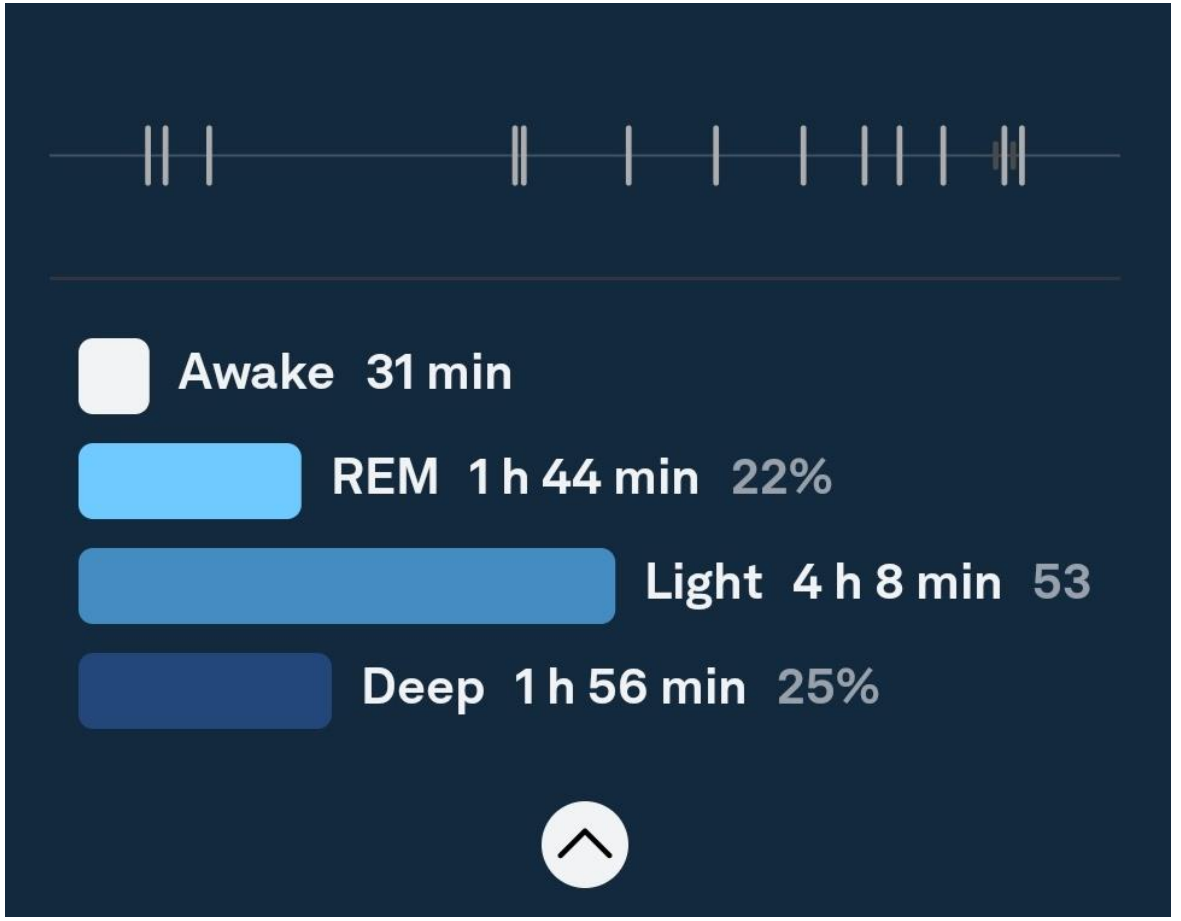
Stage **N1**: 2-5% Total sleep time
Stage **N2**: 45-55% Total sleep time
Stage **N3**: 10-20% Total sleep time

REM: 20-25% Total sleep time

Sleep Architecture on Wearables

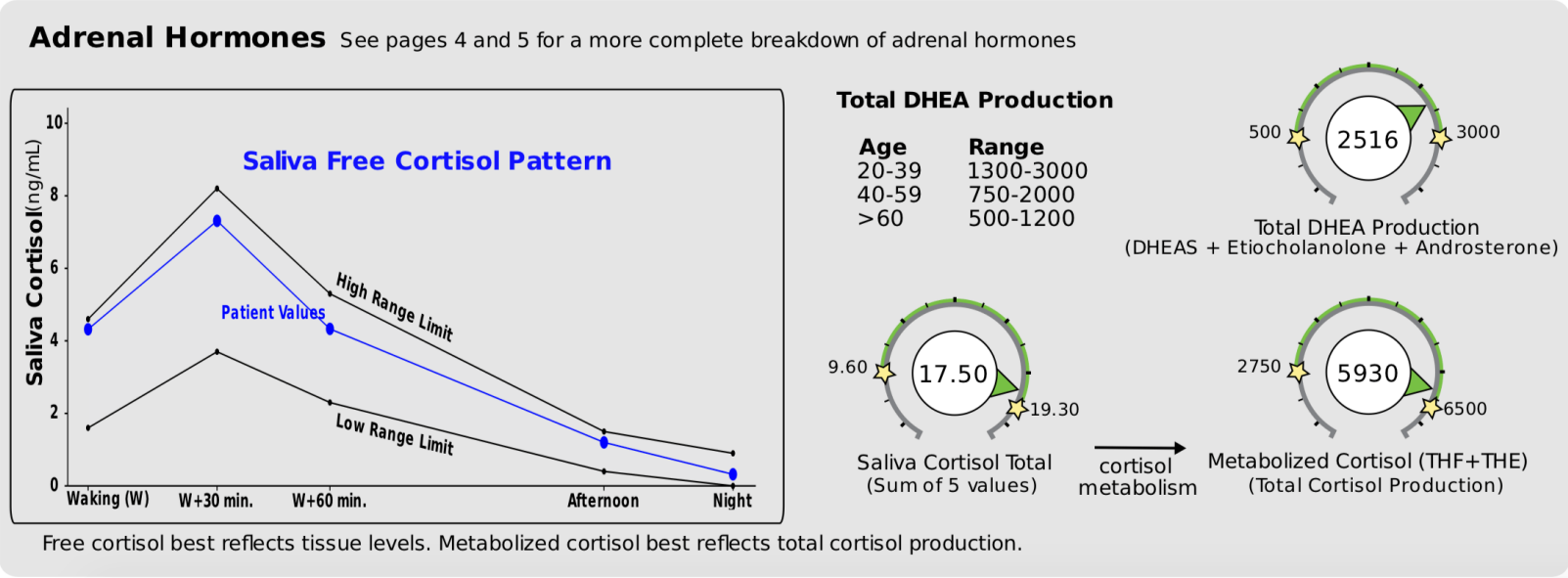
25% REM / 50% LIGHT / 25% DEEP

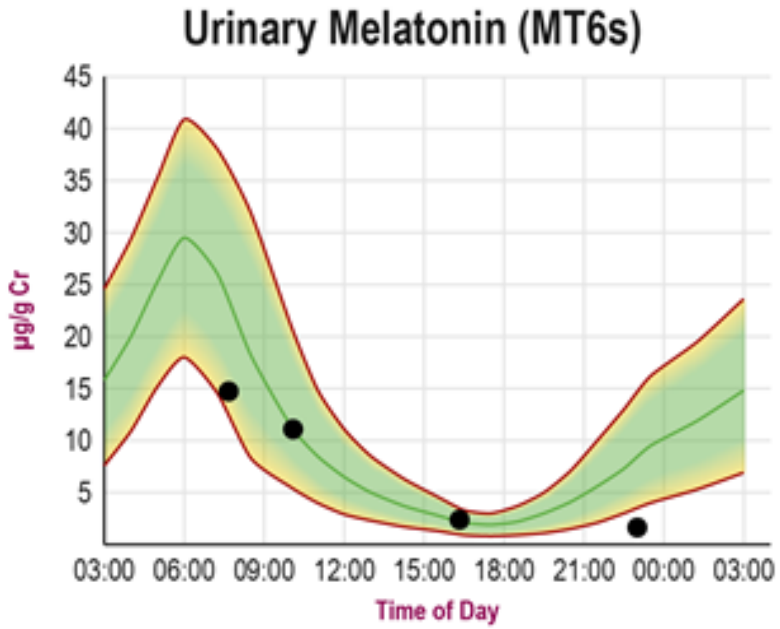




Testing for Circadian Rhythm

Functional Testing of Urinary or Salivary Cortisol Pattern



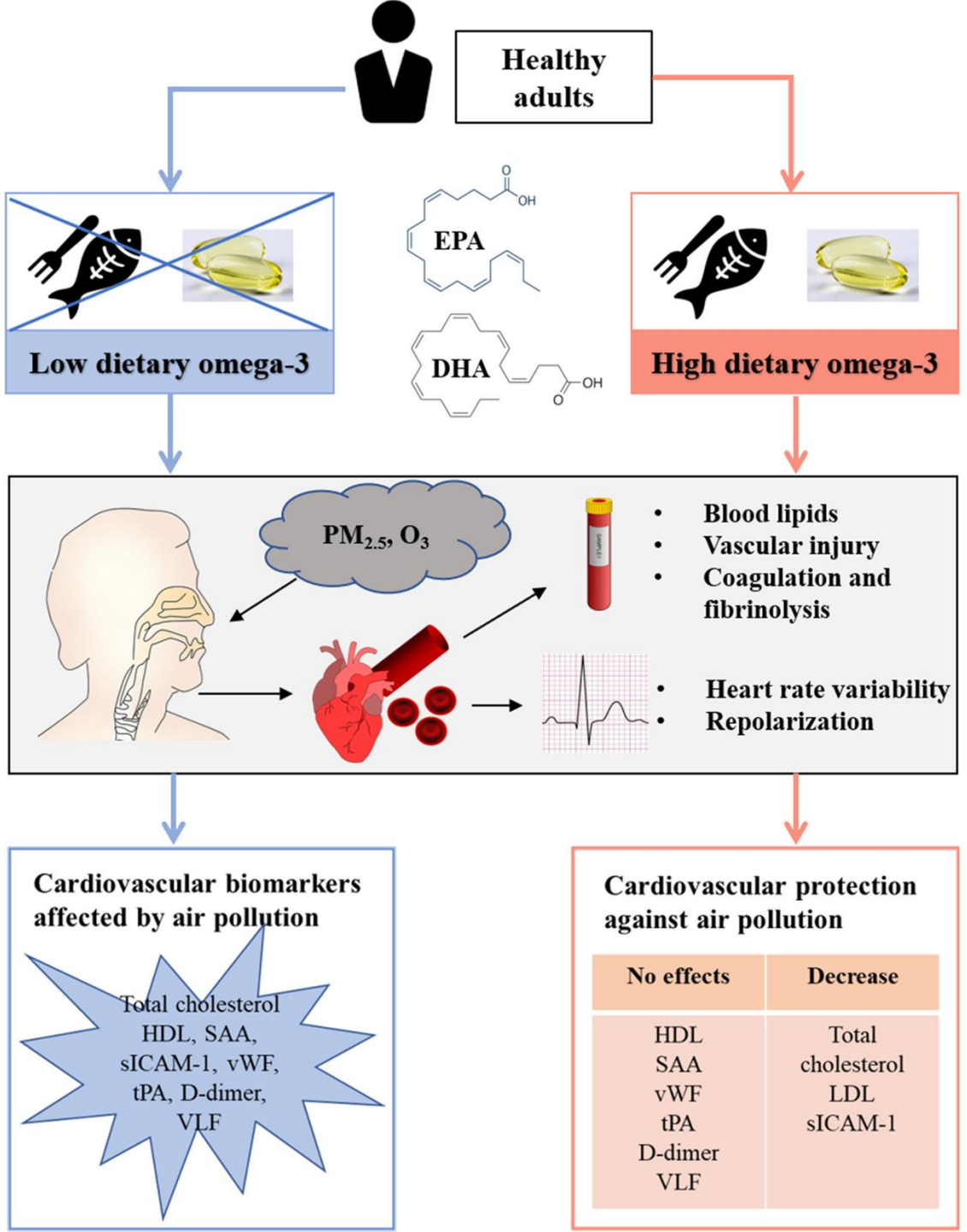


Omega-3 Index

Omega-3 Index

- % of EPA and DHA in RBCs
  - Low < 4%
  - Normal = 4-8%
  - Optimal = 8-12%
  - High > 12%

- EPA and DHA have powerful anti-inflammatory function



Strategies for Upgrading Vagus Nerve and Sleep

Action Steps for Upgraded Sleep

- Good Sleep Hygiene
  - Room should be cool, dark, happy and SAFE!
- Consistent Bed and Wake Times
  - Consistency is key to getting good sleep – habit forming!
- Morning Sunlight (First Light)
  - 10-30 minutes of natural light exposure, first thing in the morning
- Practice Vagus activation exercises before bed
  - Breathing exercises to put you into parasympathetic “rest” state
- Stop Bright and Blue Light for 1-2 hours before bed
  - At minimum, turn on Night Shift on electronics

Action Steps – Daily Timing

- Meal Timing
  - Eat meals at consistent and regular Intervals
  - Stop eating 2-3 Hours before bedtime
  - Avoid caffeine within 1.5 hours of waking and after 12 noon
  - Avoid sugar early and late in the day

- Movement
  - Exercise/move daily, in the morning or early afternoon
  - Aim for 8000+ steps daily

Article

Transcutaneous Vagus Nerve Stimulation Could Improve the Effective Rate on the Quality of Sleep in the Treatment of Primary Insomnia: A Randomized Control Trial

Yating Wu [1,2], Lu Song [3], Xian Wang [1], Ning Li [1], Shuqin Zhan [1], Peijing Rong [4], Yuping Wang [1] and Aihua Liu [1,*]

5. Conclusions

In conclusion, the results of this study show that auricular t-VNS at 20 Hz for 1 month is effective for primary insomnia patients; the patients obtained an absolute reduction in PQSI scores. The t-VNS treatment also significantly relieved the level of anxiety and depression assessed by the HAMD and HAMA scores, with good safety and high compliance with daily stimulation.

- Several studies have shown that transcutaneous vagus nerve stimulation (t-VNS) can improve sleep quality in patients with primary insomnia
  - A randomized control trial demonstrated that t-VNS effectively enhanced sleep quality, with a significantly higher success rate compared to the control group

- T-VNS was found to increase the number of periods in the rapid eye movement (REM) phase, prolong the REM phase, and extend total night sleep time, especially second stage sleep time

- Another study showed that low-intensity VNS prolonged average sleep latency

Morning Strategies

- First morning sunlight
  - Regulates the circadian rhythm
  - Increases Serotonin production
  - Decreases conversion to Melatonin

- Exercise/movement
  - Get outside
  - Go for a walk or bike ride
  - Start using muscles to start the day

Daytime Strategies

- Spend time outdoors
  - Eat lunch outside of office
- Movement/Exercise
  - Go for a midday walk
- Minimize use of Sunglasses
  - Expose eyes to natural sunlight

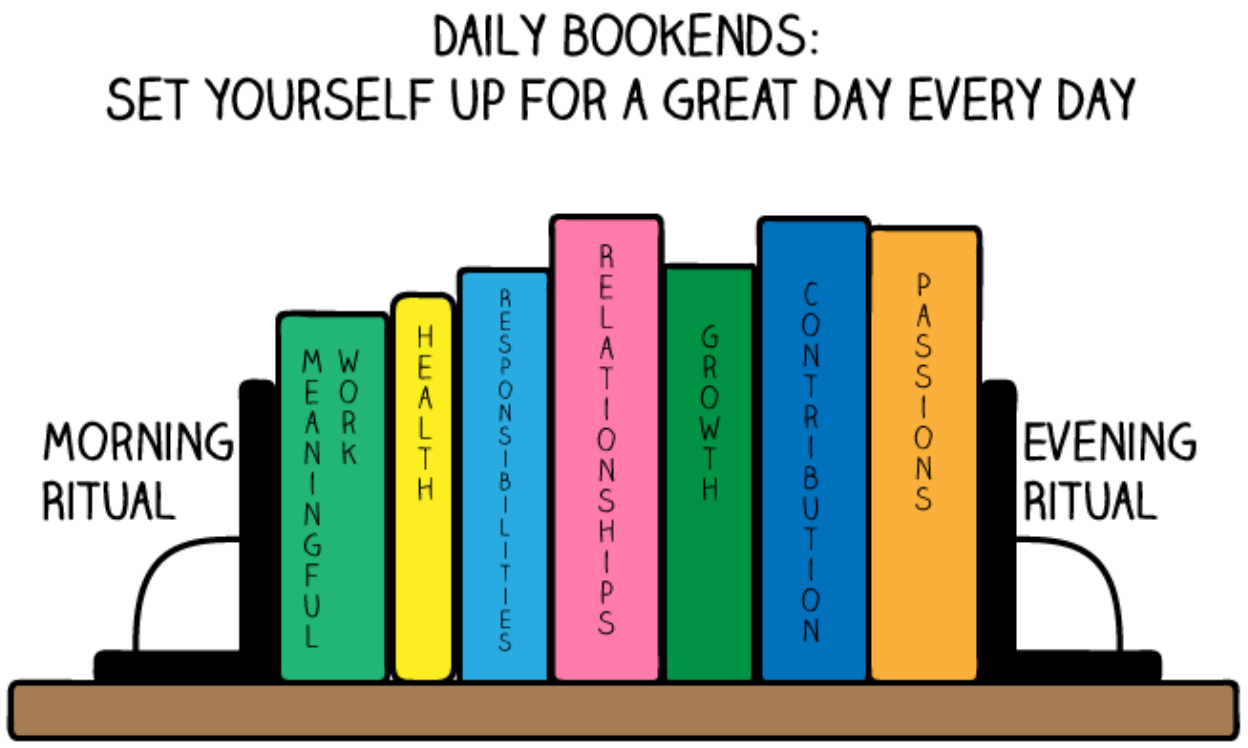
Evening Strategies

- Bookend with WIND DOWN routine
- Stop eating 2-3 hours before bed
- Watch the sunset
- 3-2-1 Circadian Rhythm Rule
- Supplements
  - Magnesium Bisglycinate
  - L-Theanine
  - Low Dose Melatonin

Pre-Sleep Strategies

- Bookend/Winddown Routine
  - Breathing practice
  - Meditation
  - Journaling
- Minimize/stop phone use
  - Charge phone in a separate room
- Minimize emotional stressors
  - Connecting with partner

Bookending your Day



- Consistent wake and sleep routines
- Short personalized routines at the beginning and end of day
  - Journaling
  - Breathing
  - Meditation
  - Vagus Nerve Stimulation
- Routines help to normalize routine and engage the polyvagal ventral vagal safety

During Sleep Strategies

- Mouth taping
  - Stop mouth breathing at night
- Nasal dilators
  - Enable nose breathing
- Wearable sleep trackers

Deep Breathing Exercises and Meditation

Acute Effects on Heart Rate Variability during Slow Deep Breathing

V Malhotra [1], R Bharshankar, N Ravi, O L Bhagat

high level of statistical significance during the manoeuvre. Frequency Domain parameters: Low Frequency (LF), High Frequency (HF), LF/HF ratio increased significantly. Parasympathetic activity is represented by LF when respiration rate is lower than 7 breaths per minute or during taking a deep breath. Thus, when the subject is in the state of relaxation with a slow and even breathing, the LF values can be very high indicating an increase in parasympathetic activity rather than an increase in sympathetic regulation. Practice of pranayama naturally slows the breathing, which in

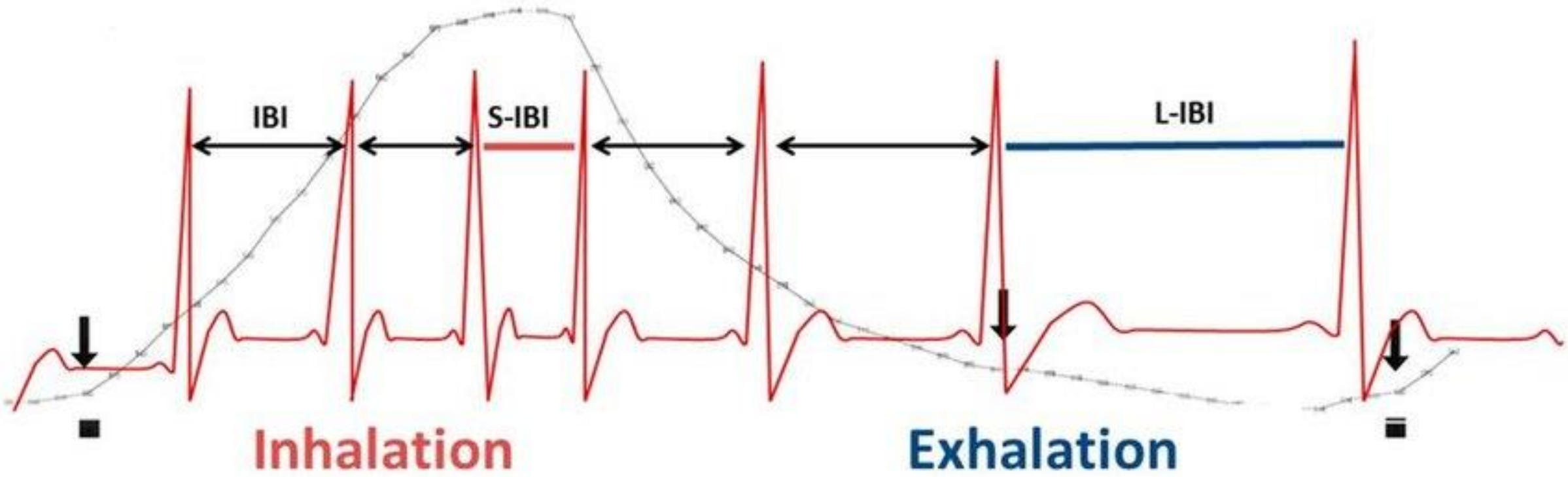
and central mechanisms. Slow yogic breathing (pranayama) may serve as a physiologic method to draw upon cardio-vagal reserve and regular practice of these manoeuvres may beneficially affect cardiovascular autonomic regulation in health and in various cardiovascular diseases.

PMID: 33397876


S 200
Ex: 5727/A10031741640
Se: 0
Im: 20
-0:16

Learn To Breathe Correctly

Respiratory Sinus Arrhythmia, the driver of HRV



The heart rate increases during inhalation and decreases during exhalation, resulting in the longest heart period during exhalation (L-IBI) and the shortest heart period during inhalation (S-IBI)

https://doi.org/10.1088/1361-6579/ab299e

Cold Exposure/Cryotherapy

A systematic review of HRV during diving in very cold water

Richard Viking Lundell [a] and Tommi Ojanen [b]

Conclusions

HRV is a useful method to study divers, because it is an easily applicable method that provides a great amount of information on the ANS status. More research is needed to confirm how the human ANS responds to diving in different conditions. Especially when it comes to very cold water, the knowledge is limited. However, results in published studies are surprisingly coherent and show a predominant activation of the parasympathetic nervous system during exposure. The cold seems to strengthen the PNS responses of diving.

PMID: 37079282

Aggressive Gargling & Gag Reflex Activation

The Effect of Gag Reflex on Cardiac Sympatovagal Tone

S. Mehran Hosseini, Mohsen Jamshir, Alireza Maleki

Received: 28 Jan 2012 / Accepted: 09 Mar 2012

Discussion

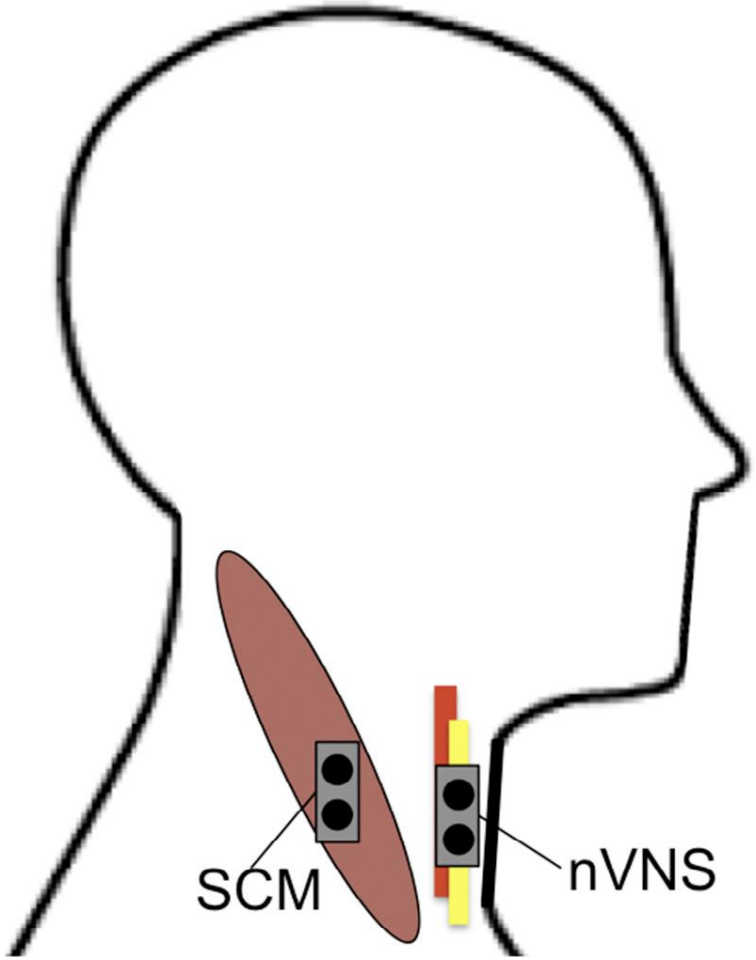
Gagging caused statistically significant increase in average heart rate but illustrated the changing trend of autonomic tone in favor of parasympathetic division over 5 minutes interval. Despite some increase in parasympathetic activity (not significant), there was about 50% reduction in normalized LF and LF/HF ratio. The paradoxical relation between average heart rate and HRV indexes may be due to unequal rate of change in autonomic fiber activities which was masked by 5 minutes averaging following gag stimulation.

PMID: 22811779

Transcutaneous Vagus Nerve Stimulation (VNS)

- Electrical Stimulation of Vagal fibers along the anterolateral neck
- Easily accessible within the carotid sheath
- Activation of both afferent and efferent axonal fibers
- 100,000 fibers on left side and 200,000+ on the right side

How does nVNS Work?

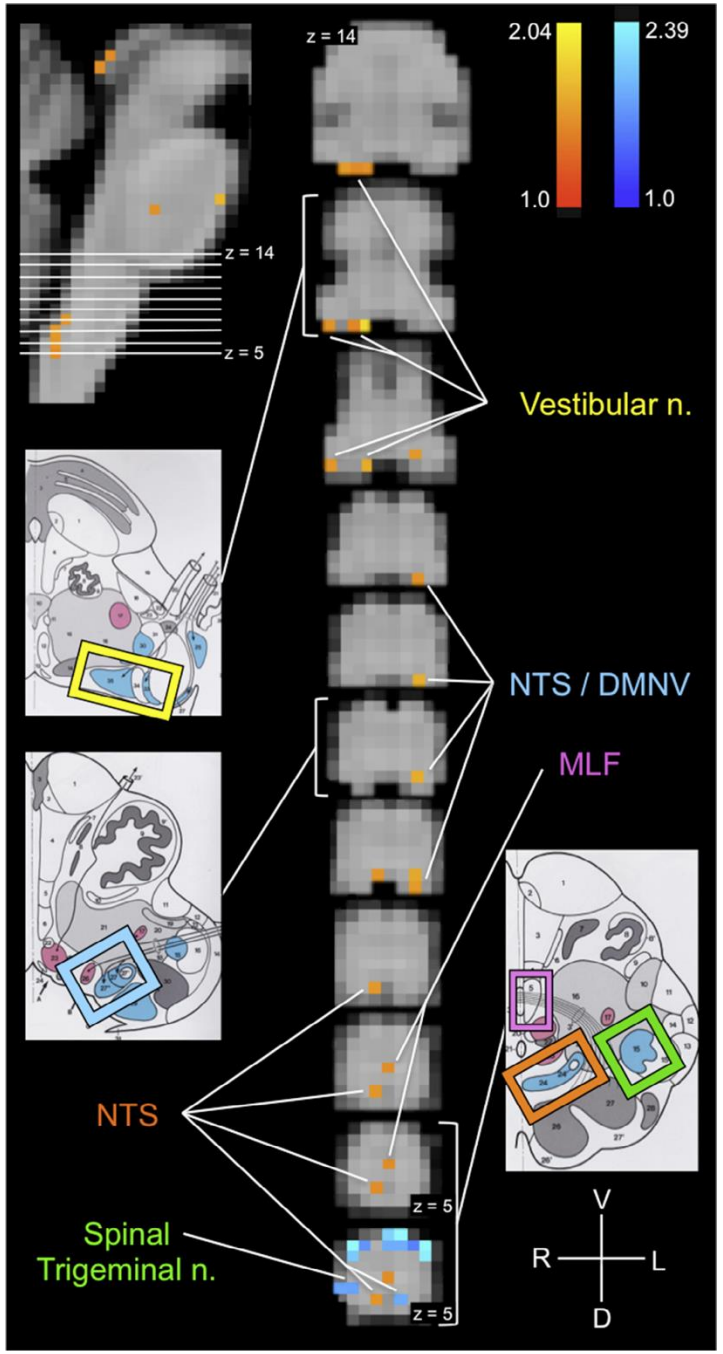


Activation of Brainstem Nuclei:

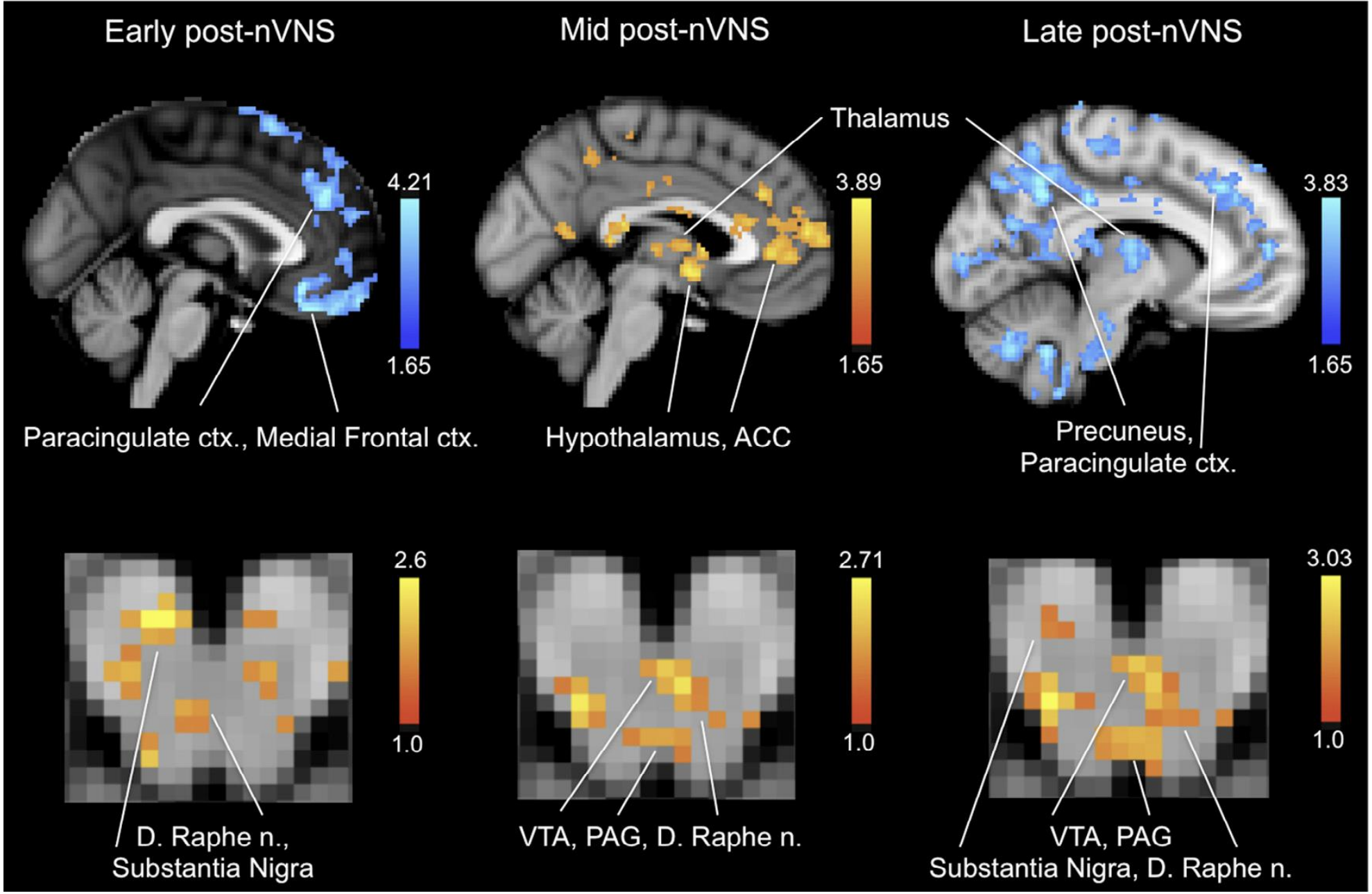
- **Nucleus of the Solitary Tract**
- **Dorsal Motor Nucleus of Vagus**
- Vestibular Nuclei
- Medial Longitudinal Fasciculus

Inhibition of Brainstem Nuclei:

- Spinal Trigeminal Nucleus

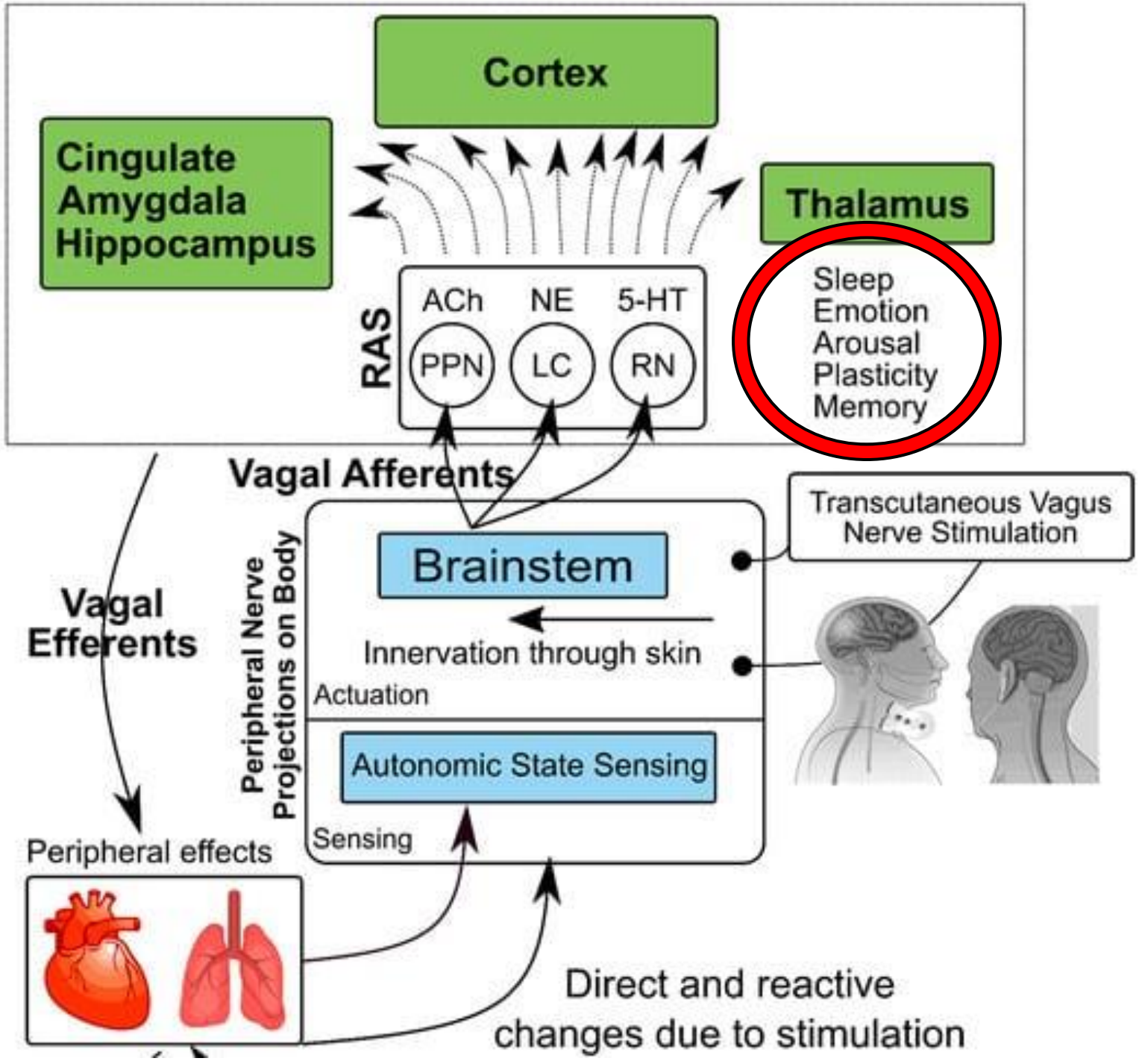


Access to Vagal Projections via Cutaneous Electrical Stimulation of the Neck: fMRI Evidence in Healthy Humans. Frangos, E. Komisaruk, B. Brain Stimulation. DOI: 10.1016/j.brs.2016.10.008

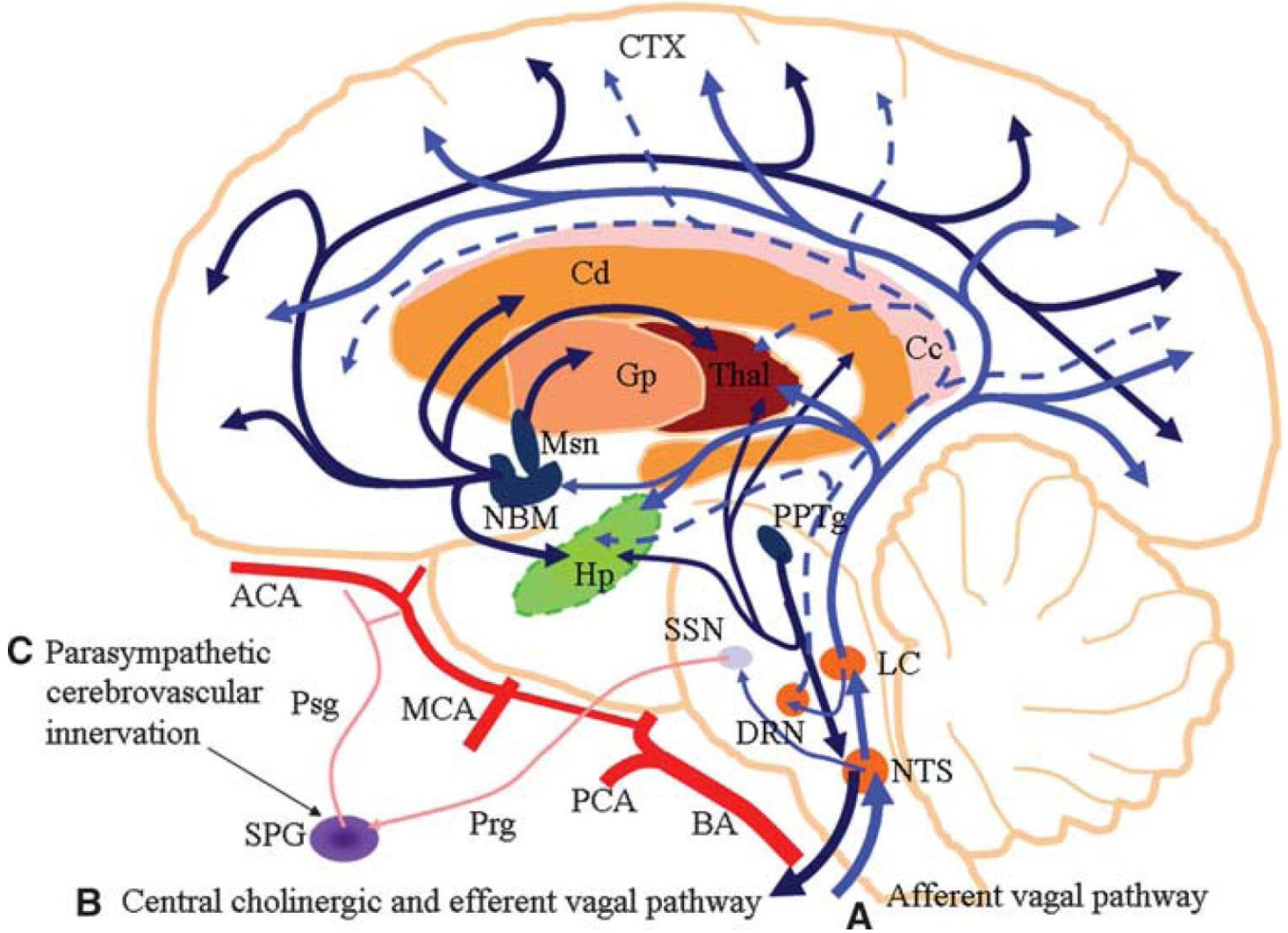


Early Phase (3-5 mins) Mid Phase (7-9 mins) Late Phase (13-15 mins)

Access to Vagal Projections via Cutaneous Electrical Stimulation of the Neck: fMRI Evidence in Healthy Humans. Frangos E, Komisaruk B. Brain Stimulation. DOI: 10.1016/j.brs.2016.10.008

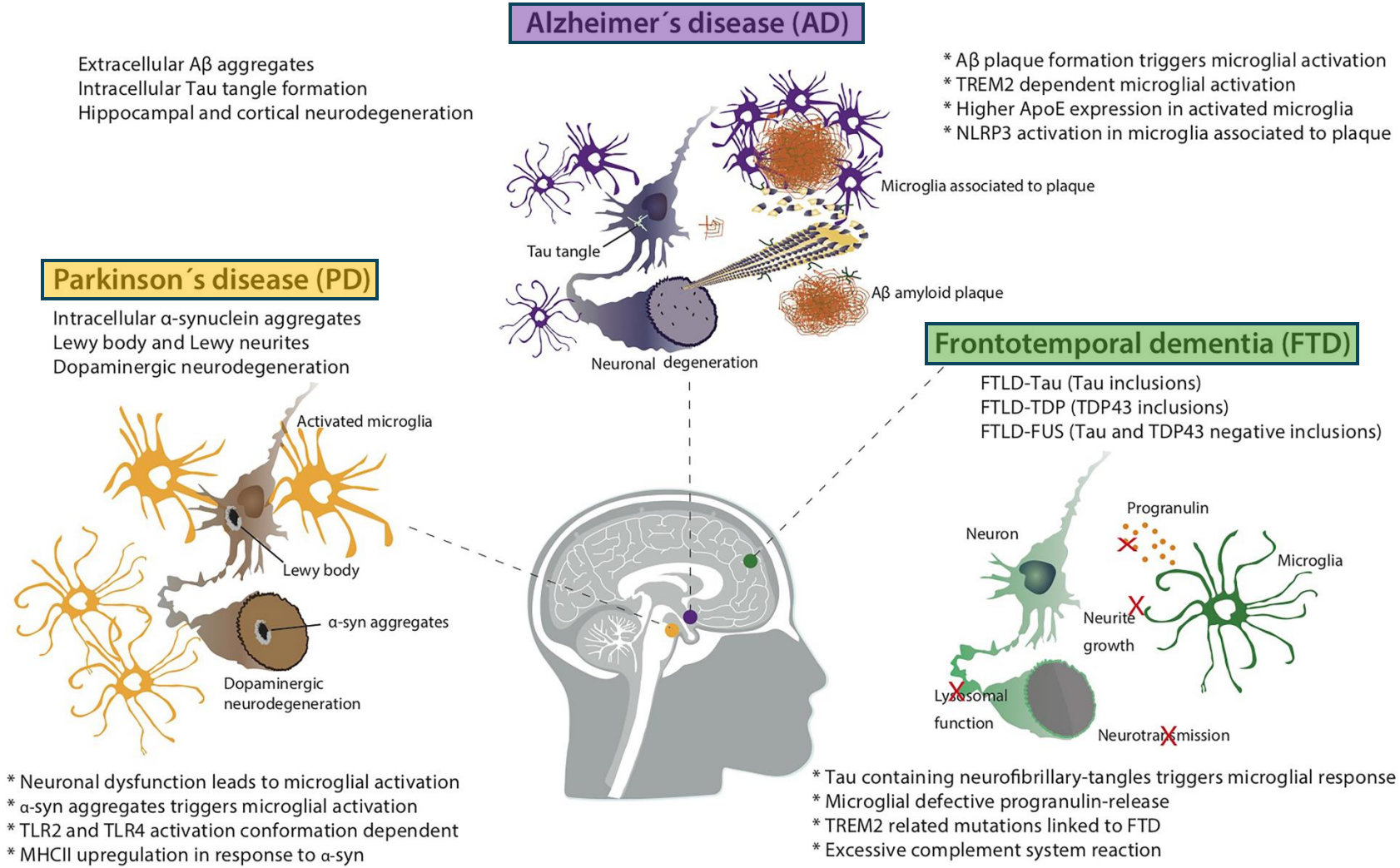

Cortex
Cingulate
Amygdala
Hippocampus
Thalamus
Sleep
Emotion
Arousal
Plasticity
Memory
RAS
ACh
NE
5-HT
PPN
LC
RN
Vagal Afferents
Vagal
Efferents
Peripheral Nerve
Projections on Body
Brainstem
Innervation through skin
Actuation
Autonomic State Sensing
Sensing
Transcutaneous Vagus
Nerve Stimulation
Peripheral effects
Direct and reactive
changes due to stimulation

Acetylcholine in the CNS



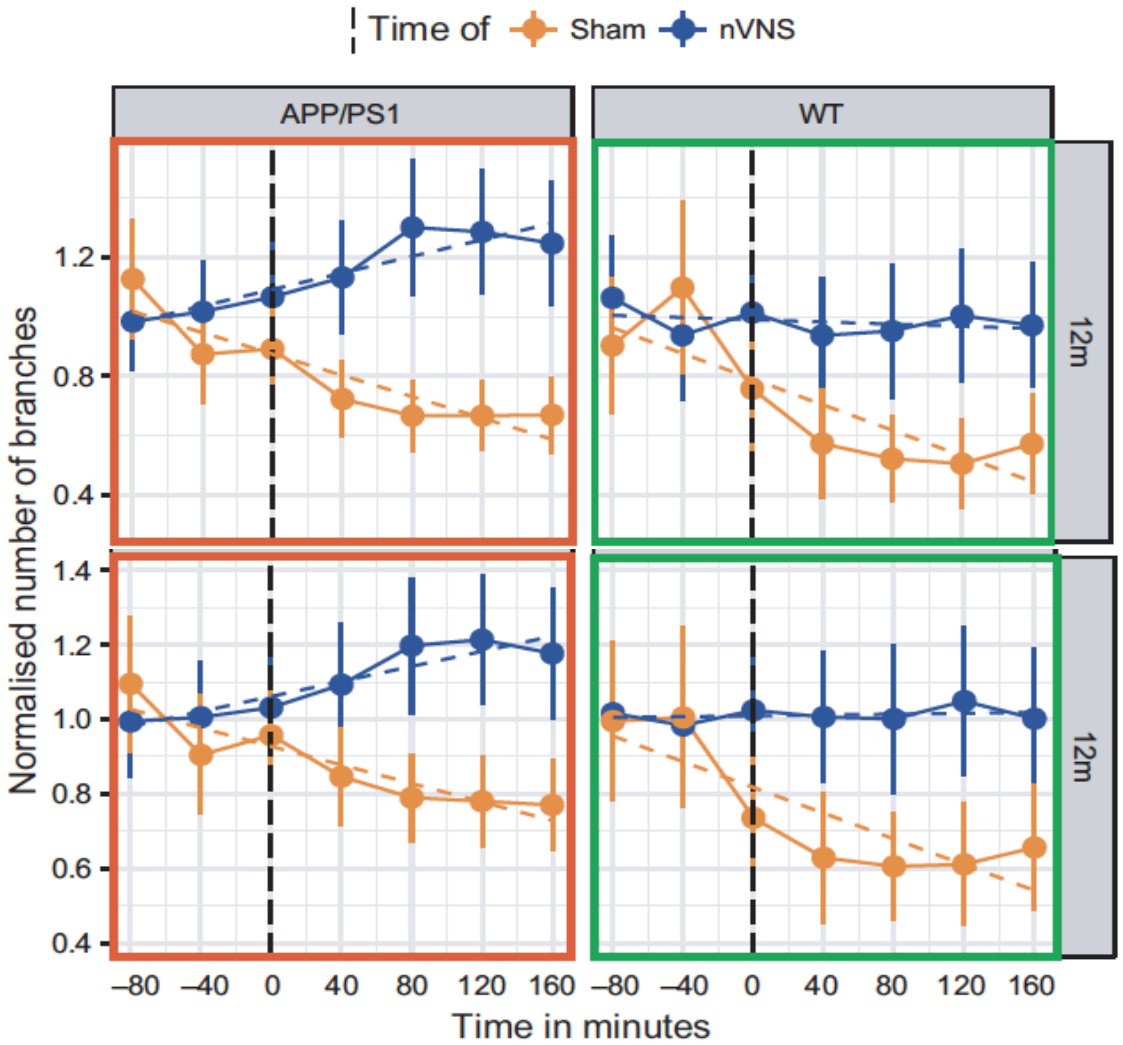
Cheyuo C, Jacob A, Wu R, Zhou M, Coppa GF, Wang P. **The Parasympathetic Nervous System in the Quest for Stroke Therapeutics**. *Journal of Cerebral Blood Flow & Metabolism*. 2011;31(5):1187-1195. doi:10.1038/jcbfm.2011.24

Microglia in Neurodegenerative Diseases



Microglia in Neurologial Diseases: A Road Map to Brain-Disease Dependent Inflammatory Response Front. Cell. Neurosci., 18 December 2018 Sec. Non-Neuronal Cells Volume 12 - 2018 |

VNS Alters Microglia Morphology



"VNS can promote M2 microglia polarization and inhibit M1 microglia polarization to alleviate brain injury via inhibition of the TLR4/MyD88/NF-κB pathway in microglia"[1]

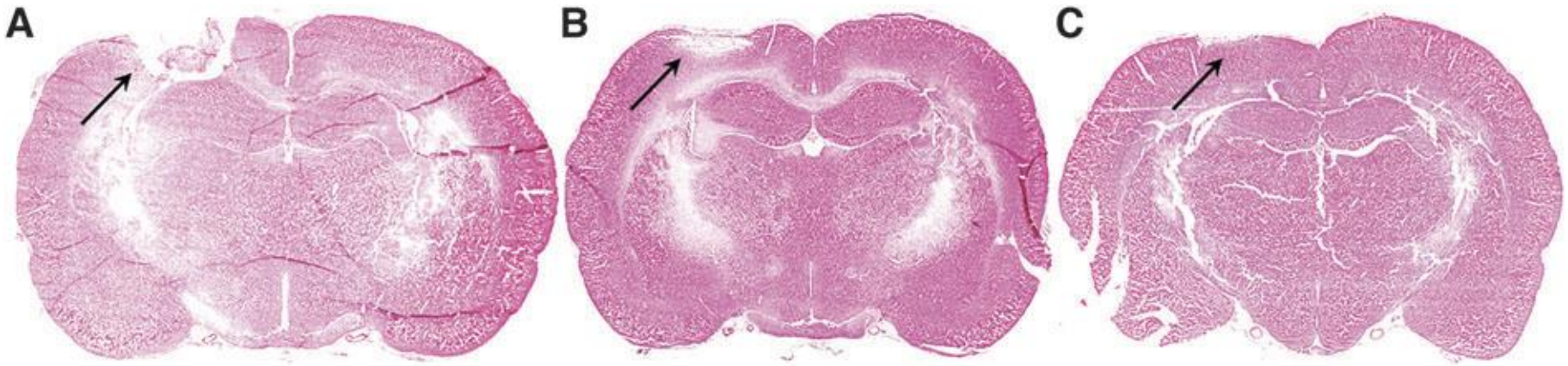
VNS promotes microglial M2 polarization through upregulating α7nAChR to reduce neuroinflammation … VNS could significantly decrease the concentrations of the pro-inflammatory cytokines and elevate the concentrations of the anti-inflammatory cytokines."[2]

"Our data show for the first time that morphological changes in activated microglia may be directly reversed by nVNS."[3]

[1]Zhang, et al., Vagus nerve stimulation promotes the M1-to-M2 transition via inhibition of TLR4/NF-κB in microglia to rescue the reperfusion injury, *Journal of Stroke and Cerebrovascular Diseases*, Vol. 31, Iss. 9, (2022)

[2]Chen, et al., Vagus Nerve Stimulation Reduces Neuroinflammation Through Microglia Polarization Regulation to Improve Function al Recovery After Spinal Cord Injury, *Frontiers in Neuroscience*, Vol. 16, 813472 (2022)

Acute Anti-Inflammatory Effects of nVNS



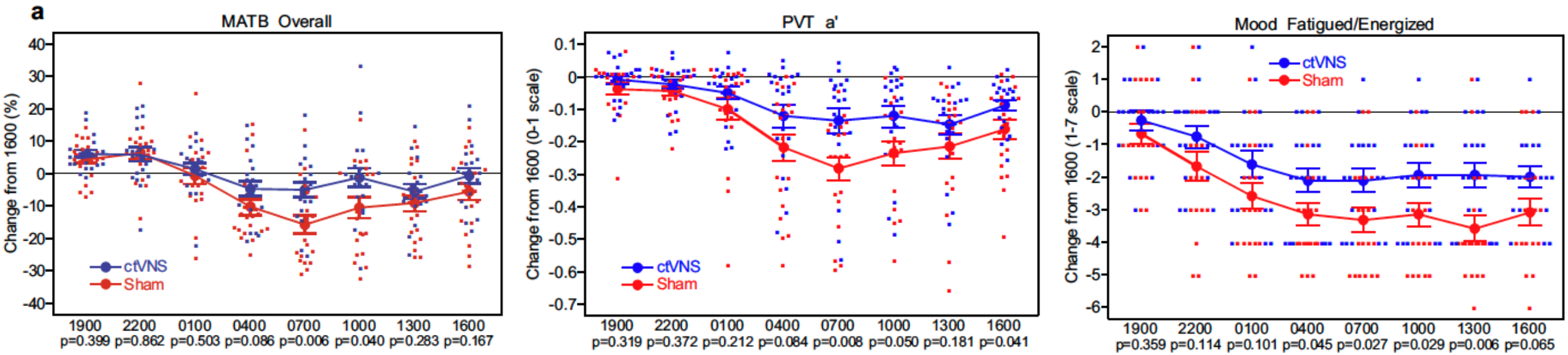
Control | Five 2-min stimulations | Five 2x2-min stimulations

Observed a statistically significant reduction in post-TBI lesion volume among both nVNS groups (2-min and 2 x 2-min).

The brain damage reduction in the higher dose (2 x 2-min) nVNS group was large enough to translate into a significant improvement in the neurobehavioral outcome measures (motor function and anxiety).

Divani, A. et al. **Non-Invasive Vagus Nerve Stimulation Improves Brain Lesion Volume and Neurobehavioral Outcomes in a Rat Model of Traumatic Brain Injury**. *Journal of neurotrauma*, *40*(13-14), 1481–1494. https://doi.org/10.1089/neu.2022.0153

ctVNS Improves Cognitive Performance Under Sleep Deprivation Stress



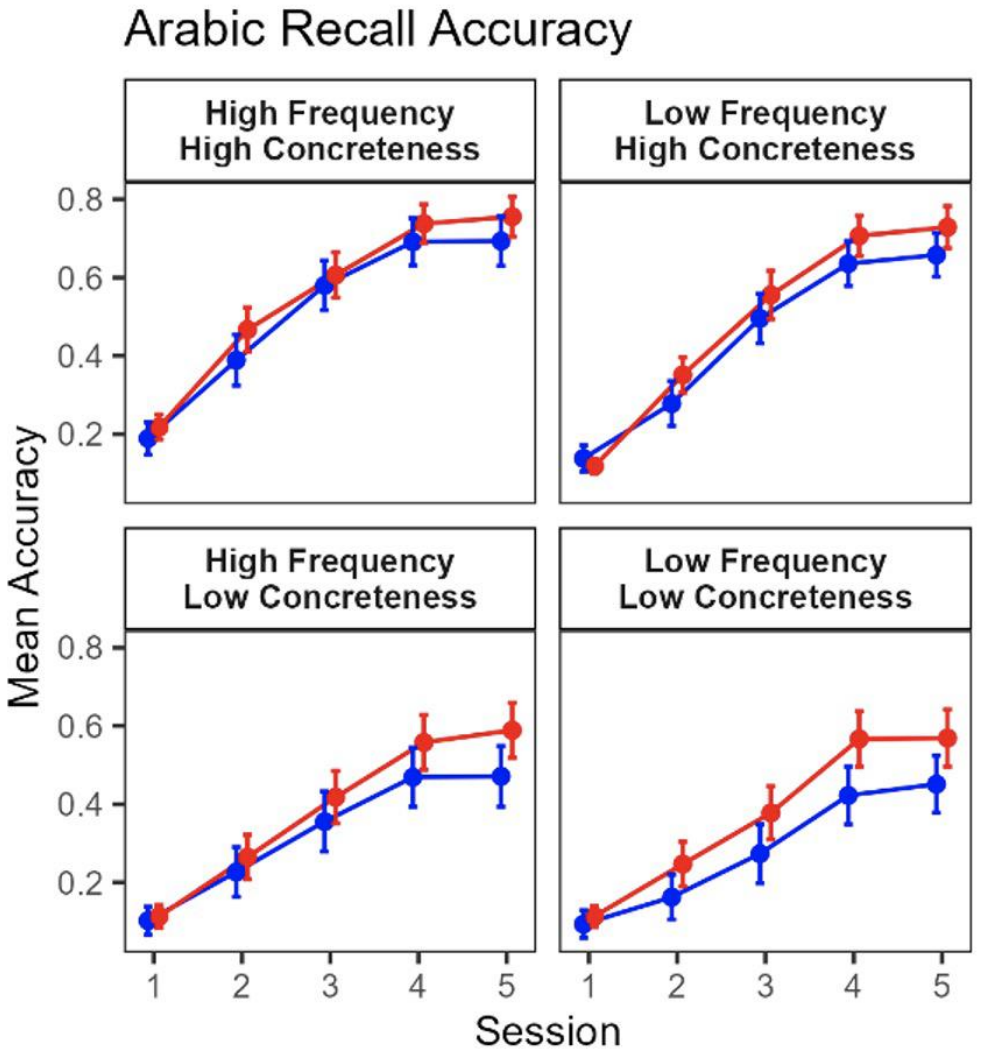
The ctVNS group performed significantly better on arousal, multi-tasking, and reported significantly lower fatigue ratings compared to sham for the duration of the study. ctVNS could be a powerful fatigue countermeasure tool that is easy to administer, long-lasting, and has fewer side-effects compared to common pharmacological interventions.

McIntyre, L.K. et al. (2021). **Cervical transcutaneous vagal nerve stimulation (ctVNS) improves human cognitive performance under sleep deprivation stress.** *Communications biology*, *4*(1), 634. https://doi.org/10.1038/s42003-021-02145-7

tcVNS Improves Language Recall Accuracy

The study showed a signicant positive effect of tcVNS over sham (p=0.025) on language recall, thereby suggesting tcVNS ability to significantly improve the recall of a foreign language compared to sham.

The improvement achieved through tcVNS treatment on days 2-4 was maintained on day 5 demonstrating that the recall advantage that emerged during training was sustained after the completion of treatment.

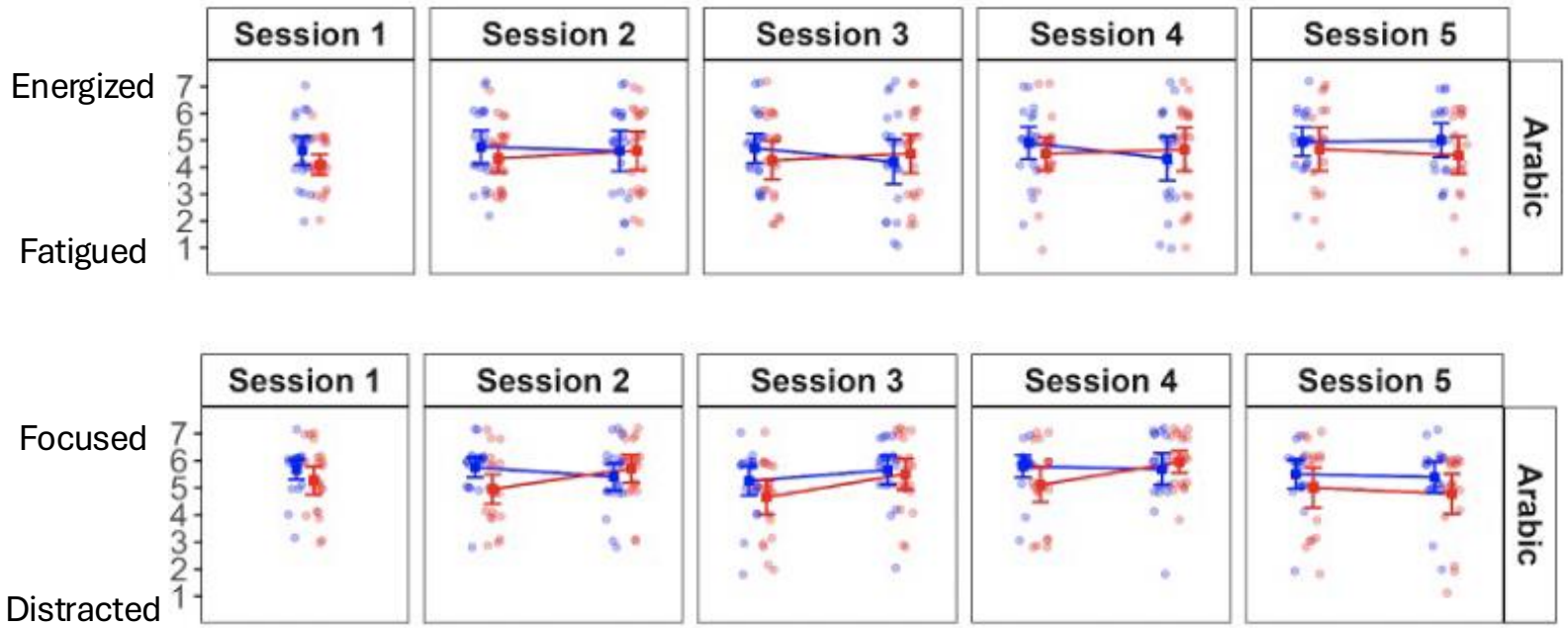


Miyatsu T. et al. **Transcutaneous Cervical Vagus Nerve Stimulation Enhances Second-Language Vocabulary Acquisition while Simultaneously Mitigating Fatigue and Promoting Focus.** Poster Presented at: American Academy of Neurology 75th Annual Meeting; April 2023; Boston MA.

ctVNS promotes Energy and Focus

Equally impressive were the improvements in the subject's energy and mood despite the rigors of the training program.

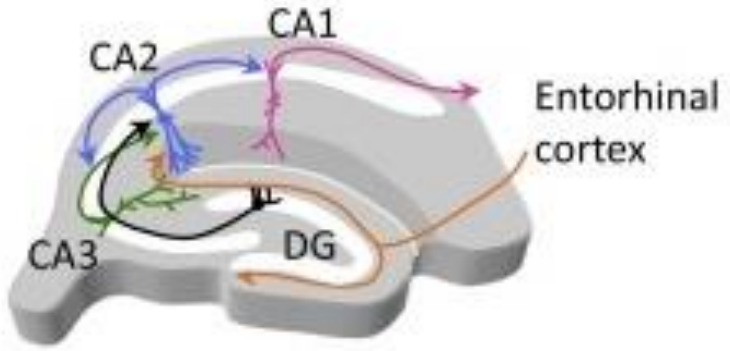
This study compliments our findings that suggest ctVNS could be a valuable tool to enhance war fighter training and resilience in a range of areas.

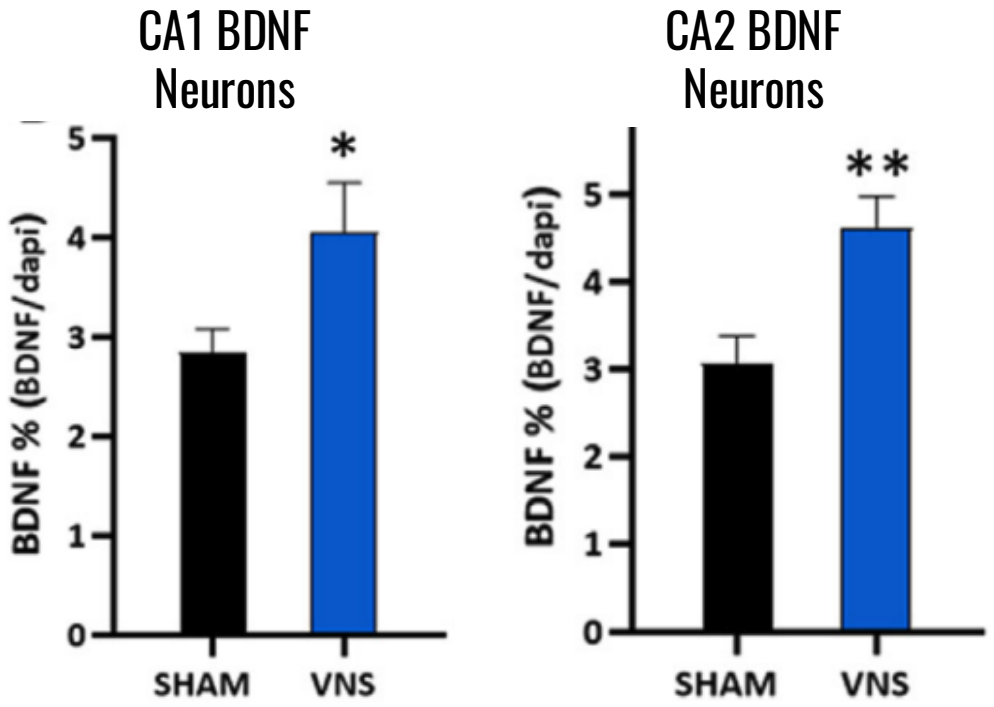


Miyatsu T. et al. **Transcutaneous Cervical Vagus Nerve Stimulation Enhances Second-Language Vocabulary Acquisition while Simultaneously Mitigating Fatigue and Promoting Focus.** Poster Presented at: American Academy of Neurology 75th Annual Meeting; April 2023; Boston MA.

VNS Induced Hippocampal Neuroplasticity and Cognitive Enhancement

BDNF Expression in the CA1 and CA2 regions of the Hippocampus are increased after VNS. IHC staining identified a higher number of BDNF positive cells in the CA1 and CA2 regions of the hippocampus of stimulated rats compared to unstimulated rats.



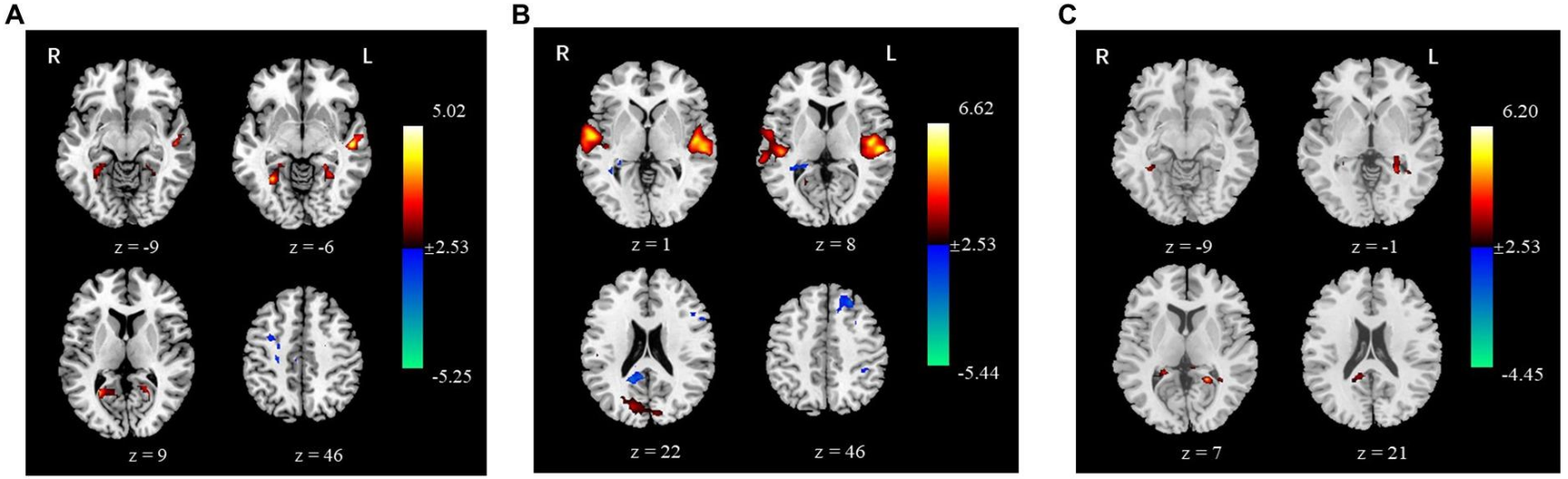


Olsen, L. K., Moore, R. J., Bechmann, N. A., Ethridge, V. T., Gargas, N. M., Cunningham, S. D., Kuang, Z., Whicker, J. K., Rohan, J. G., & Hatcher-Solis, C. N. (2022). **Vagus nerve stimulation-induced cognitive enhancement: Hippocampal neuroplasticity in healthy male rats.** *Brain stimulation*, *15*(5), 1101–1110. https://doi.org/10.1016/j.brs.2022.08.001

Cognitive function and brain activation before and after transcutaneous cervical vagus nerve stimulation in healthy adults: A concurrent tcVNS-fMRI study

Han Zhang[1,2,3,4†], Zhiwei Guo[5†], Yun Qu[1,3,4*], Yu Zhao[2], Yuxuan Yang[2], Juan Du[2] and Chunlan Yang[1,3,4]

- tcVNS improved cognitive performance in healthy adults, particularly in memory and language skills
  - Better performance on verbal fluency tasks, recalling more words and making fewer errors
- Increased activity in the calcarine gyrus, fusiform gyrus, lingual gyrus, and parahippocampal gyrus



doi: 10.3389/fpsyg.2022.1003411

Long-term Sustained Cognitive Benefits of Vagus Nerve Stimulation in Refractory Depression

Desbeaumes Jodoin, Véronique PhD[*]; Richer, François PhD[*]; Miron, Jean-Philippe MD[†]; Fournier-Gosselin, Marie-Pierre MD[‡]; Lespérance, Paul MD, MSc[†]

Results

Vagus nerve stimulation patients significantly improved on cognitive and clinical measures. Learning and memory improved rapidly after 1 month of stimulation, and other cognitive functions improved gradually over time. Cognitive improvements were sustained up to 2 years of treatment. At 1 month, improvement in Montgomery-Åsberg

Conclusions

In recent years, a growing interest in cognitive dysfunction in depression has emerged. Our results suggest that chronic VNS produces sustained clinical and cognitive improvements in TRD patients, with some mental functions improving as soon as 1 month after the initiation of the VNS therapy. Vagus nerve stimulation seems a very promising adjunctive therapy for TRD patients with cognitive impairment.

DOI: 10.1097/YCT.0000000000000502

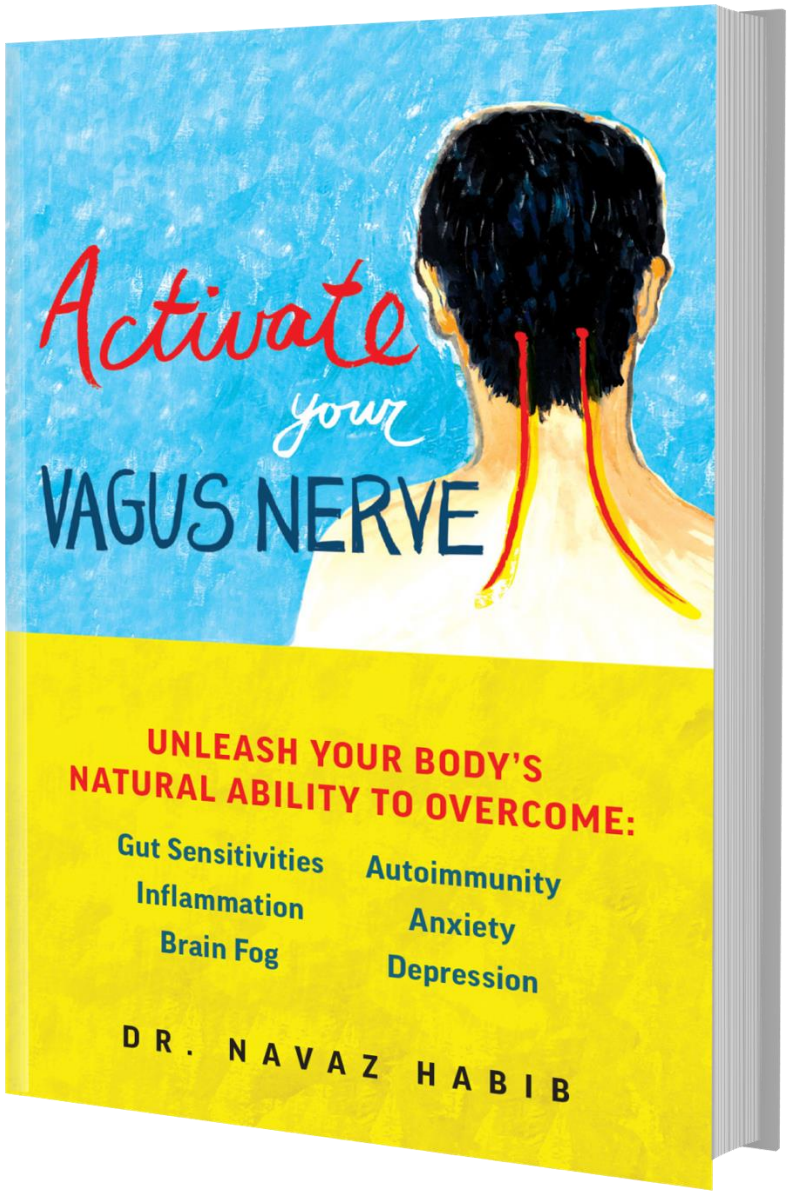
HRV Boosting Nutrients

1. **Choline (Phosphatidylcholine)**
2. **B-vitamins**
3. **Magnesium (bis-Glycinate)**
4. **Omega-3 Fatty Acids (EPA/DHA)**
5. Vitamin D3
6. Antioxidants
7. Coenzyme Q10 (CoQ10)
8. Electrolytes
9. Beet Root Extract
10. Potassium Nitrate

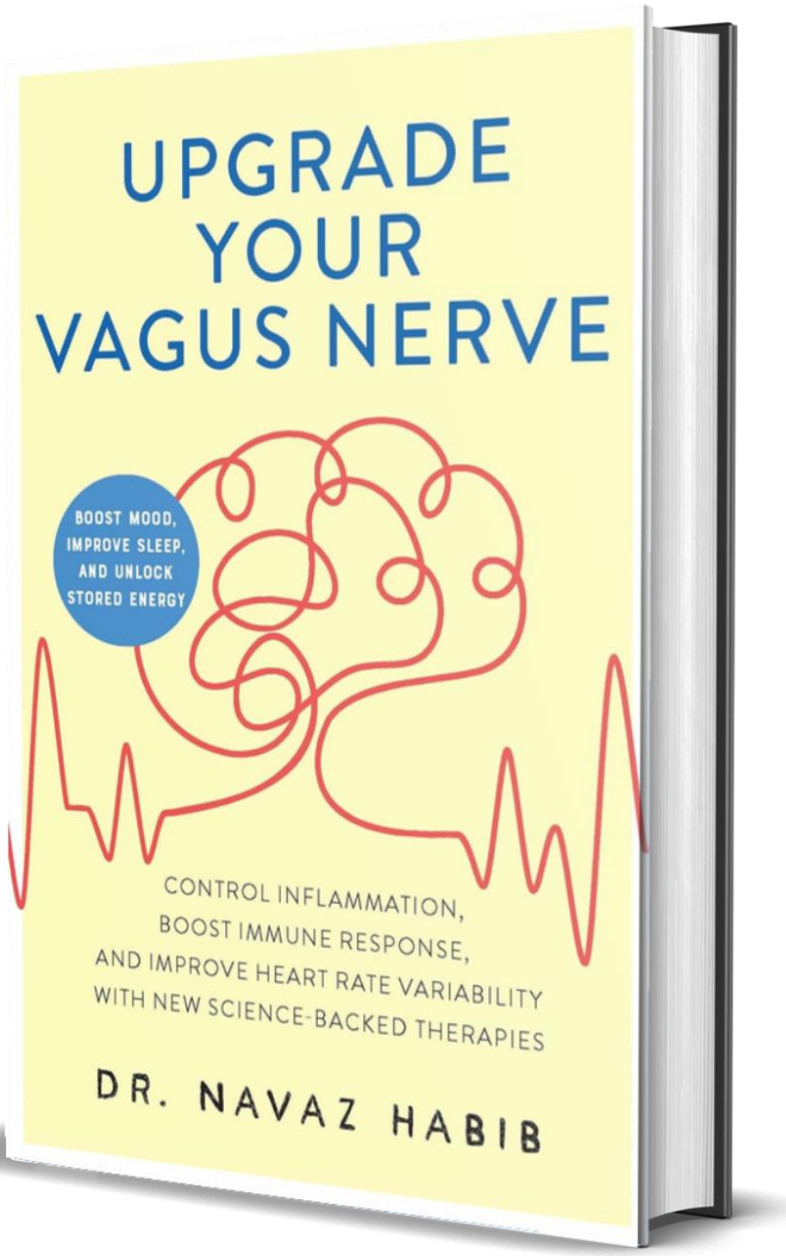
Activating the Vagus Nerve
facilitates a STATE SHIFT
from Sympathetic Fight-Flight
to Parasympathetic Rest-Digest-Recover.

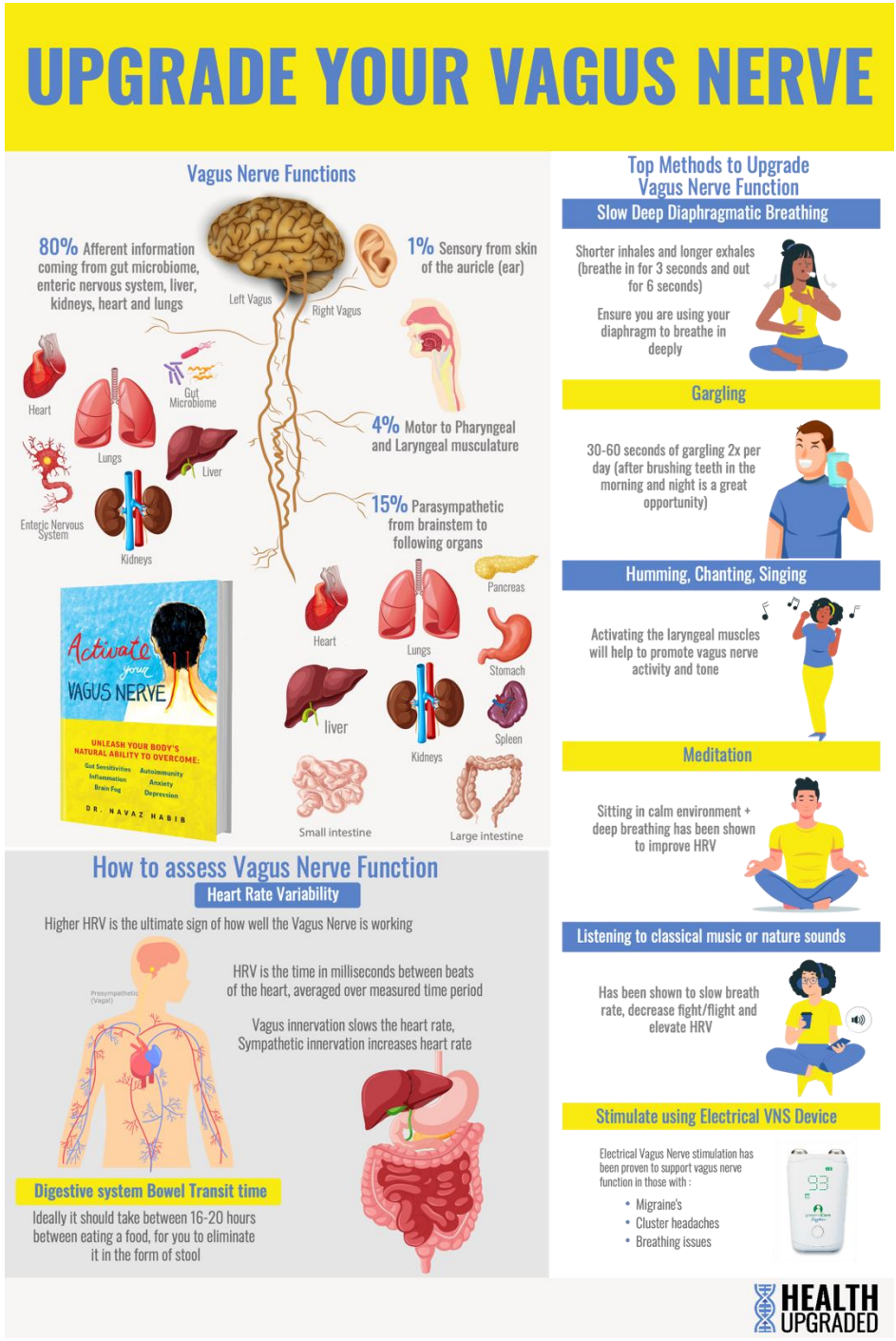
Our bodies cannot heal in fight/flight.

Healing can only happen in a
parasympathetic state!



THE HEALTH UPGRADE PODCAST





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