STRESS:
How to Recover and Start Strong this Year!

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dutch®

Remember

1. The information in this presentation is provided for informational and educational purposes only and is not medical or treatment advice.

2. Any information and statements regarding dietary or herbal supplements have not been evaluated by the Food and Drug Administration and are not intended to diagnose, treat, cure, or prevent any disease.

3. The use of any information provided in this presentation is solely at your own risk.

Objectives

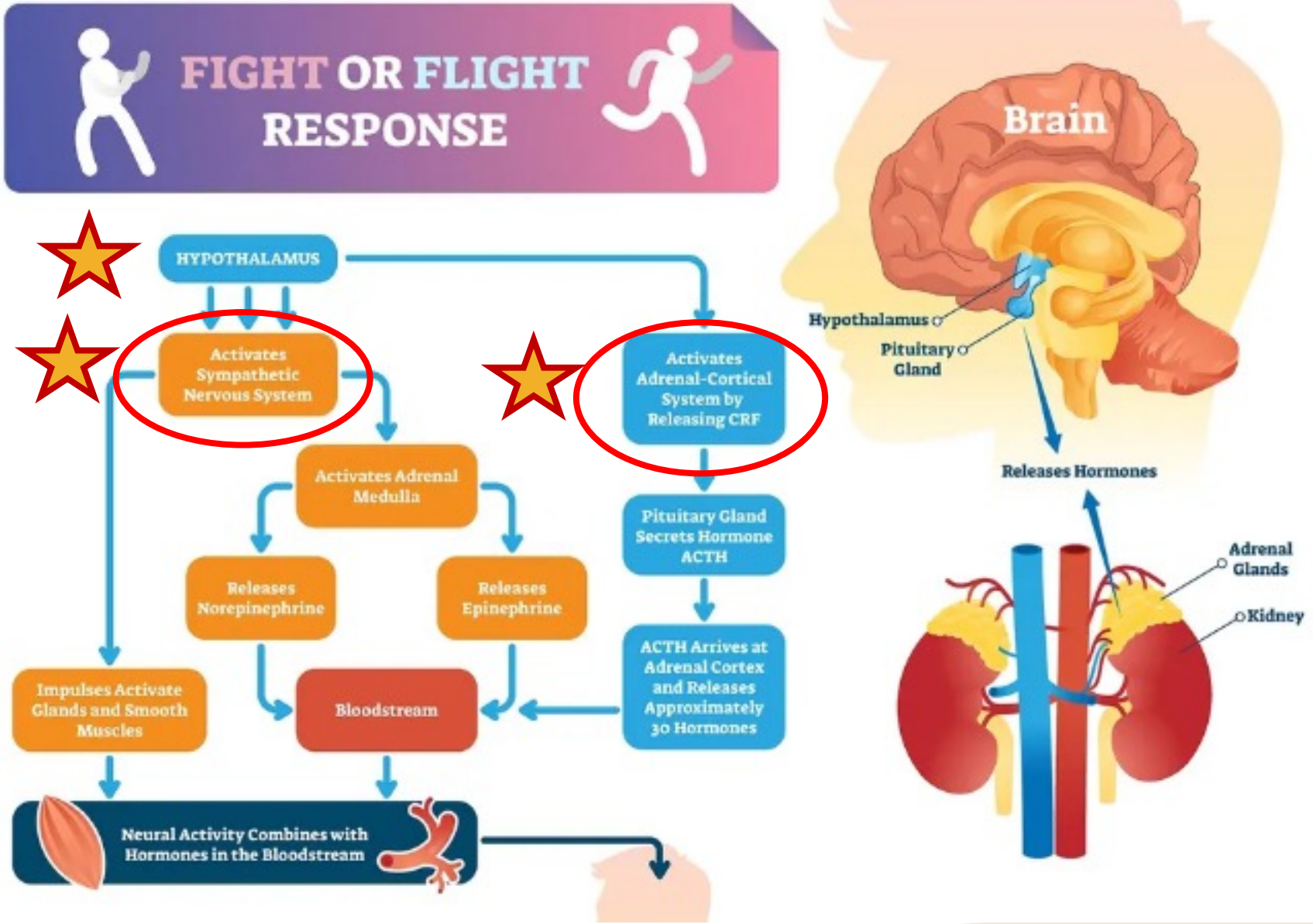
1. **Understand what stress is and how the body reacts to stress**
2. **Understand the major hormones influencing our stress response**
3. **Review important factors affected by cortisol and stress**

What is Stress?

- Stress is anything that creates an imbalance in your system
- Homeostasis: maintain a steady state, or optimal stability (think temperature, fluid balance, mood, energy, blood sugar, etc)

Where does stress come from?

- REAL vs
- PERCEIVED
  - All the same response
  - The body does not have a “good” or “bad” category of stress



https://www.simplypsychology.org/fight-flight-freeze-fawn.html

Autonomic Nervous System

Sympathetic

- Fight or Flight
- GO
- RUN
- DO

Parasympathetic

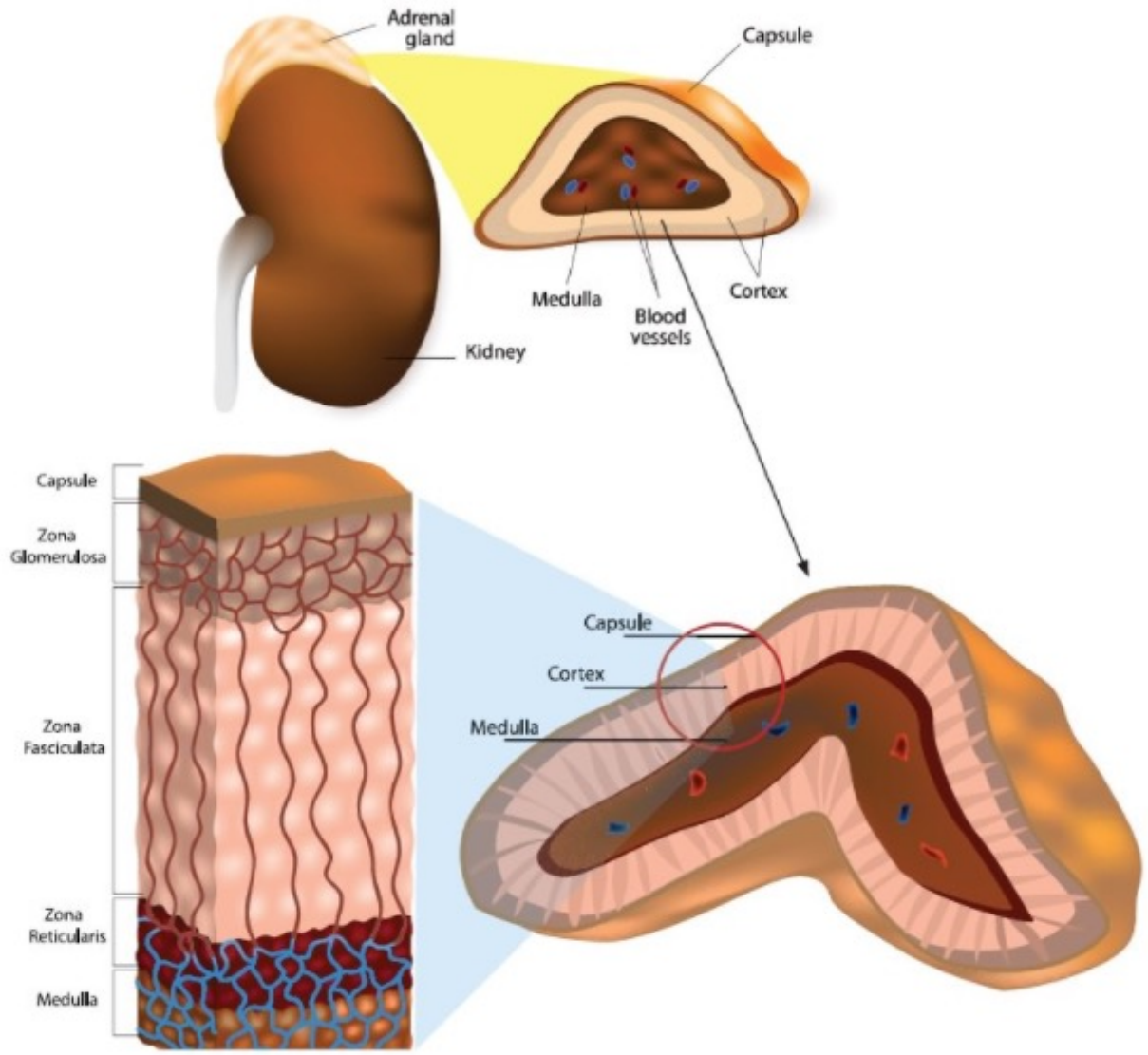
- Rest
- Digest
- Relax

Stress response

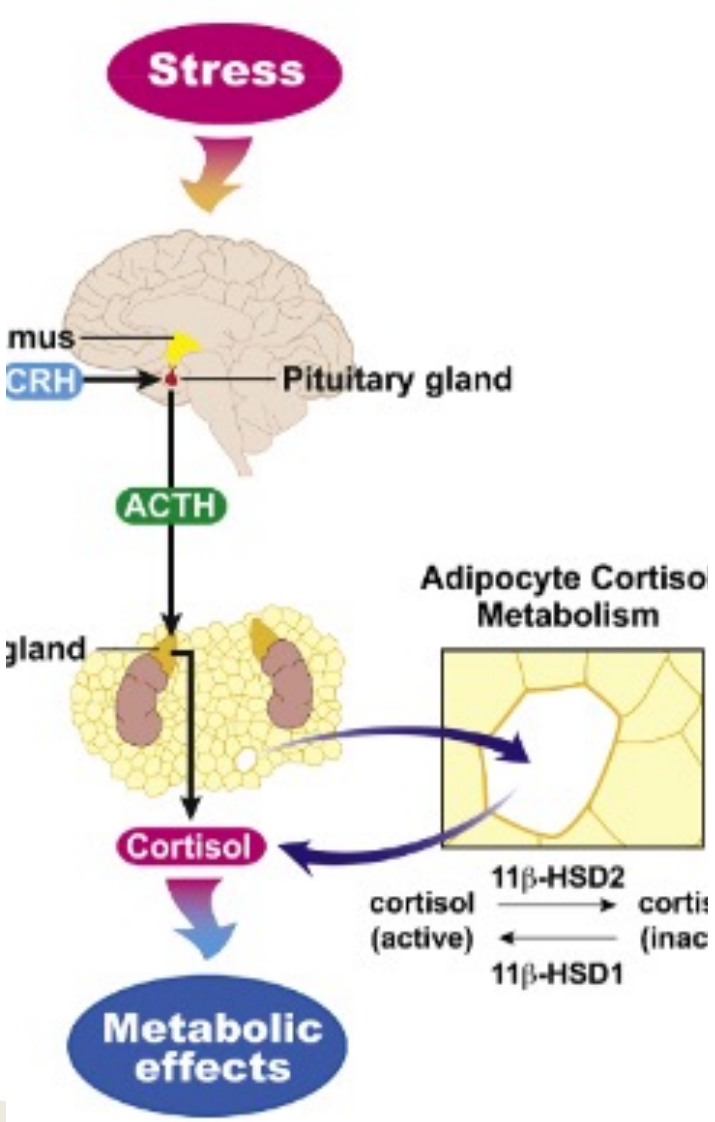
- Adrenal Glands Produce:

(3 zones for hormone production in the adrenal cortex)

- **Cortisol**
  - Adrenal Cortex: Zona Fasciculata
- **DHEA/DHEA-s**
  - Adrenal Cortex: Zona Reticularis
- **Aldosterone**
  - Adrenal Cortex: Zona Glomerulosa
- **Catecholamines**
  - Adrenal Medulla: Epinephrine and
  - Norepinephrine



The HPA response to stress



HPA = **H**ypothalamic – **P**ituitary – **A**drenal Axis

Hypothalamus → CRH (In the paraventricular nucleus PVN)

CRH → Pituitary Gland

Pituitary Gland → ACTH

ACTH → Adrenal Glands

Adrenal Glands → Cortisol

MORE ACTH = more cortisol **LESS ACTH = less cortisol**

Cortisol Physiology

- **Cortisol**
  - Produced in the **zona fasiculata** in the adrenal cortex of the adrenal glands
  - It is a **glucocorticoid**
    - steroid hormone that utilizes sugar and fats to mediate a response; can influence immune response and reduce inflammation
  - Cortisol is released in response to stress. It is also released in the presence of low blood sugar (which is a stressor).

Cortisol and the stress response

- Cortisol
  - Because cortisol is a glucocorticoid – it uses glucose for its actions:
    - Cortisol blocks insulin to keep glucose in the blood stream
    - Cortisol induces gluconeogenesis (break down of glucose from fat cells/liver)
    - Cortisol reduces protein uptake (diverts it to gluconeogenesis to keep glucose in circulation)
    - Cortisol suppresses the immune system to deal with the stress
    - Cortisol increases blood pressure (vasoconstriction)
    - Cortisol improves focus (mental and physical), eyesight, and hearing

Cortisol and the stress response

- Short Term Effect of Cortisol Release:
  - Anti-inflammatory
  - Ability to have energy to fight, deal with stress

  - Increased focus
  - Increased blood pressure (vasoconstriction)
  - Increased HR and blood flow to muscles

  - Decreased digestive effort
  - Decreased sex hormone response
  - Decreased immune response

Cortisol and the stress response

- Long Term Effect of Cortisol Release:
  - Blood sugar irregularities/dysglycemia – diabetes and insulin dysregulation
  - Weight gain, specifically around the middle
  - Immune suppression, immune dysregulation – get sick easier, more difficult to recover
  - Chronic Fatigue
  - Gastrointestinal Issues – parasympathetic nervous system suppression = constipation, diarrhea, heartburn, stomach upset, etc
  - Cardiovascular Concerns – blood vessel constriction, over-compensation of the cardiovascular system (high blood pressure)
  - Sex Hormone Imbalances, infertility, irregular periods, heavy periods, low libido/sex drive

Cortisol and the stress response

Cortisol's short-term purpose:

TO KEEP YOU SAFE

To enable you to run from your saber-tooth tiger

- Your saber-tooth tiger may look like:
  - Work stress
  - Relationship stress
  - Exercise
  - Blood sugar dysregulation
  - Etc…

The HPA response to stress

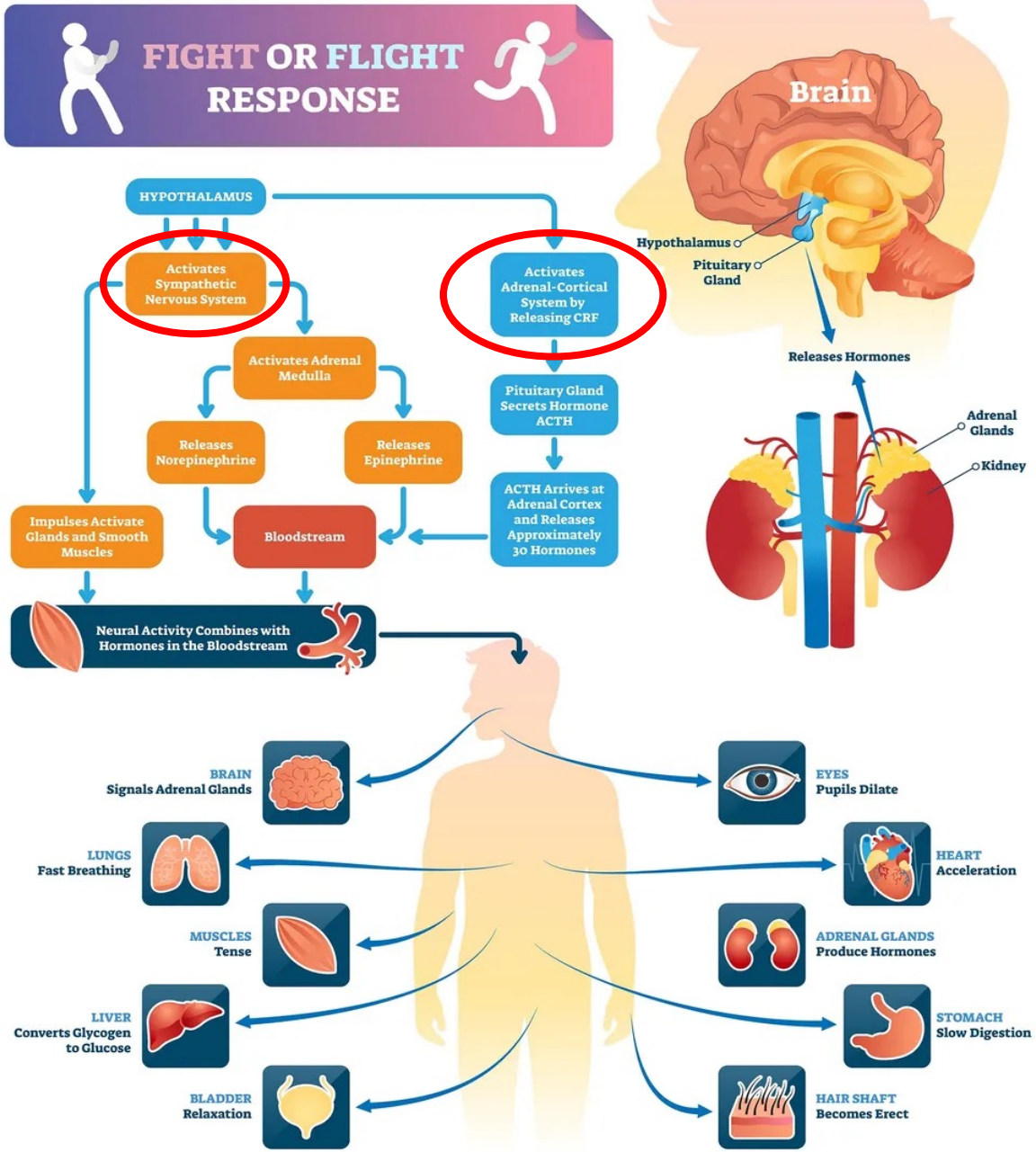
- We need to understand that the stress response begins in the BRAIN – not the adrenal glands

- The brain signals the adrenal glands for a cortisol response

The HPA response to stress

Cortisol Response vs Catecholamine Response

- Cortisol (Adrenal Cortex) - SLOW
  - The body makes cortisol as needed when signaled – it is not made then stored
  - This usually occurs after a stressor signals the **BRAIN**
  - Lag time is usually about 10 minutes after Epi/Norepi have been released
- Catecholamines Epinephrine/Norepinephrine (Adrenal Medulla) - FAST
  - Immediate release of stored epinephrine and norepinephrine
  - These are amines the body makes then stores to be at the ready for a threat!
    - This is signaled through the nervous system



https://www.simplypsychology.org/fight-flight-freeze-fawn.html

Stress Response

- **Now we know**:

  1) The stress response starts in the brain – from the Hypothalamus

  2) It triggers a response from the

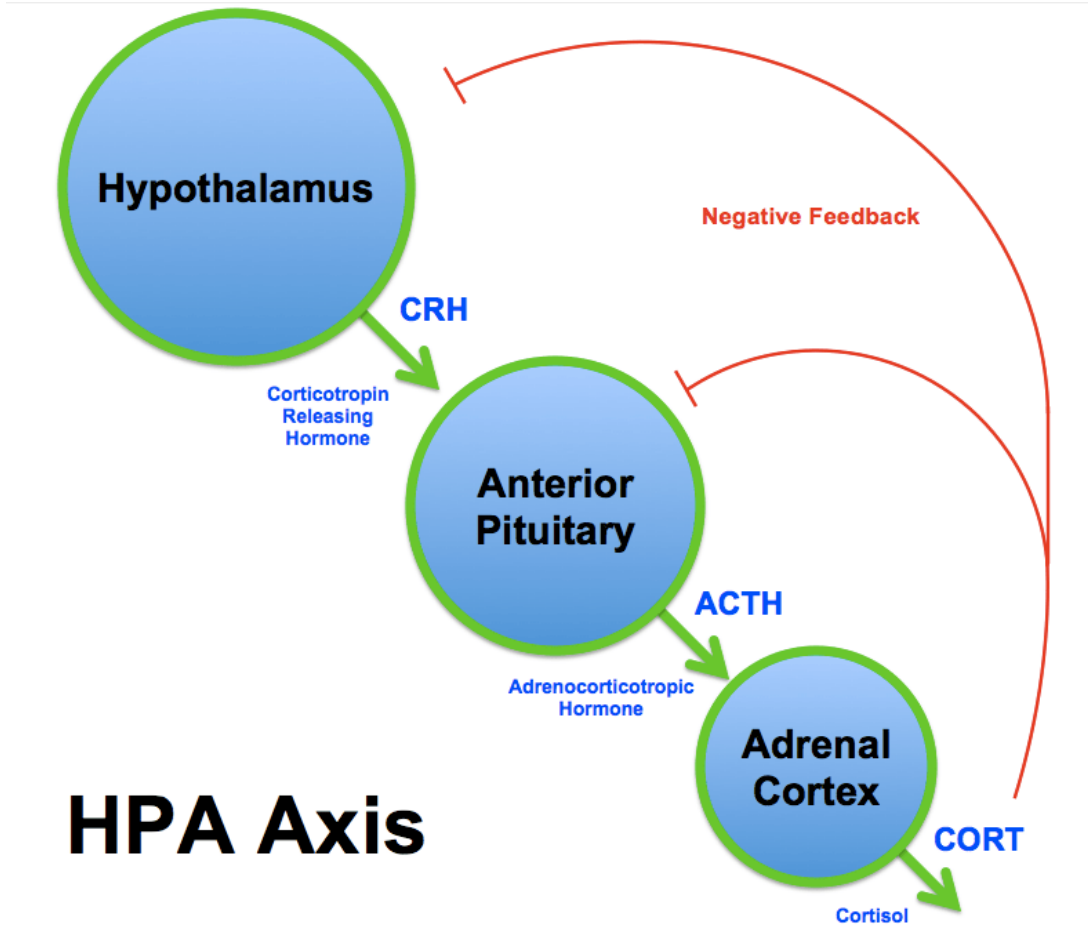
  Autonomic Nervous System (the Sympathetic part)

  And

  The Adrenal Gland Cascade

Stress Response

- Our stress response relies on a negative feedback loop, so our brain knows to stop signaling the stress response
- This means when there are appropriately high levels of cortisol, it signals back to the Hypothalamus to stop stimulating the HPA Axis and the Sympathetic Nervous System response

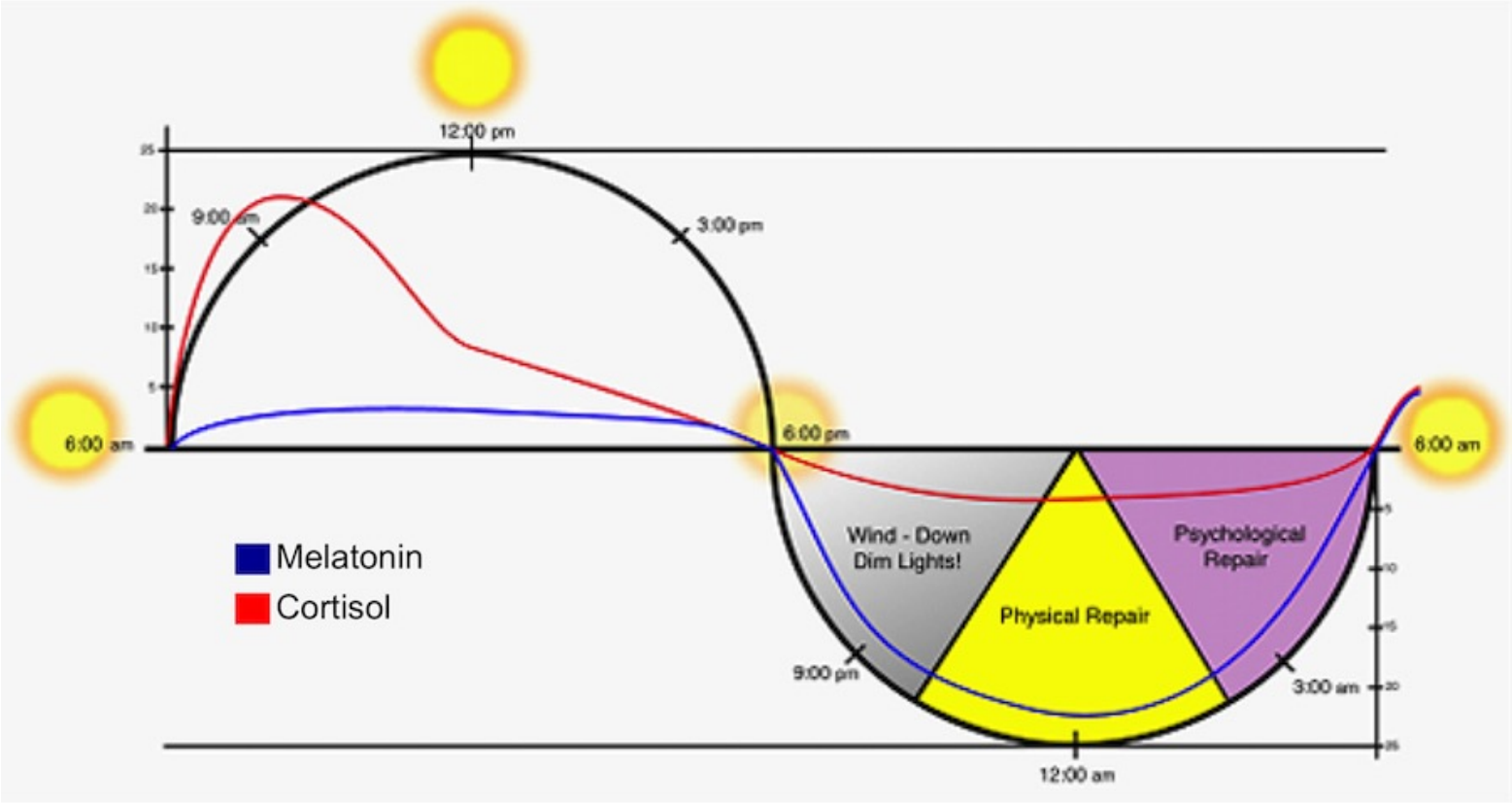


HPA axis activation, proceeding from the hypothalamus to the pituitary gland to the adrenal glands. *Image courtesy of Brian M Sweis.*

https://neuroscientificallychallenged.com/posts/what-is-the-hpa-axis

Cortisol and daily rhythm

- DHEA has a diurnal pattern similar to Cortisol
- Cortisol should follow a ***diurnal [circadian] pattern***
- Cortisol starts to rise before waking
- Cortisol peaks around 9 am, then wanes into the evening
- Melatonin takes over at night when cortisol levels should be low



Cortisol and circadian rhythm

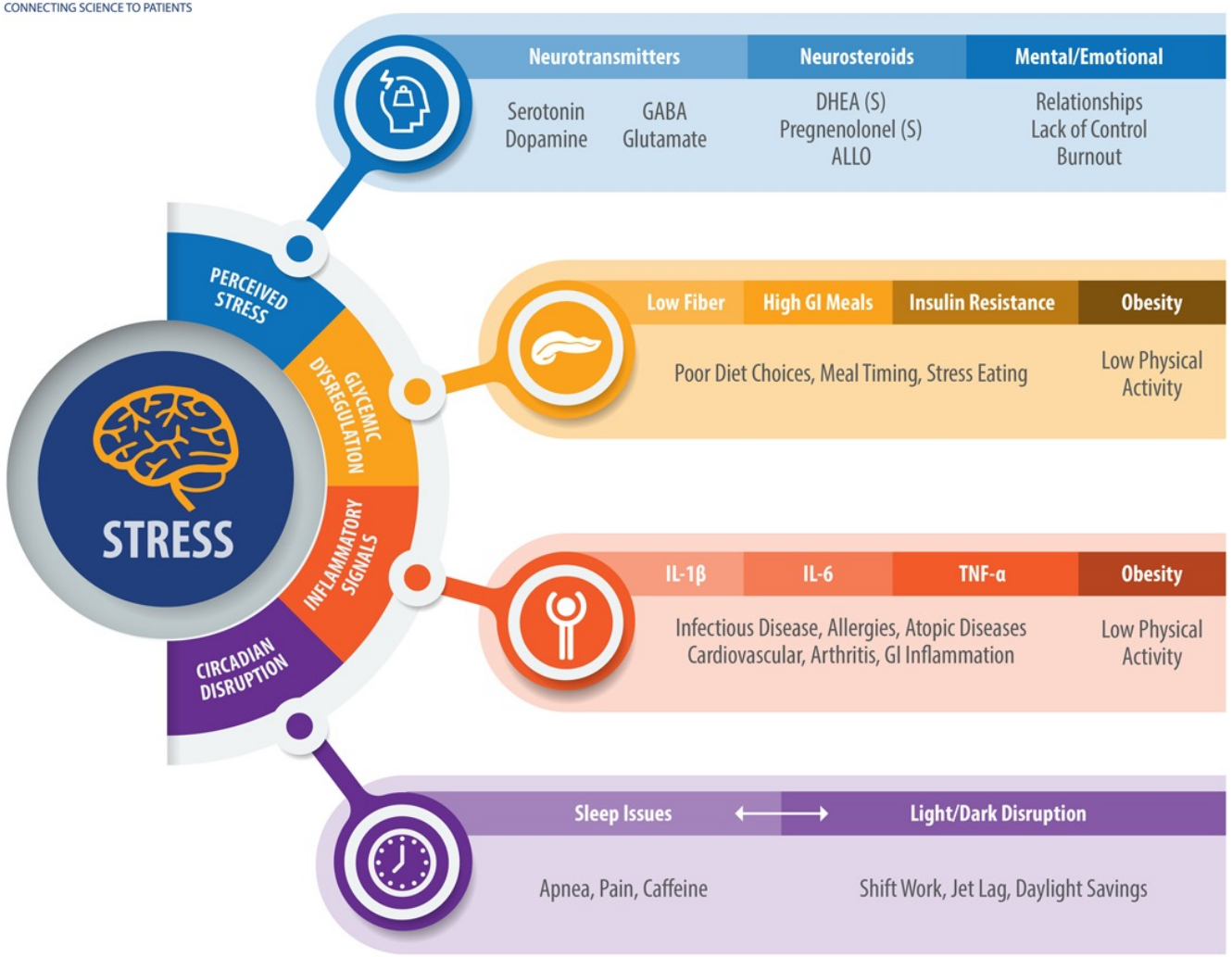
- Circadian rhythm is a 24 hour internal clock that is regulated by the Suprachiasmatic Nucleus (SCN) and measures the sleepiness and wakefulness for our brain and body in the 24 hour cycle
- The nuclei of this part of the brain signal the hypothalamus and are responsible for signaling cortisol and melatonin release
- The SCN is sensitive to any sort of light – daylight, screen light (blue light), false light (house lights)
- The rhythm is determined from light, not dark

SLEEP

Sleep is regulated by the HPA Axis

- If HPA dysfunction is present, sleep disturbance is also likely present
- Sleep is affected by cortisol, norepinephrine (NE), melatonin

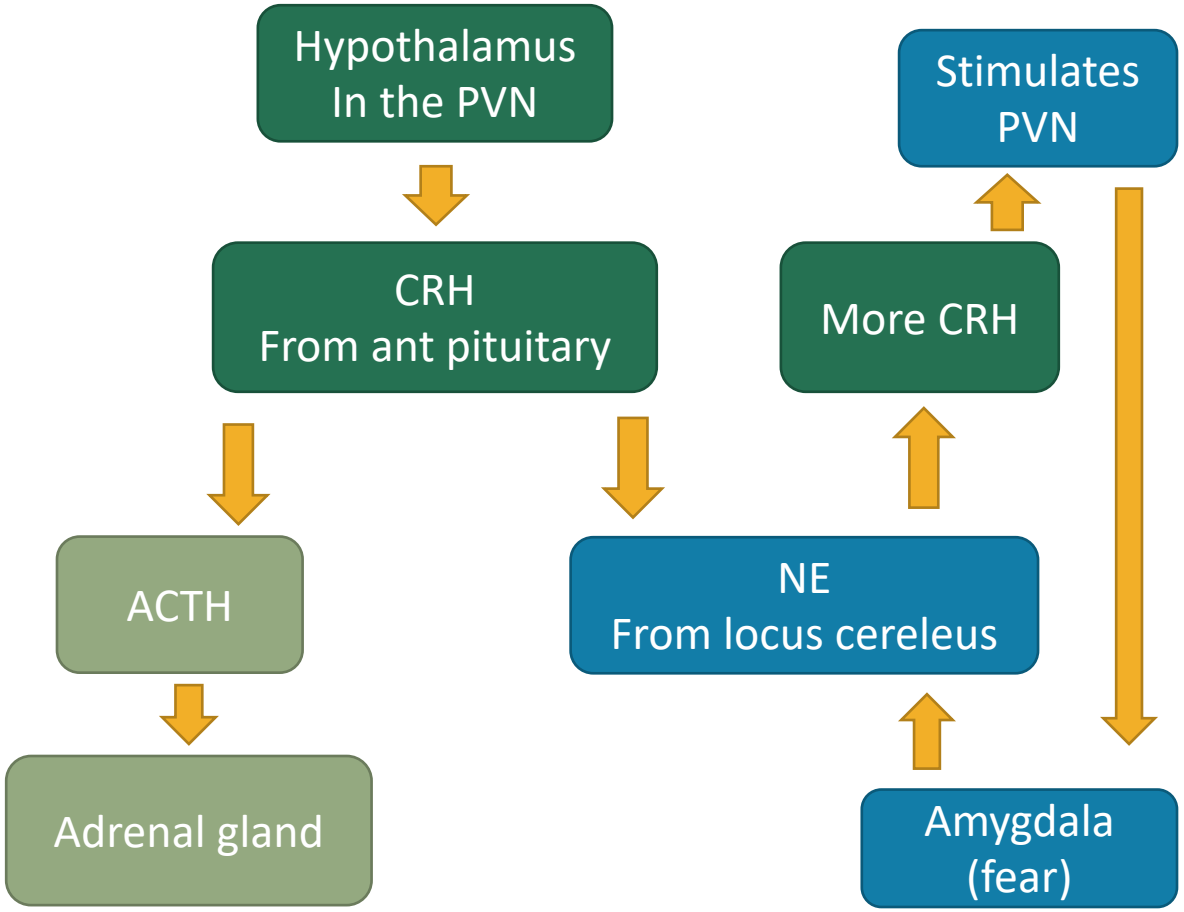
Chronic HPA Axis Dysregulation Stressors



Gorski, J. , (2019) Stress Keeping You Up at Night? Blame Your HPA Axis - Crown Bioscience. https://blog.crownbio.com/circadian-clock-stress-response

Excitatory signaling for the stress response

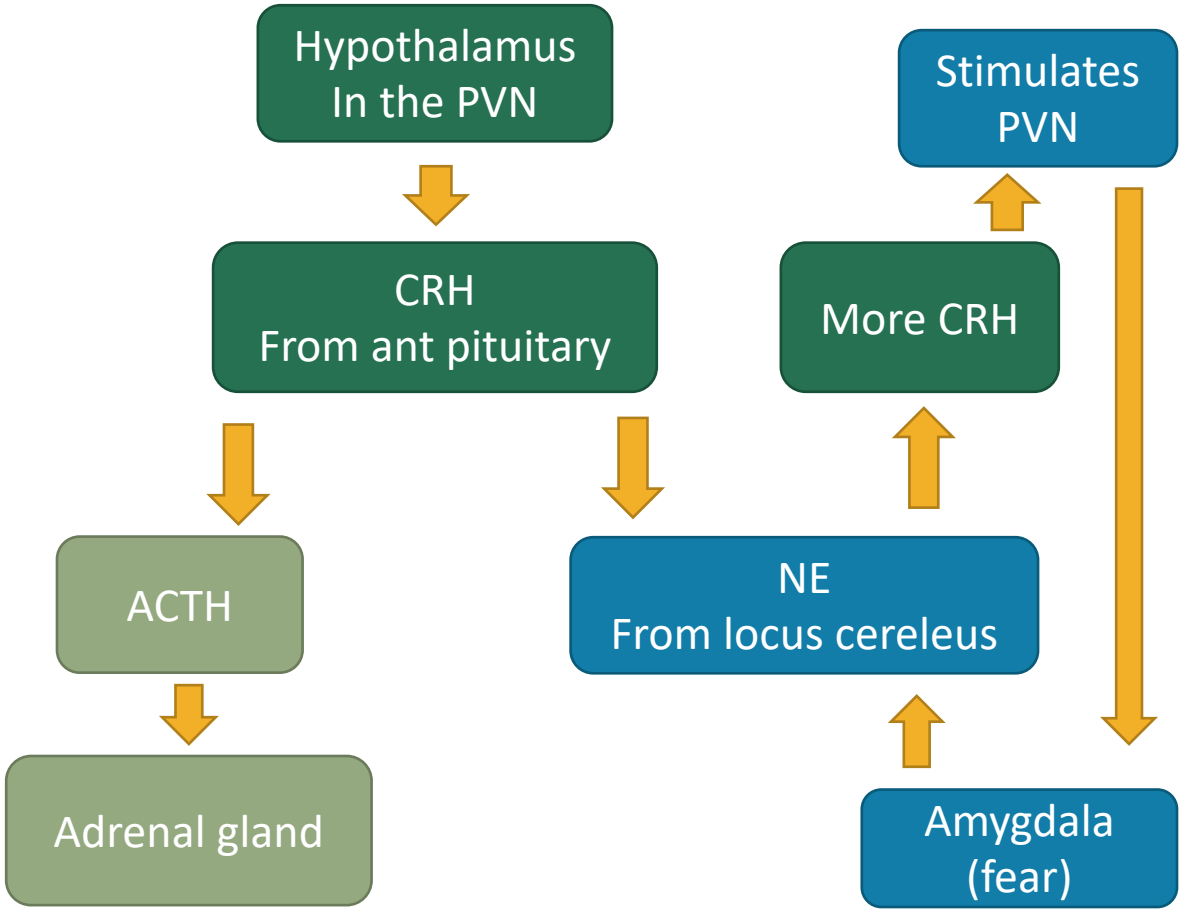
- HPA Axis and NE signaling



- HPA axis signaling increases ACTH to signal adrenal gland release of cortisol
- High cortisol results in negative feedback to shut down cortisol production
- When NE is also involved, there is another trigger to release more CRH, which continues to stimulate ACTH signaling, and ongoing stimulation for the brain release of NE

Excitatory and inhibitory signaling for the stress response

- HPA Axis and NE signaling



This signaling is stimulating, or excitatory

Excitatory = Sympathetic nervous system

Excitatory hormones for the stress response include:

Cortisol

NE

Glutamate

Calming the stress response

Inhibitory = Parasympathetic nervous system

Inhibitory hormones for the stress response include:

GABA

Cortisol

STRESS RESPONSE – Sympathetic vs Parasympathetic Nervous System response

- When the body is in Sympathetic drive for too long, and does not have the capacity to balance with Parasympathetic rest, we become

"Sympathetic Dominant"

- This means:
  - Our threshold to turn on that stress response is more easily reached
  - We are not able to create enough down time to allow for appropriate rest

Great, Debbie….then how am I supposed to sleep?

?

https://www.pinterest.com/pin/349732727282473230/

Great, Debbie….then how am I supposed to sleep?

In a pillow fort

That’s how

https://www.pinterest.com/pin/349732727282473230/

Sleep physiology **from Dr. Bradley Bush

- Our normal sleep should include cycles of light sleep, deeper slow-wave sleep, and REM sleep.
- **Light sleep**
- Stage 1:
  - start of the sleep cycle, considered transitioning from wakefulness to sleep, lasting about 5-10 minutes
  - Theta waves (slow brain waves)
  - Slow, rolling eye movement
- Stage 2:
  - about 20 minutes
  - Mixed frequency brain waves with rapid bursts of rhythmic brain activity known as sleep spindles
  - Body temperature decreases and heart rate slows

Bush, Bradley. The Role of Cortisol in Sleep. Natural Medicine Journal. January 2014.

Sleep physiology

Deeper, slow wave sleep – Stages 3 and 4

Stage 3:

- 20-50% of slow brain waves, delta waves
- Transitional between light and very deep sleep

Stage 4:

- about 30 minutes
- >50% delta waves, often referred to as delta sleep

Stage 5: **REM sleep**

- Increased breath rate and brain activity
- REM is mixed theta waves with rapid eye movement
- REM occurs about every 90 minutes in adults

Bush, Bradley. The Role of Cortisol in Sleep. Natural Medicine Journal. January 2014.

Sleep patterns

In adults

- Slow wave sleep is generally the first half of the night
- REM is the second half of the night

- Sleep starts out sequentially until it cycles through the stages, then it will go in and out of sequence
- Sleep begins in Stage 1, then 2, 3, and 4. After Stage 4, then Stage 3, then 2 are repeated before REM
- Stage 2 usually occurs after the last REM cycle
- The first REM cycle usually occurs after 90 minutes of sleeping but for a very short time, and each time REM is repeated, it lasts longer

Bush, Bradley. The Role of Cortisol in Sleep. Natural Medicine Journal. January 2014.

Sleep importance

The sleep/wake cycle influences:

Metabolism – hunger hormones like leptin and grehlin
Immunity
Cognition
Muscular function and capacity
Overall recovery

- Sleep enables the body to reduce wakefulness, conserving energy and allowing rest
- Sleep allows brain waste clearance, as well as overall lymphatic clearance (detoxification)
- Wakefulness creates more waste in the body and needs clearance during and through sleep

Cortisol and sleep

- How does cortisol affect sleep, or vice versa?
- Because cortisol and melatonin are partners in the circadian rhythm response, it may be difficult to know from where the issue came:
  - Stress?
  - Poor sleep?
  - Immune dysfunction?
  - Inflammation?

- 2 major contributors to poor cortisol response:
  - Obstructive Sleep Apnea (OSA)
  - Insomnia

Cortisol and daily rhythm

- When sleep is not optimal, it negatively affects our cortisol rhythm
- Optimal sleep includes:
- Appropriate bedtime
  - Optimal bedtime is around 11 pm for quality of sleep
- Sufficient time to sleep
  - This can vary from person to person, but most adults require at least 5-7 consistent hours of sleep for optimal cortisol signaling
- Ability to sleep through the night
  - Interrupted sleep can affect cortisol signaling

Cortisol and daily rhythm

- When sleep is not optimal, cortisol may be triggered too soon and wake our body too soon

OR

- It can also create latent cortisol response
  - Secondary to not sleeping well, then one may fall asleep finally and be forced to wake earlier than they are ready, which may lead to poor cortisol awakening response (not sleeping a sufficient amount of time)

Circadian rhythm and sleep wake cycle regulation

- Increased signaling to cytokines which activates immune cells and inflammatory response(s)

"

Cytokines are protein, glycoprotein, or peptide cell signaling molecules that are found throughout the central nervous system (CNS) and periphery that function in autocrine, paracrine, or endocrine fashion [2]. Cytokines play a role in regulation of cognition, performance, appetite, pain, fatigue, sleepiness, sleep, and vasohemodynamics. Cytokine dysregulation occurs in much pathology that involve sleep disturbance, including type 2 diabetes [131], cardiovascular disease [132], and cancer [133]. Cytokine dysregulation is implicated in most sleep-related pathologies including sleep apnea and insomnia [134, 135].

"

Zielinski, 2016

- Increased inflammation in brain (glial) cells negatively influences cognition: brain fog, anxiety, mood changes

Zielinski, M, et al. *Functions and Mechanisms of Sleep*. AIMS Neuroscience. 2016; 3(1): 67-104.

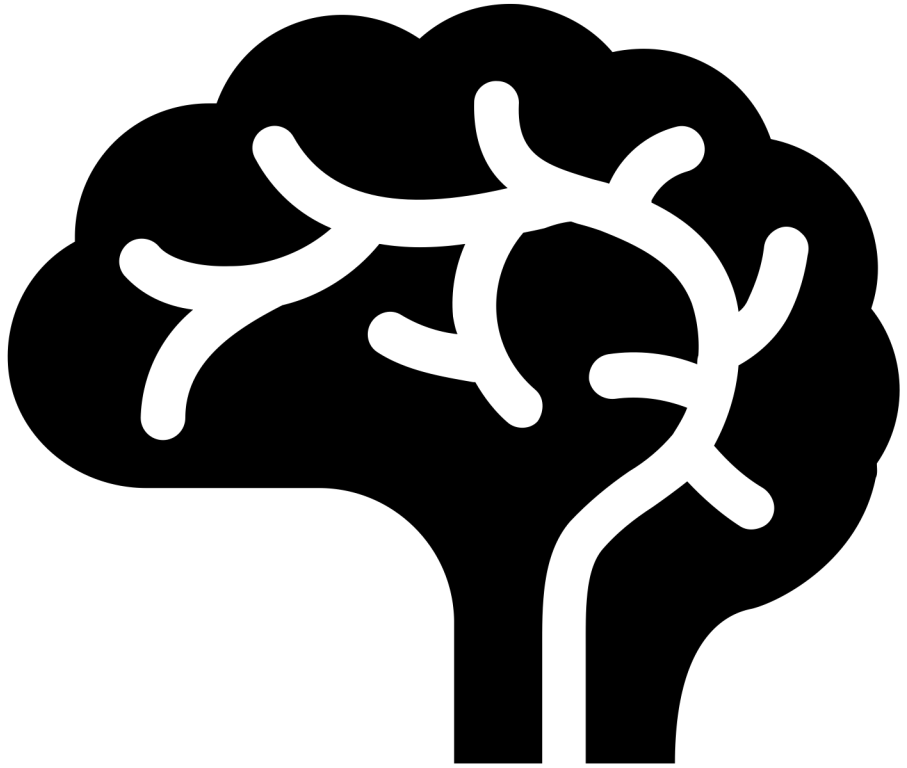
Circadian rhythm and sleep wake cycle regulation

Dysregulation in the sleep wake cycle has been shown to increase risk for:

- Diabetes
- Cardiovascular disease
- Immune stimulation
- Inflammation
- Cognition deficits
  - Brain fog
  - Mood changes (depression, anxiety, focus
- Metabolic dysregulation
  - Appetite dysregulation
  - Movement, physical activity

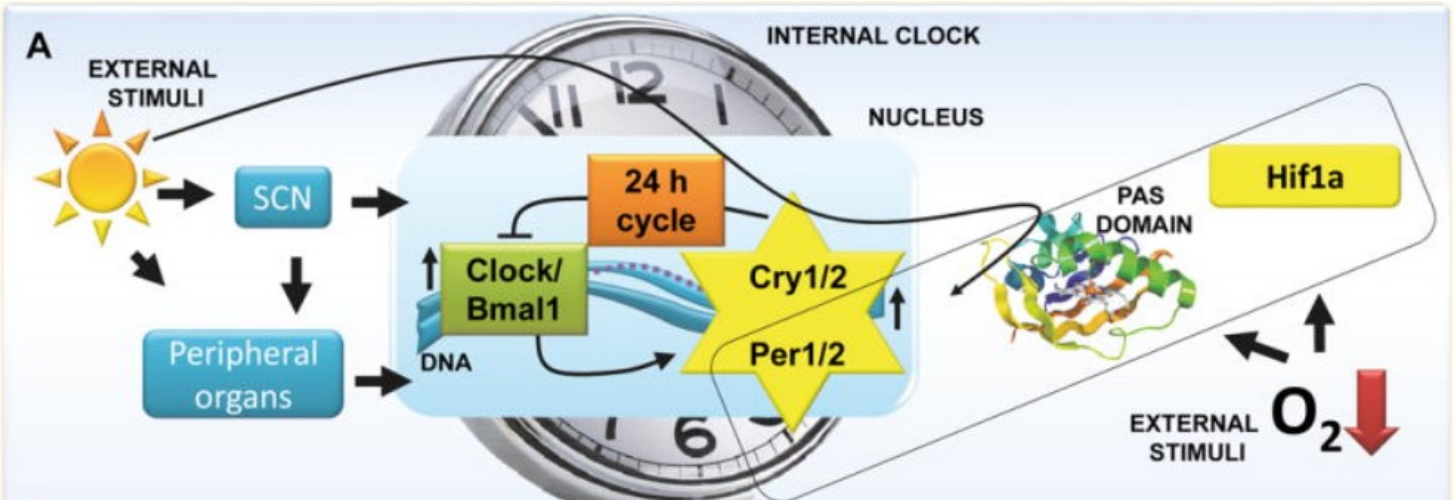
Circadian rhythm and our health

- Because our body relies on natural light to help stabilize the circadian clock, natural light may be an option for treatment
- Not only does our brain register natural light to facilitate the rhythm of our clock, our cells are also sensitive to the 24 hour rhythm

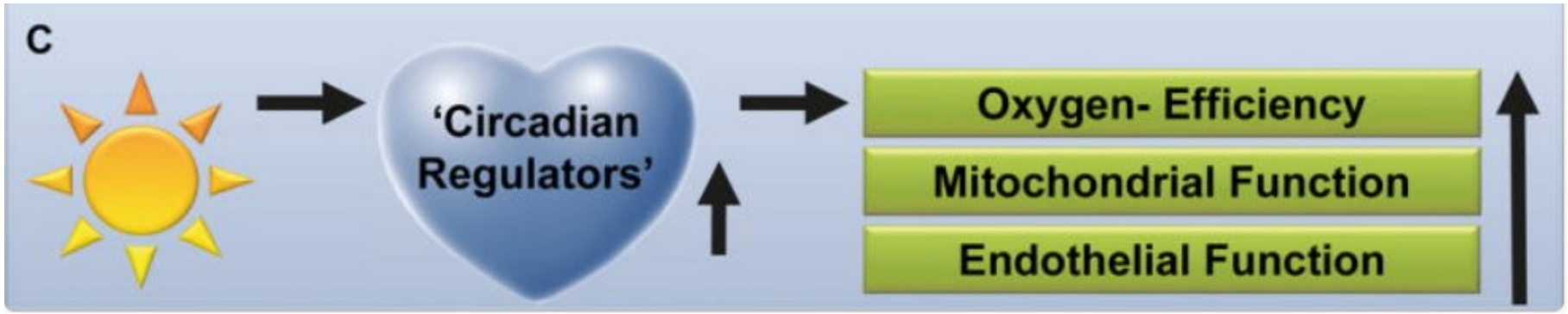


Brainard, J, et al. Health implications of disrupted circadian rhythms and the potential for daylight as therapy. 2015 May; 122(5): 1170-1175.

Circadian rhythm and our health



- This shows that sunlight influences not only the brain, but individual cell types throughout the whole body – which is why sleep has a multisystem effect



Brainard, J, et al. Health implications of disrupted circadian rhythms and the potential for daylight as therapy. 2015 May; 122(5): 1170-1175.

HOW TO EVALUATE SLEEP AND CORTISOL

Free Cortisol Curve vs Cortisol Awakening Response (CAR)

- **BOTH** the diurnal rhythm of cortisol AND the Cortisol Awakening Response (CAR) affect health outcomes
- These outcomes may include:
  - Mood stability
  - Mental health including dementia, depression, etc
  - Cardiovascular disease
  - Diabetes
  - Immune regulation

Cortisol: CAR

The **CAR** looks at:

- Stress resilience - the capacity for the body to respond appropriately to stressors, whatever they may be (real vs perceived)

- It is like a "mini stress test" to ensure appropriate HPA response to stress

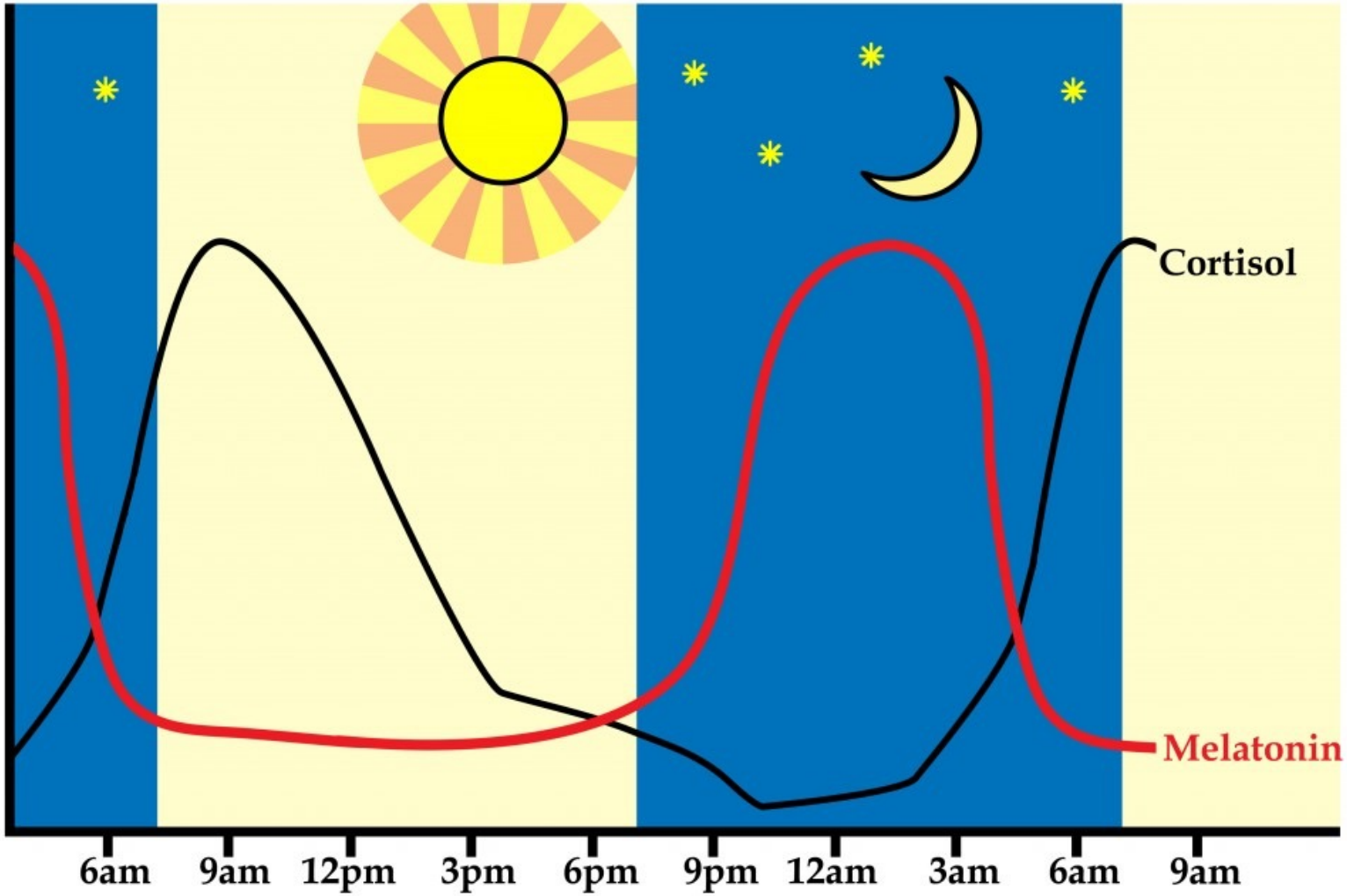
Cortisol: CAR testing

- "…. **If you can't get your CAR right, how do you expect to get the rest of your stress response right?"**

  -Dr. Carrie Jones

- Knowing that the CAR is a mini stress test on the HPA axis, if this is not responding appropriately, we have a problem with how the body is dealing with stress!

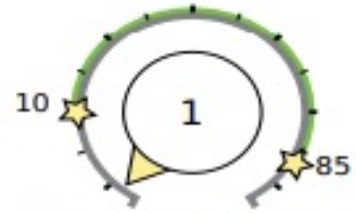
Cortisol: diurnal pattern



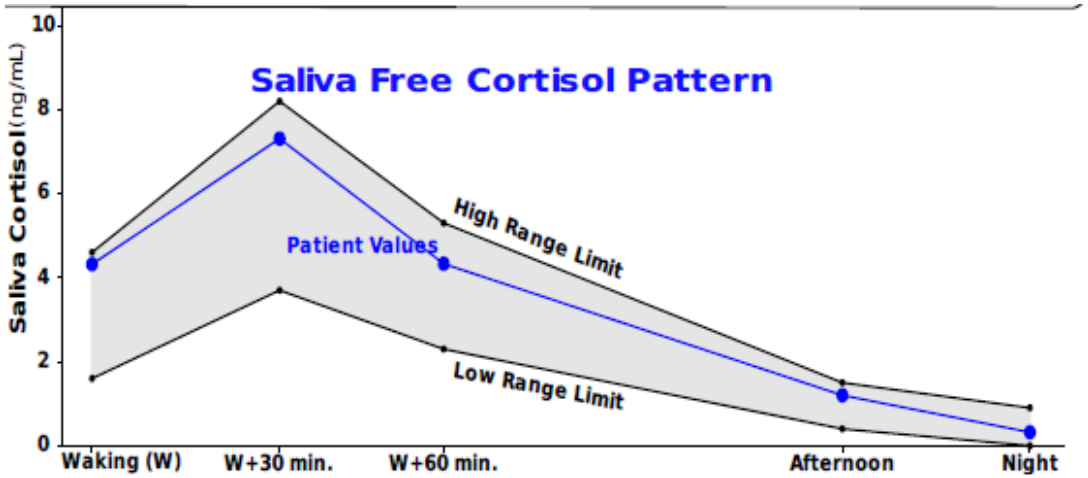
https://www.thepaleomom.com/wp-content/uploads/2014/02/Melatonin-and-Cortisol.jpg

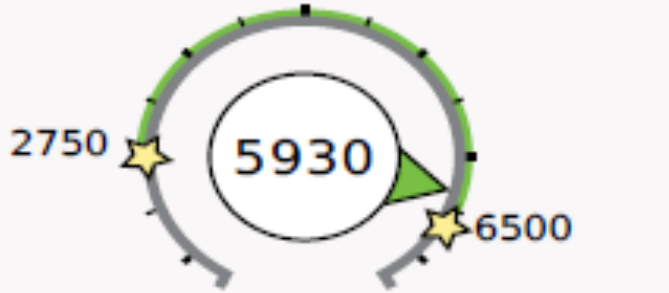
Cortisol testing:

- **We want to see:**
- Cortisol Production capacity (Met Cort)
- Amount of Free Cortisol
- How the cortisol is used throughout the day (pattern)
- Melatonin production

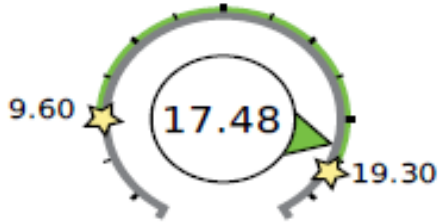


Melatonin* (Waking)





Metabolized Cortisol (THF+THE)
(Total Cortisol Production)



Saliva Cortisol Total
(Sum of 5 values)

Cortisol: DUTCH testing

Flagship test: DUTCH COMPLETE

Dried Urine only

4 **urine** samples done throughout the day and dried

1. Dinner time
2. Before bed
3. First thing upon waking
4. 2 hours after waking

- Optional 5th (3rd) strip if wake and urinate in the middle of the night

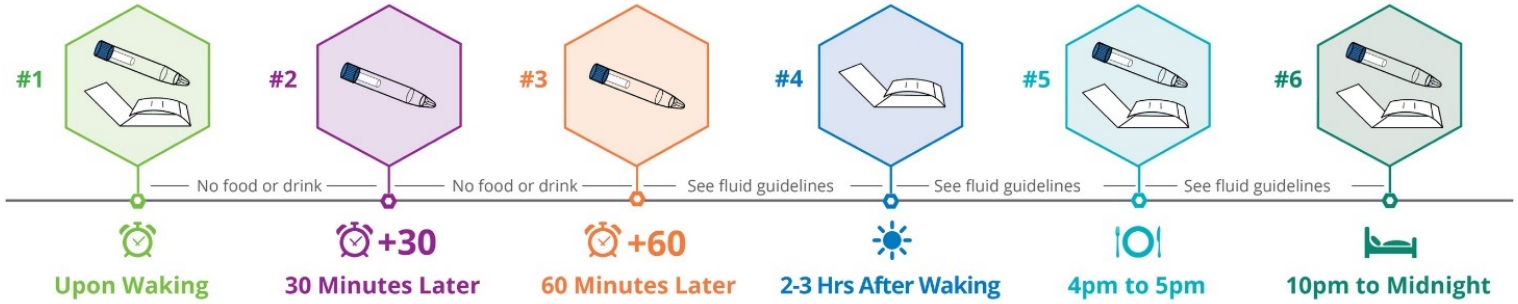
Cortisol: DUTCH testing with CAR

DUTCH PLUS – Urine PLUS Saliva for the CAR

5 **Saliva** collections

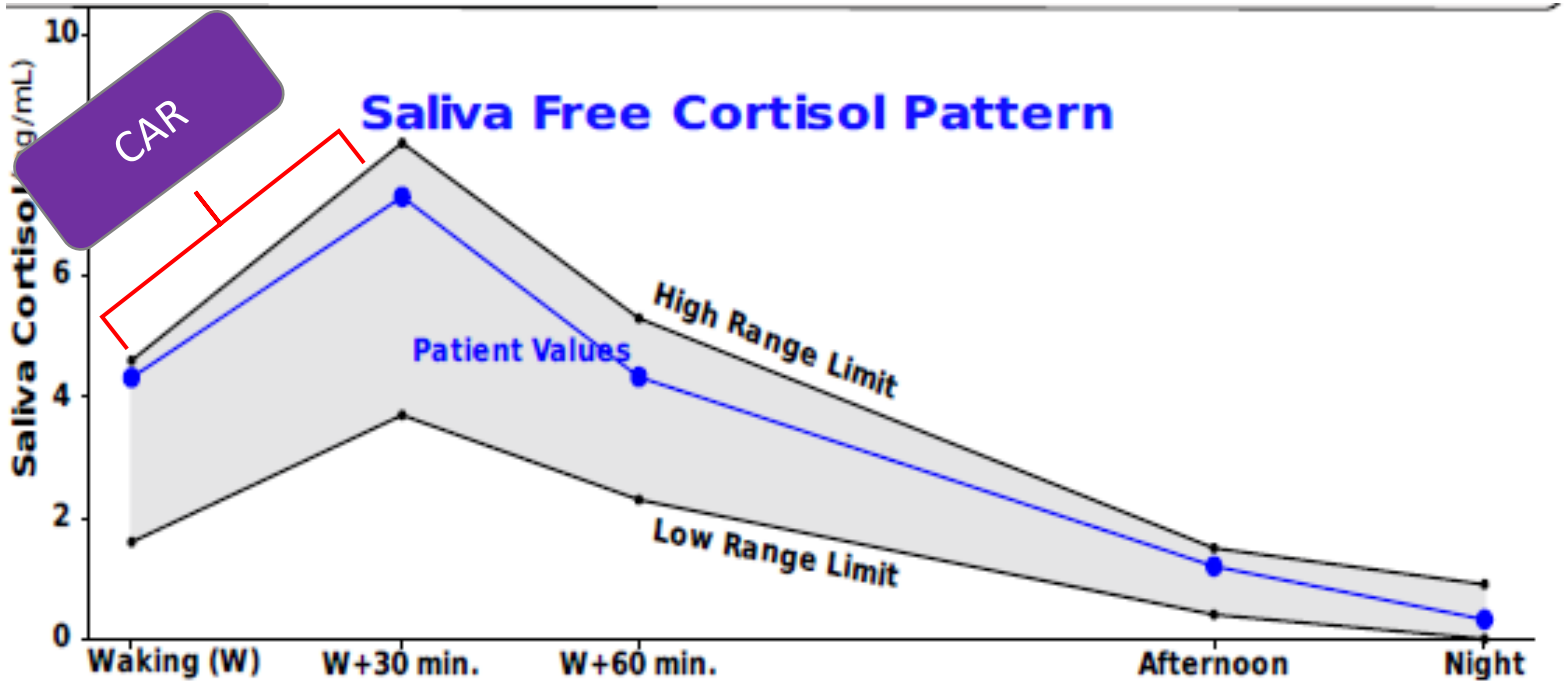
- Waking, +30 min, +60 min, 5pm, Bedtime
- Easier collections using cotton swabs

4 **Dried urine** collections (for metabolites)

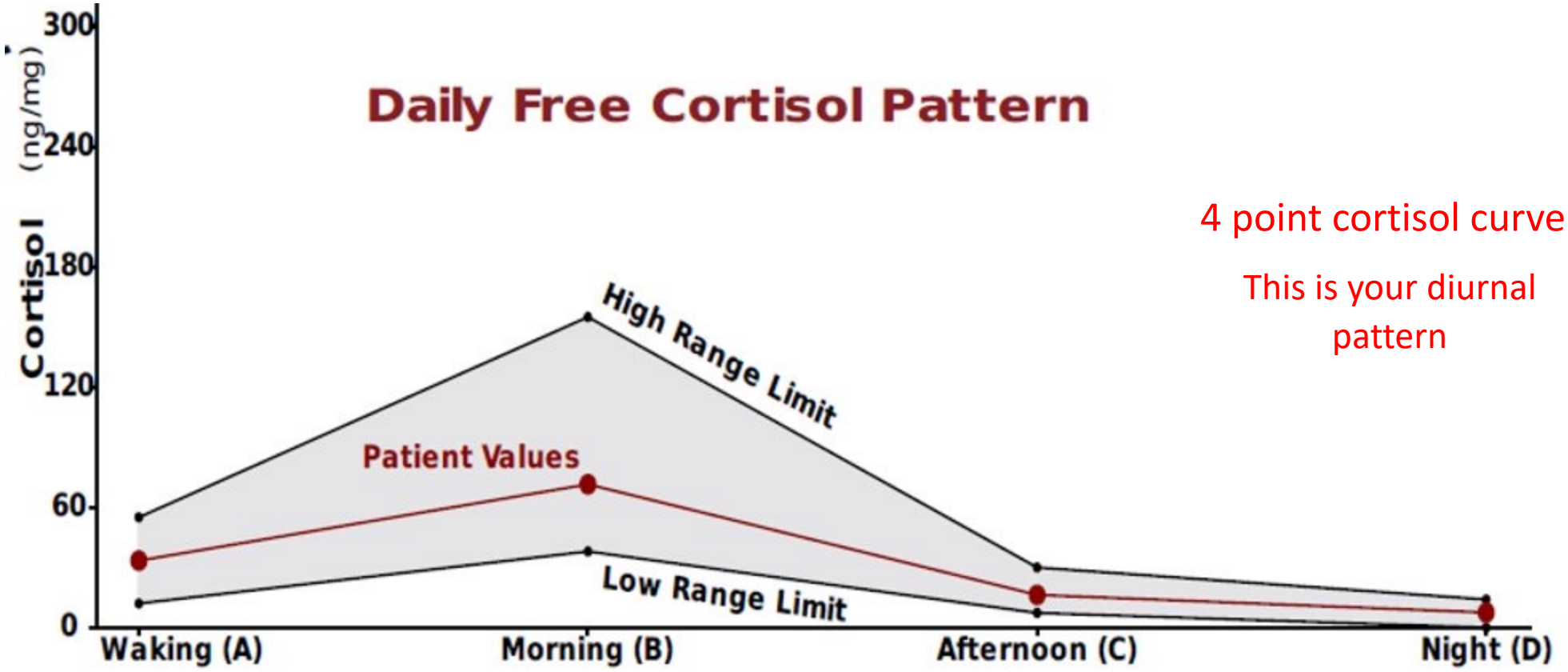


Cortisol: CAR

- CAR – Cortisol Awakening Response
- Mini stress test for HPA Axis function
  - Looking at the rise of cortisol from waking through 30 min post waking



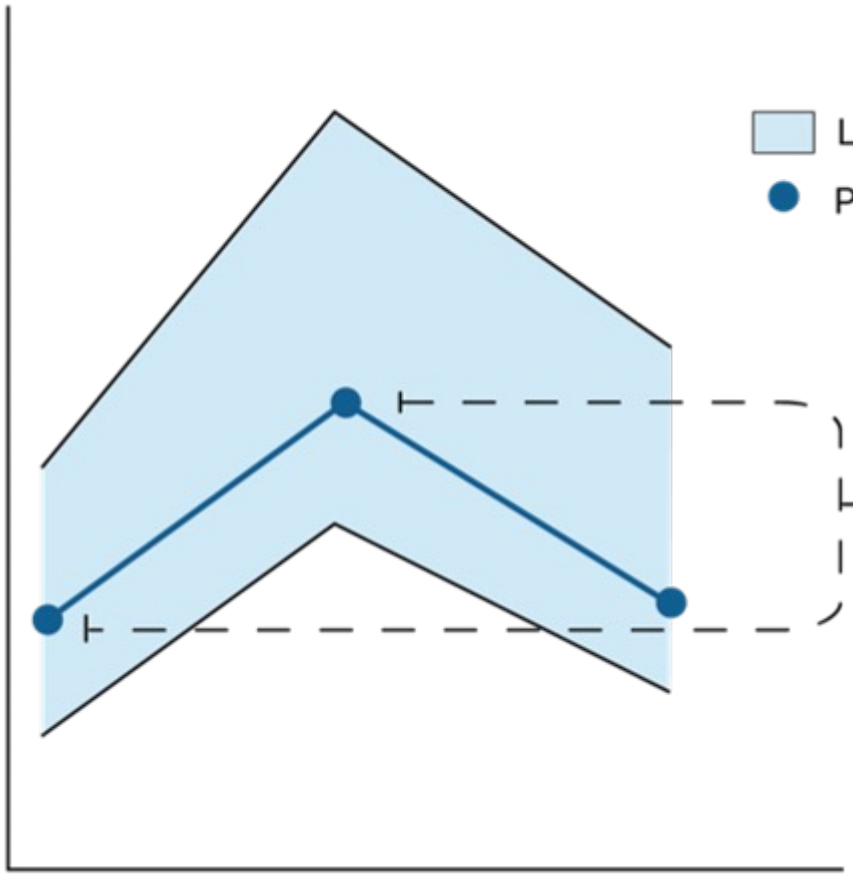
Cortisol: 4 point diurnal curve



4 point cortisol curve!

This is your diurnal pattern

Cortisol: CAR



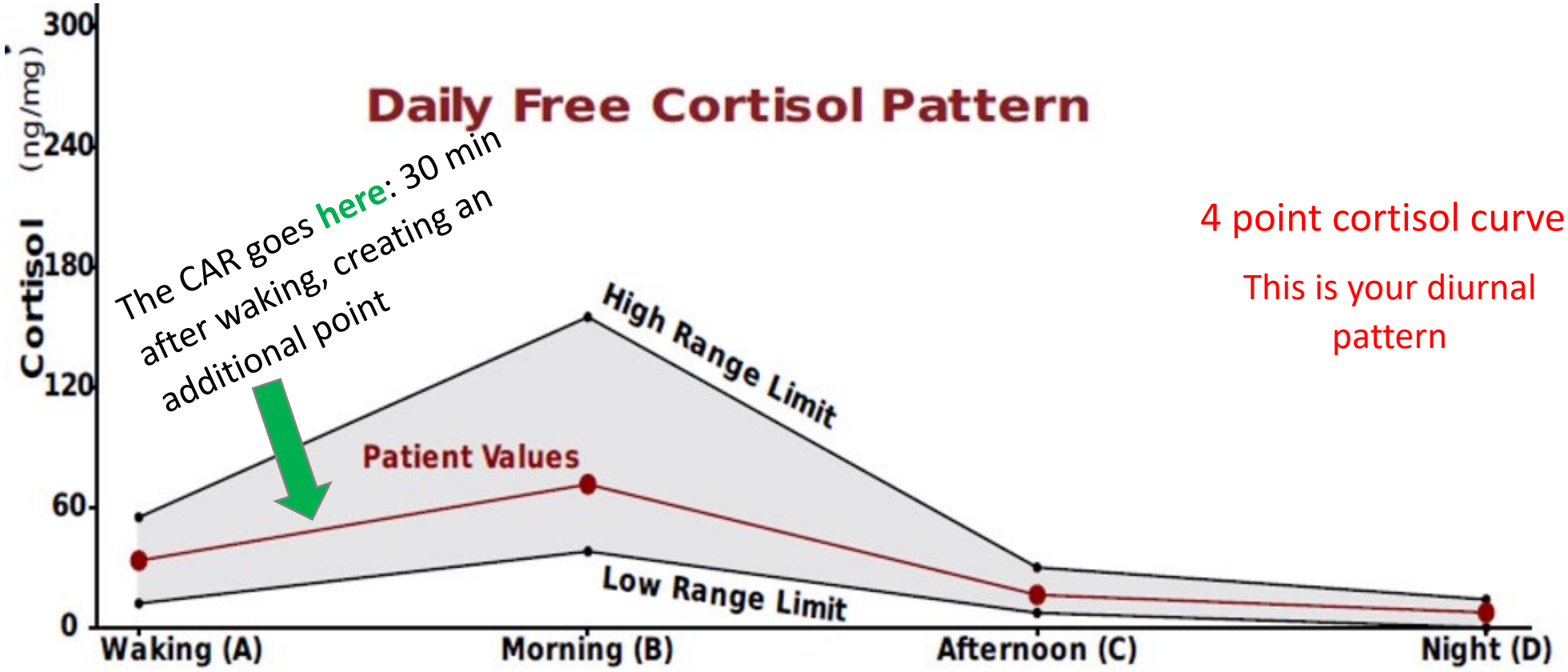
CAR	2.5 ng/mL	100%
Expected CAR	1.5 - 4 ng/mL	50 - 160%

Important to know about the CAR:

1.What is the CAR percent rise/change from waking to 30 min?

2.What are the actual numbers?

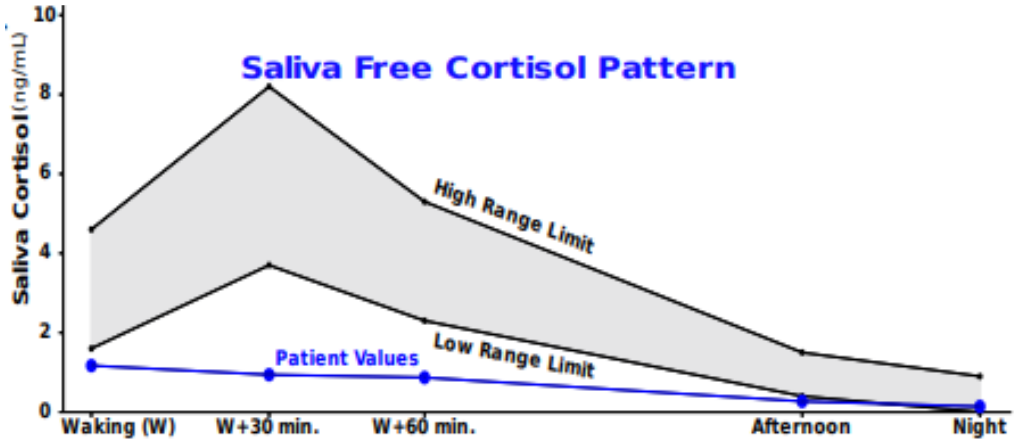
Cortisol: 4 point diurnal curve

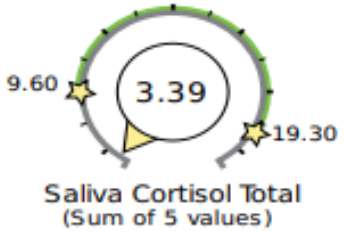


4 point cortisol curve!

This is your diurnal pattern

Cortisol: CAR





CAR

- This shows poor HPA axis function in the diurnal curve
- This shows a negative CAR

=

- Poor HPA resiliency
- Contributing factors:
  - Stress
  - Sleep
  - Inflammation

Cortisol: CAR and health outcomes

- Poor CAR and poor HPA response correlates with:
  - Mood dysregulation
  - Immune stress/autoimmune disease
  - Cognitive risks/decline
  - Metabolic dysfunction

REDUCED QUALITY OF LIFE

Cortisol and stress: how to make it better

The idea is SIMPLE
The implementation may be DIFFICULT

REGULATE SLEEP

MOVE YOUR BODY during the day
STABILIZE your blood sugar
MANAGE your stress

LIFESTYLE SUPPORT

Cortisol, stress, sleep and ….better

Herbal and Nutritional supplements that may be helpful:

- Vitamin C
- Vitamin B6
- NAC (N-Acetyl Cysteine)
- CoQ10
- PQQ
- Ashwagandha
- Rhodiola
- Phosphatidyl Serine
- Magnolia

*I am not your doctor

Please discuss the best option for your individual case with your provider

Good luck and choose wisely!

You have the information to make educated decisions about your daily health

Dr Debbie Rice

Thank you for learning with me today!

QUESTIONS?

drrice@dutchtest.com

Instagram: drrice.Debbie

New Providers Receive 50% Off up to 5 Testing Kits

- **Additional Benefits Include:**
  - Easy At-Home Collection
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- Zielinski, M, et al. *Functions and Mechanisms of Sleep*. AIMS Neuroscience. 2016; 3(1): 67-104.
- Bush, Bradley. The Role of Cortisol in Sleep. Natural Medicine Journal. January 2014.
- Brainard, J, et al. Health implications of disrupted circadian rhythms and the potential for daylight as therapy. 2015 May; 122(5): 1170-1175.

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3812410/
- https://www.simplypsychology.org/fight-flight-freeze-fawn.html (image SNS/PNS)
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Thank You!

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