Cortisol and Weight Gain: The connection between

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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.

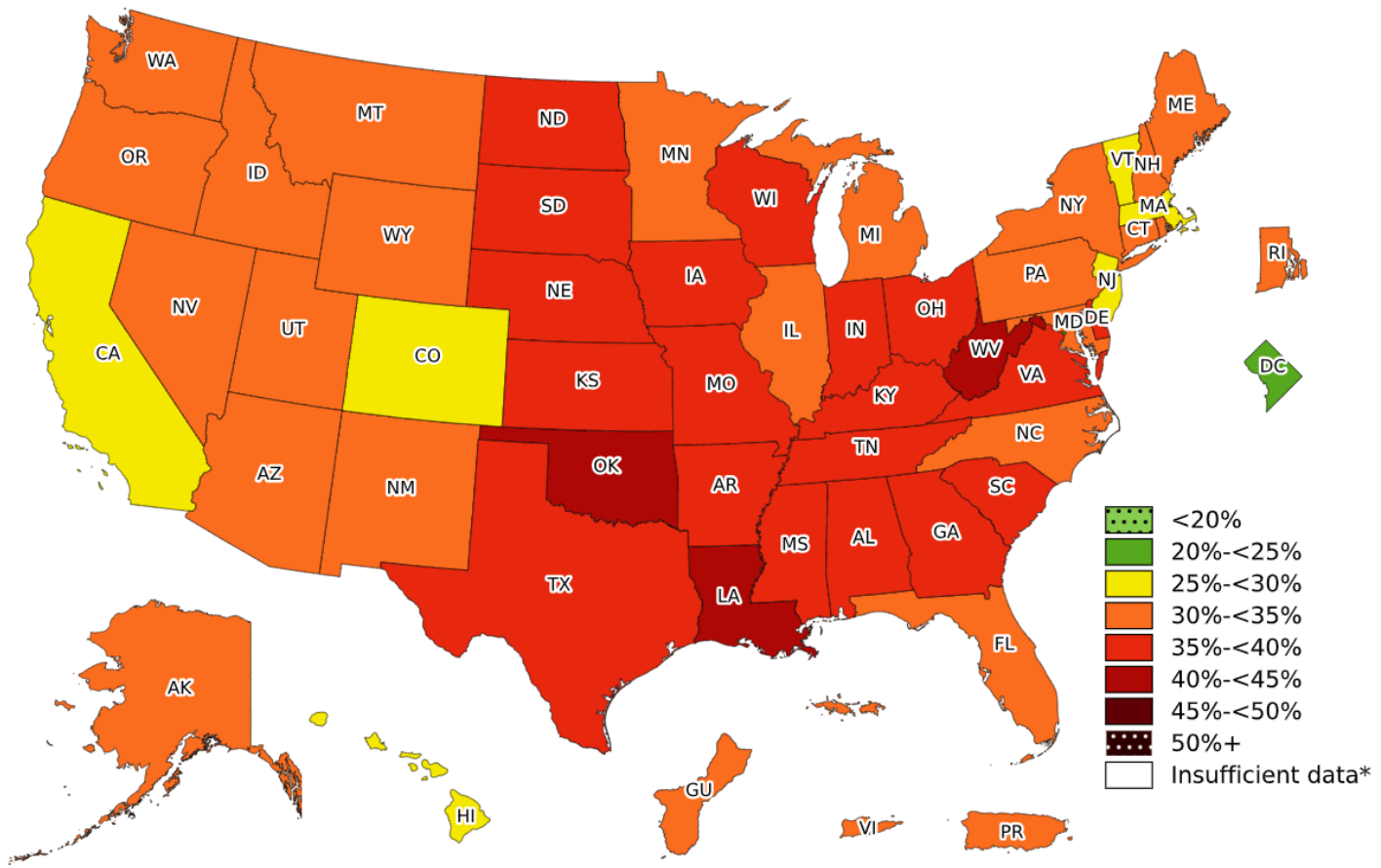
3. The use of any information provided in this presentation is solely at your own risk.

Obesity Pandemic

- Multiple studies cite that obesity has become a pandemic
- United States: 2022
- Risk factors listed include:
- Education
- Poverty level
- Race/ethnicity
- Location

(does not include the world numbers)

Prevalence† of Obesity Based on Self-Reported Weight and Height Among U.S. Adults by State and Territory, BRFSS, 2022



Adult Obesity Prevalence Maps | Overweight & Obesity | CDC

Obesity/Weight Changes

- The WHO states this as an epidemic across the world of overweight and obesity – naming it

  "Globesity" (WHO)

- There is differentiation that males have higher risk of being overweight, while females have higher risk of obesity
- This is not just for Western and developed countries
- Includes developing countries as well

- Because of this, we see the risk for diseases which include diabetes/metabolic syndrome, cardiovascular disease including stroke, cancer, and more.

https://www.who.int/activities/controlling-the-global-obesity-epidemic

Contributing Factors and Considerations:

- When evaluating HOW did we get here?

Consider:

- *Increased stress* of a connected society and economy – 24/7!
- *Increased pressure* to perform for work

Deprioritizes healthy habits

- Whole food nutrition (fast food instead)
- Physical activity (sedentary)
- Appropriate sleep habits (work deadlines, family dynamics)

https://www.shutterstock.com/image-photo/young-businesswoman-tons-documents-calling-phone-130051355

Contributing Factors to Obesity and Overweight:

- When we think about increased stress, we think about

- CORTISOL
- Cortisol is our main stress hormone

- So HOW does Cortisol tie in to weight gain and obesity….

Welcome to your Tour!

- Sit back and relax
- I will be your tour guide through this awesomely complex yet straightforward discussion

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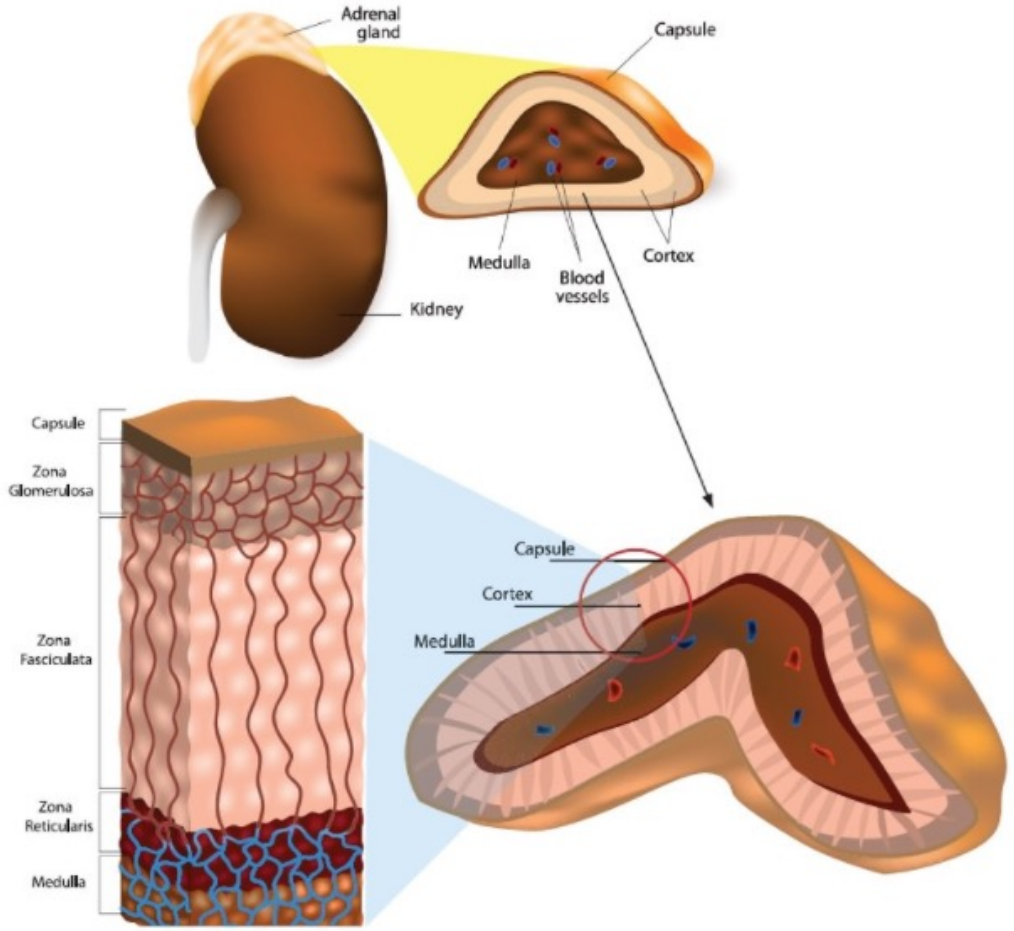
Cortisol Production

- 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



- **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: Glucocorticoid

- **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: Glucocorticoid (GC)

Cortisol as a glucocorticoid (GC)

- Influences metabolism of glucose, fat, and protein

Properties include:

- Anti-inflammatory
- Anti-allergic
- Immuno-suppressive
- Metabolic optimization

Cortisol: Glucocorticoid

Goal of Cortisol

Maintain Homeostasis

- Cortisol creates a state of hyperglycemia
- Stress induced need for glucose to critical organs (brain, skeletal muscle)
- Cortisol blocks insulin action on the cells to keep glucose in the blood stream
- Increases enzymes responsible for glycogenolysis and gluconeogenesis
- Induces catabolism in peripheral muscle to mobilize amino acids for gluconeogenesis
- Activates Hormone Sensitive Lipase (HLP) to promote beta oxidation of free fatty acids for glucose

Cortisol: Short Term effect

- 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

SYMPATHETIC NERVOUS SYSTEM

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

PARASYMPATHETIC NERVOUS SYSTEM

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
  - Not sleeping well
  - Etc...

Cortisol: Long Term Effect

- 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

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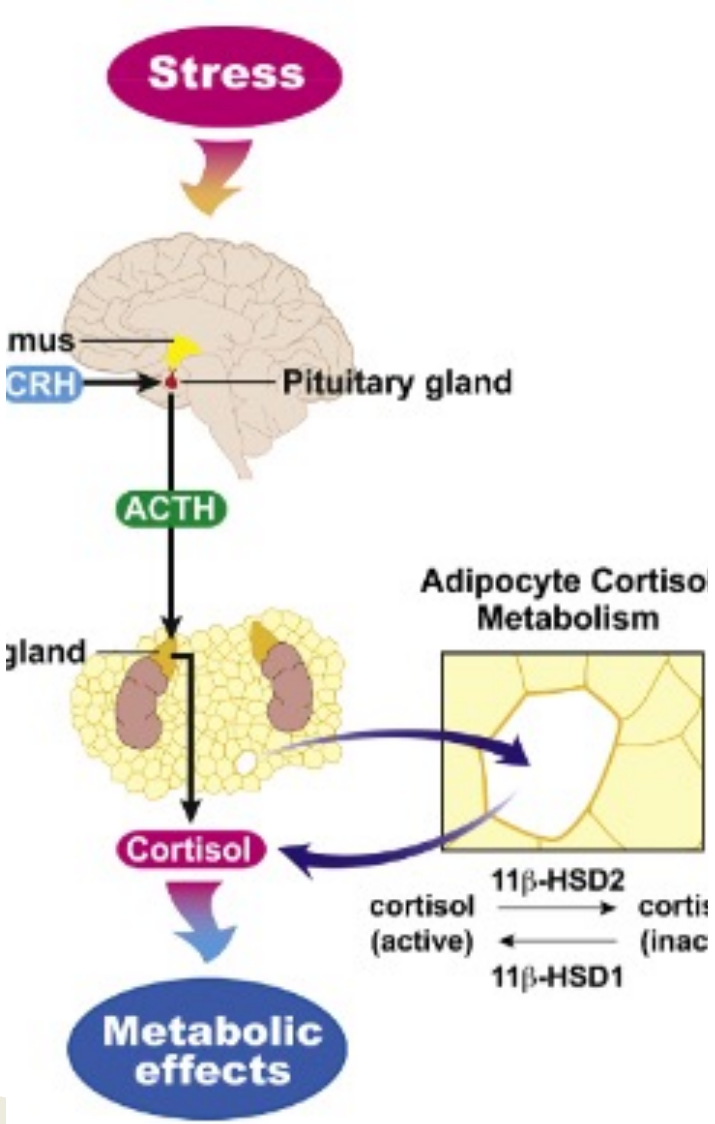
Cortisol Physiology



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

Hypothalamus → CRH (In the paraventricular nucleus PVN)

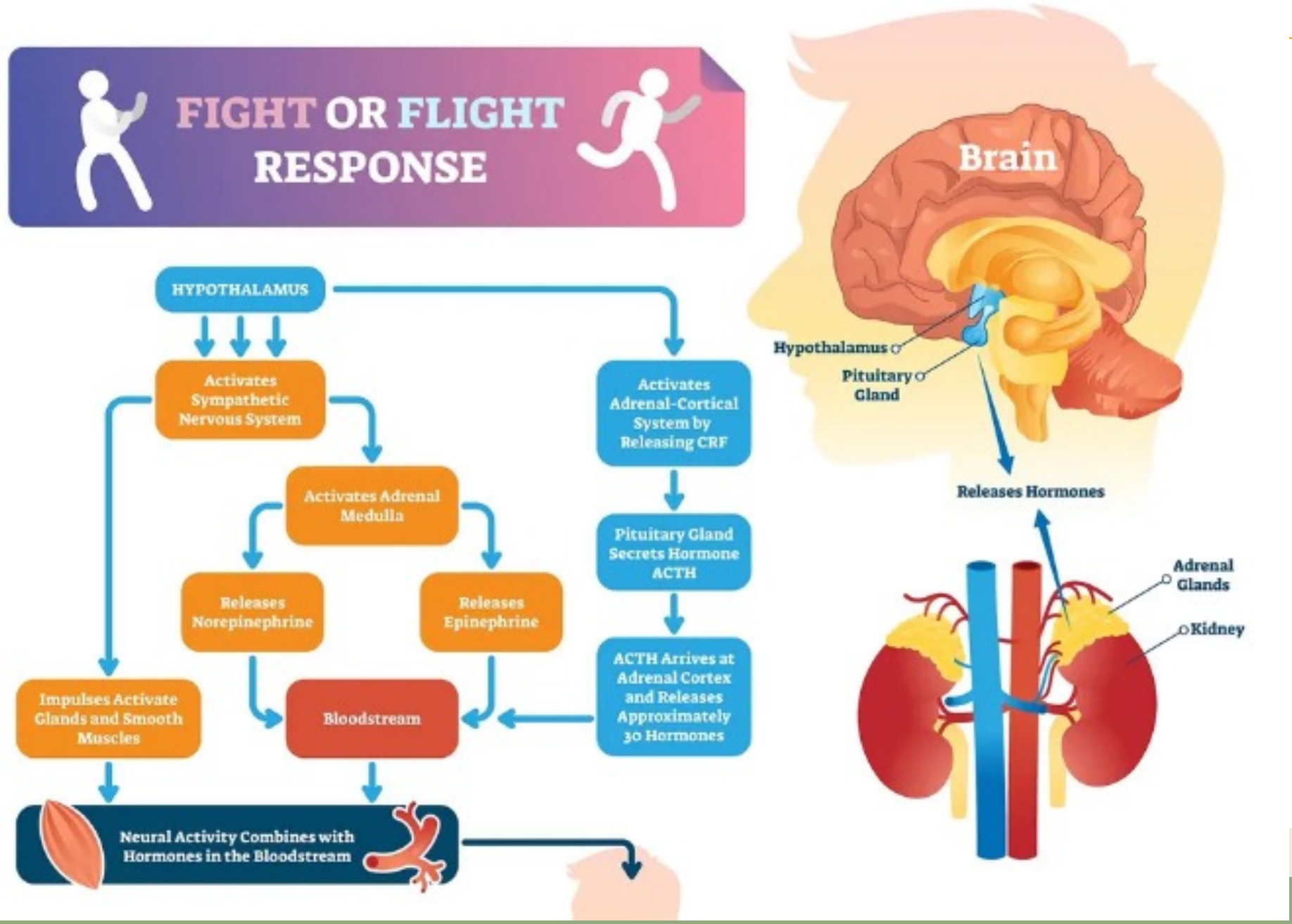
CRH → Pituitary Gland

Pituitary Gland → ACTH

ACTH → Adrenal Glands

Adrenal Glands → Cortisol

MORE ACTH = more cortisol LESS ACTH = less cortisol



Stress Response Hormones

- We all “know” that stress contributes to or exacerbates disease states
- We know that cortisol is commonly or frequently referred to as the “stress hormone”
- We also know that our stress response involves our catecholamines:

  Epinephrine and Norepinephrine, as well as Dopamine

- Therefore we can connect that cortisol and our catecholamines influence disease states

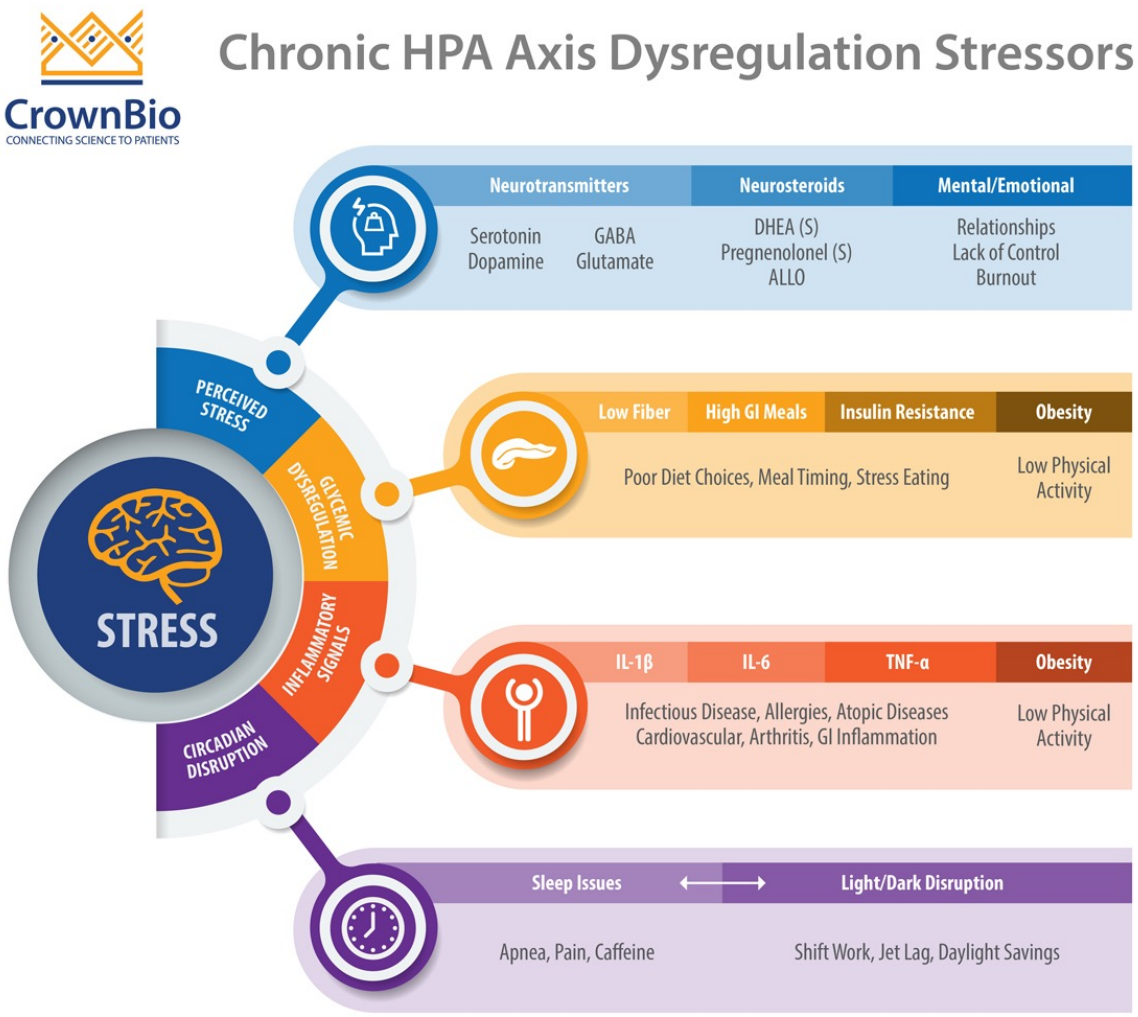
Stress Response Begins in the Brain

- 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 brain signals the SNS for a catecholamine response

HPA function and Stress Response



Stress and physiologic response:

Real vs perceived stress:

- Results in mental/emotional dysregulation

Blood sugar imbalance:

- Ultimately insulin resistance then obesity

Inflammation:

- Ultimately obesity

Day/Night disruption:

- HPA imbalance

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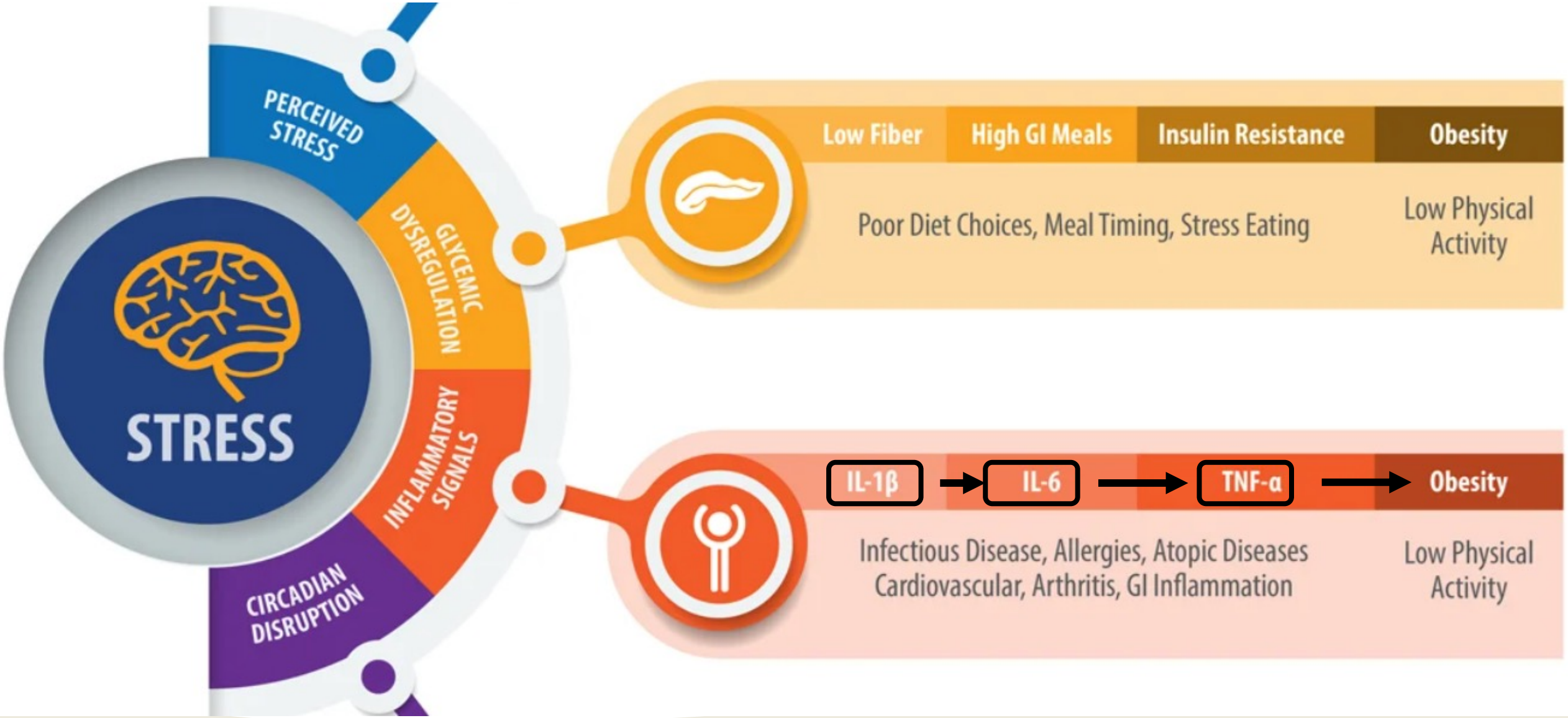
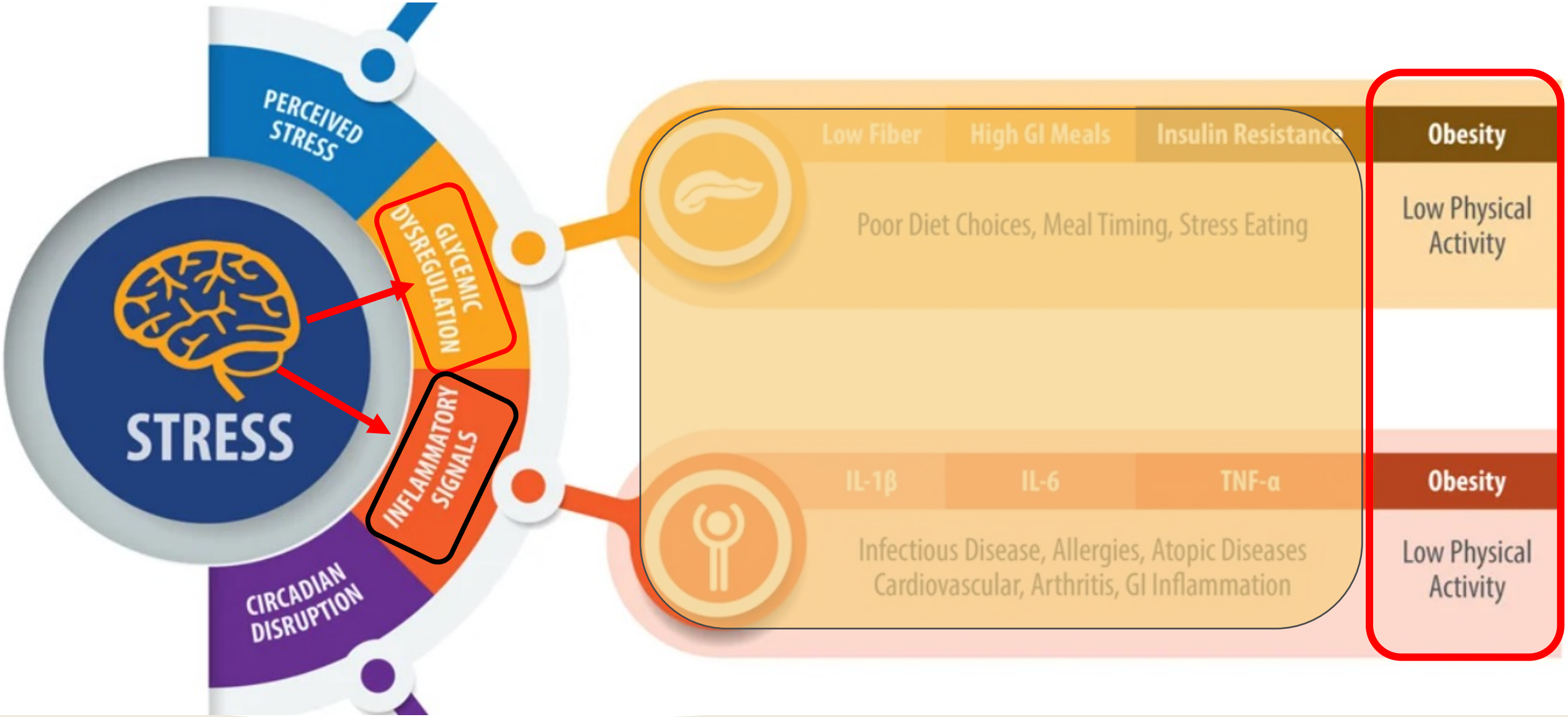
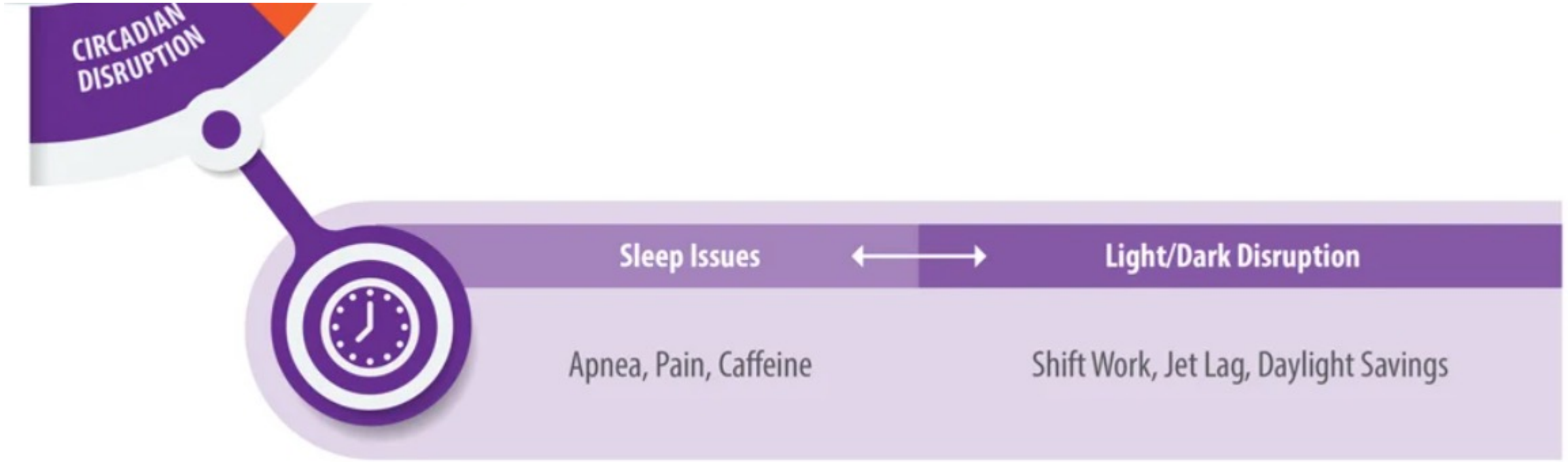
HPA function and Stress Response: Obesity



HPA Function and Stress Response: Obesity



HPA Response and Sleep:



Circadian Disruption:

- Cortisol responds to sunlight
- **All** our cells respond to sunlight
- Sunlight determines our wakefulness and sleepiness

We should be wakeful during the light
And sleepy during the night

Circadian Rhythm and Hormones

Hormones that regulate metabolism include:

- Growth Hormone
- Cortisol
- Leptin
- Ghrelin
- Thyroid
- Estradiol
- Testosterone
- DHEA
- Progesterone

Circadian Rhythm and Hormones

Hormones that regulate metabolism include:

- Growth Hormone
- Cortisol
- Leptin
- Ghrelin

These hormones need a healthy sleep pattern to do their jobs correctly

When there is sleep deprivation, these hormones are unable to work optimally

- Thyroid
- Estradiol
- Testosterone
- DHEA
- Progesterone

Sleep and Metabolism

We know that sleep is an important contributor to overall health

Sleep is integral to our circadian modulation

When sleep loss occurs, we are susceptible to increased disease states, disrupted metabolism, and confused hormone signaling

Sleep and Sex Differences

Here we can see the impact of sleep disturbance on sex and inflammation:

KEY POINTS:

Females:

Are at higher risk for inflammatory disease

More likely to have sleep issues

More likely to develop higher levels of systemic inflammation associated with sleep loss

Higher levels of CRP and IL-6 (inflammatory markers)

Box 3 | **Sex and ethnic differences in the effects of sleep disturbance on inflammation**

The effects of sleep disturbance on inflammation vary by sex and ethnicity.

Sex differences

Females are at higher risk than males for most inflammatory diseases[136], are more likely to experience sleep complaints[1], are more likely to have high levels of systemic inflammation[32] and are more likely to have increased inflammation associated with sleep disturbance[12]. In adults with established heart disease, poor sleep quality prospectively predicted increases in inflammation, but only in females[137]. Likewise, in another sample of adults, long sleep duration predicted higher levels of C-reactive protein and IL-6 in females more so than in males[138], although some studies have found greater increases in males than in females[139]. Experimental sleep loss induces greater and/or more sustained increases in nuclear factor-κB signalling and in Toll-like receptor 4-stimulated monocyte production of IL-6 and tumour necrosis factor in females than in males[35].

Ethnic differences

African-Americans are more likely to have increased inflammation at the extremes of short sleep duration than are other ethnic groups[140], possibly owing to increased likelihood of concurrent social–environmental stress[2]. Importantly, only one study has addressed the influence of ethnicity on sleep and inflammation, and this issue warrants further attention in the design of future studies, given the high prevalence of sleep disturbance and of inflammatory disorders in African-American individuals compared with white individuals[2].

https://www.nature.com/articles/s41577-019-0190-z

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Sleep deprivation and inflammatory markers

Type of sleep deprivation	Findings	Refs
Systemic markers of inflammation		
Circadian misalignment over 25 days	Increased levels of TNF and CRP and of the anti-inflammatory cytokine IL-10	33
TSD, 88 hours	Increased levels of TNFR1 at 44 and 66 hours; increased levels of IL-6 at 88 hours; no change in TNFR2, sIL-2R or IL-10 levels	147
	Progressive increase in CRP level for 88 hours	148
TSD, 40 hours	Increased levels of IL-1 and IL-2	149
	Increased level of IL-6	14,150
	Increased levels of E-selectin, ICAM1, IL-1 and IL-1ra; decreased levels of CRP and IL-6	151
	Increased levels of IL-6 and ICAM1 after a night of recovery sleep	152
	No change in the level of IL-6	153
TSD, 34 hours	Increased level of TNF, but not of TNFR2, IL-6 or CRP	154
PSD for 12 nights	Increased levels of IL-6 and CRP, but not of sTNFR1	155
PSD for 10 nights	Increased level of CRP at day 10	148
PSD for 7 nights	Increased level of IL-6 in both sexes, and increased level of TNF in men but not women	156
PSD for 5 nights	Increased level of CRP after sleep deprivation and recovery sleep	148
PSD for 2 nights	No change in IL-6 level	157
PSD for 1 night	Increased levels of IL-6 and TNF in alcoholics with sleep disturbance but not in controls	158
	Increased level of IL-6	159
	No change in level of CRP	160
	No change in level of IL-6	16
Sleep fragmentation for 2 nights	No change in level of CRP or IL-6	161
Cellular inflammation		
PSD for 1 night	Increases in both TLR4-stimulated and resting production of IL-6 and TNF by monocytes	34
	Prolonged daytime increase in TLR4-stimulated production of IL-6 and TNF by monocytes in women but not men	35
	No change in TLR4-stimulated production of IL-6 and TNF by monocytes in older adults >60 years of age	36
Transcriptional measures of inflammation		
PSD for 5 nights	Increased mRNA expression levels of IL-1, IL-6 and IL-17	162
PSD for 1 night	Increased mRNA expression levels of IL-6 and TNF	37
Inflammatory signalling and transcriptional profiles		
PSD for 1 night	Increased inflammatory gene expression profiles owing to activation of AP-1 and NF-κB pathways	37
PSD for 1 night	Increased activation of NF-κB in women but not men	38
	Increased constitutive monocyte expression of activated STAT1 and STAT5 in the night following sleep loss	34

This is just good information to have ☺

https://www.nature.com/articles/s41577-019-0190-z

Sleep and Disease Risk

Sleep Needs:

- Appropriate sleep patterning (circadian rhythm)

When sleep deprivation is present, we see:

- Difficulty losing weight
- Easy to gain weight
- Imbalanced signaling for ghrelin and leptin
- Inappropriate cortisol signaling
- Cognitive Aging
- Biologic Aging
- Depression and mood shifts
- Poor metabolic resiliency

Hormones Involved in Weight Management

- Leptin
- Ghrelin
- Adiponectin
- Cortisol

….there are others, but these are our focus today

Hormones released from Fat Cells

Fat Cells release hormones

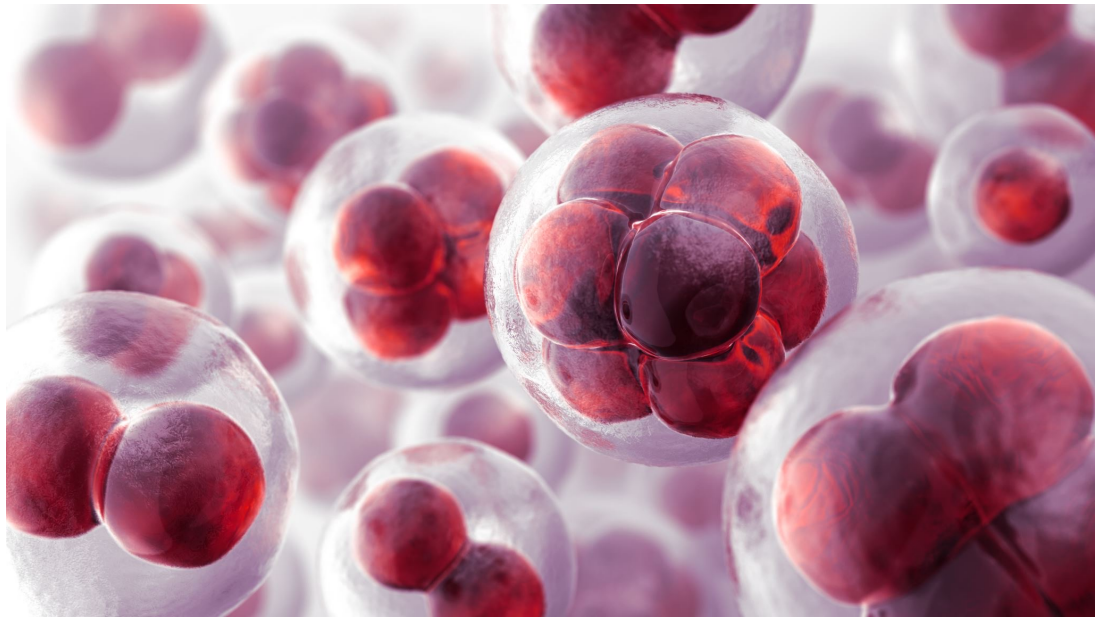
Let’s take a look at how Fat Cells communicate

Fat Cells: Adipocytes

Adipocyte physiology → Previously thought to be an inert, storage organ

We now know adipose tissue is its own endocrine organ → This means it is capable of secreting biologically active components which are called adipokines

Biologically active = metabolically active → **These are called Adipokines**



Adipocytes

Adipokine = adipose tissue + Cytokine

- Adipokines affect metabolic signaling and manage hormones affecting appetite, satiety, glucose metabolism, lipid (fatty acid) metabolism, inflammation, and immune function

- Cytokines signal cellular activity
- These can include *pro*-inflammatory or *anti*-inflammatory signals

Adipocytes

We have 2 major classes of adipose tissue:

White Adipose Tissue – **WAT**

Brown Adipose Tissue - **BAT**

Adipocytes: Different Fat Cells in the Body

- **WAT**: White Adipose Tissue
- **W**hite **A**dipose **T**issue:

- Stores excess energy as triglycerides

- Adipokines released:
- Adiponectin
- Leptin
- IL-6

- **BAT**: Brown Adipose Tissue
- **B**rown **A**dipose **T**issue:

- Stores energy as small lipid droplets
- metabolically active
- Thermogenic

- Adipokines released:
- IL-6
- IL-8
- IL-10

Adipocytes: Adipokines

Adipokines released by WAT and BAT modulate:

- thermogenesis
- energy expenditure
- glucose homeostasis
- lipid metabolism
- insulin sensitivity
- angiogenesis
- anti-inflammation

Adipokine: Leptin

Leptin Function:

- Produced from WAT mass
- Suppresses hunger
- Stimulates satiety
  (regulate appetite)
- Increases energy expenditure through fatty acid oxidation
- Results in decreased fat mass in the adipocyte

- Strong influence on immune cells (TH1)

Adipokine: Leptin

- Leptin is released in a diurnal and pulsatile fashion
- Levels are highest in the evening and early morning hours
- Circulating levels of leptin represent the amount of energy stored in fat

Low levels of fat = low levels of leptin

https://www.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&retmode=ref&cmd=prlinks&id=20083828

Adipokine: Adiponectin

ADIPONECTIN	
Liver	↓ Glycogenolysis; gluconeogenesis ↓ Lipogenesis; triglycerides
Pancrea	↑ Insulin exocytosis
Muscle	↓ Glycogen production ↑ Consumption of glucose ↑ Transport of fatty acid and fatty acid oxidation ↓ Triglycerides
Adipocytes	↑ Consumption of glucose ↑ Triglycerides ↑ Fat storage function of adipocytes

Adiponectin Function:

- Produced by WAT
- Increases fatty acid oxidation (burn fats for energy)
- Sensitizes insulin
- Anti-inflammatory
- High levels of Adiponectin are better

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7554603/

Adipokine: Adiponectin

ADIPONECTIN	
Liver	↓ Glycogenolysis; gluconeogenesis ↓ Lipogenesis; triglycerides
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Adiponectin Function:

- Anti-atherosclerotic
- Anti-proliferative
- Suppressive of carcinogens
- Modulates immune function by affecting both B and T cells

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7554603/

Adipokine: Adiponectin

- Adiponectin levels are ***decreased in disease*** states like:
- Type 2 Diabetes
- Insulin Resistance
- Obesity
- Metabolic Syndrome
- Cardiovascular Disease(s)

Adipokine: Ghrelin

Ghrelin's Gifts:

- Stimulates appetite
- Stimulates fat deposition
- Stimulates the release of growth hormone
- Inhibits insulin secretion
- Regulates hepatic glucose output
- Decreases energy expenditure
- Reduces thermogenesis
- Often called the "hunger hormone"
- Necessary for blood glucose balance
- *Gremlin Hormone ☺

Curr Opin Clin Nutr Metab Care. 2013 Nov; 16(6): 619–624

Adipokine: Ghrelin

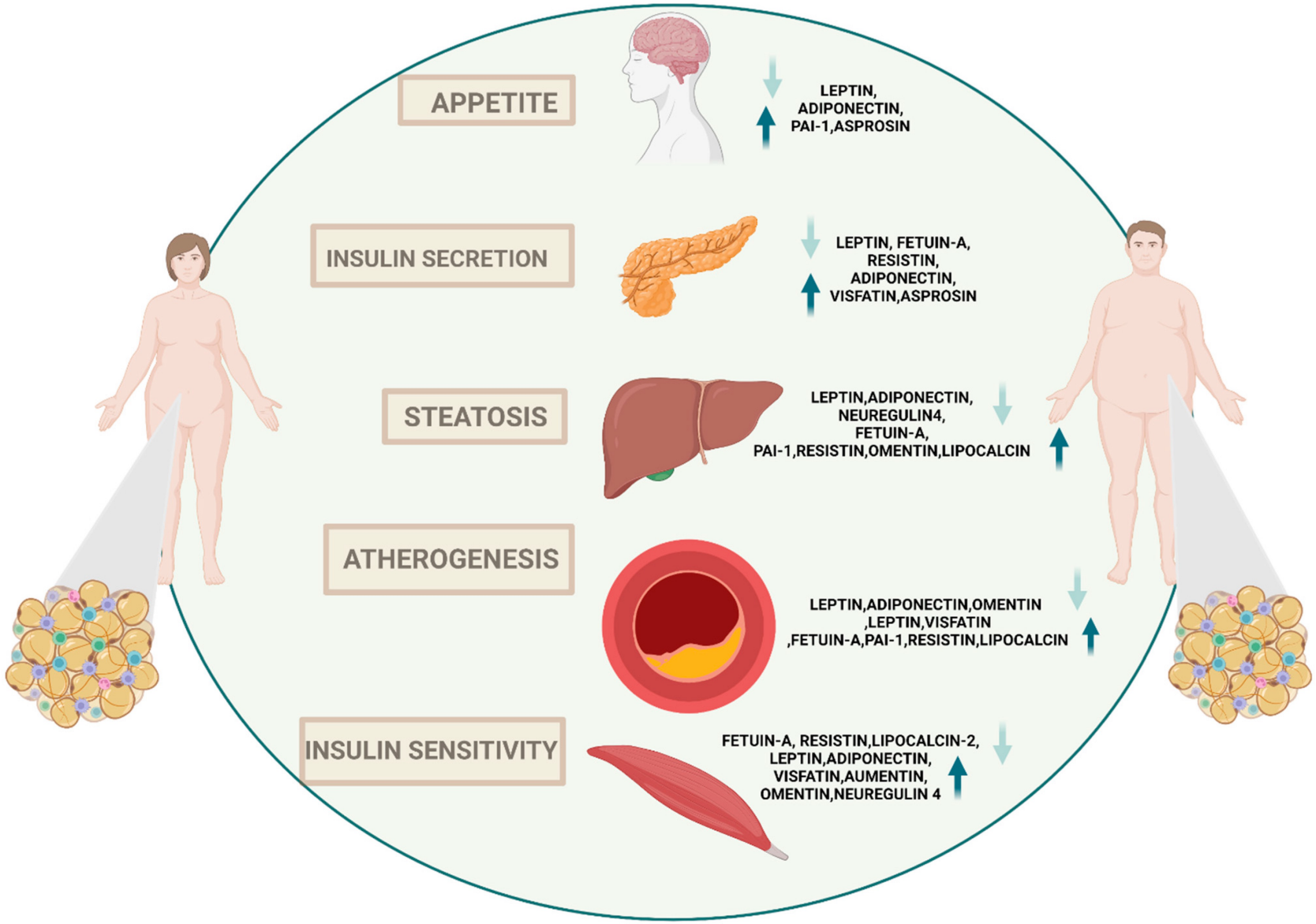
Ghrelin's Gifts:

- Reduces sympathetic nerve activity
- Prevents muscle atrophy
- Contributes to obesity and insulin resistance
- Involved in bone metabolism and formation
- May be indicated in cancer – it can have proliferative properties

- *MI, VEGF

Curr Opin Clin Nutr Metab Care. 2013 Nov; 16(6): 619–624

Adipocytes: Effects in the body



https://www.mdpi.com/2227-9059/11/5/1290

Adipocytes and Adipokines: Effects in the body

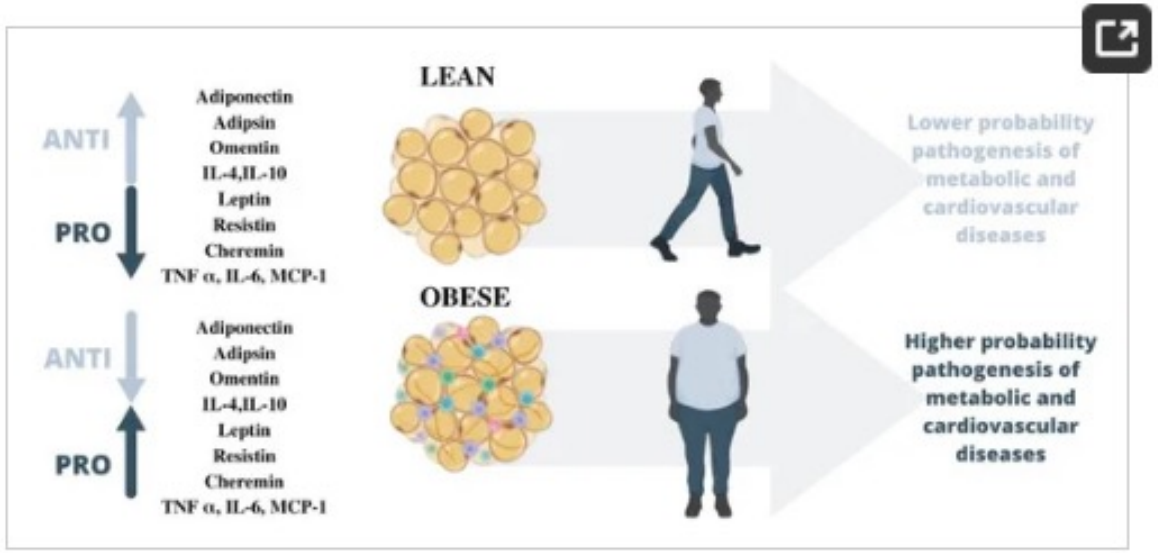


Figure 1. The behavior of adipokines in relation to the adipose tissue status of an individual. In healthy adipose tissue, anti-inflammatory adipokines increase while proinflammatory adipokines decrease, whereas the opposite is true in obese adipose tissue, increasing the likelihood of cardiovascular and metabolic diseases.

https://www.mdpi.com/2227-9059/11/5/1290

Adipokines Purpose:

- The main goal of Adipokines:

- Maintain Metabolic Integrity [homeostasis] through sensitization or resistance to insulin (Suarez, Et Al, 2023)…or regulating blood glucose levels

https://doi.org/10.3390/biomedicines11051290

Adipokines and Inflammation

- *"Adipose tissue inflammation is **initiated and sustained** over time by **aberrant** adipocytes that secrete inflammatory adipokines and by the **invasion of immune cells** formed in the bone marrow that communicates via the production of cytokines and chemokines.*
- *Low-grade inflammation of adipose tissue has a detrimental effect on distant organ function and is believed to be the core cause of obesity complications. Among them, visceral obesity plays an essential role in the development of metabolic syndrome."-Suarez, Et. Al. 2023*

https://www.mdpi.com/2227-9059/11/5/1290

So….WHY

- Why is this all important?
- Let’s pull this all together now…

Putting It All Together

KEY POINTS – Cortisol

- Cortisol is released in response to a stress
- Cortisol is meant to be acutely protective
- It is not meant to maintain chronically high levels

When your body is in Fight or Flight mode:

- Appetite decreases
- Tissue repair stops
- Reproductive processes slow/hormones slow down
- Immune system pauses

Putting it All Together

- **KEY POINTS** – Cortisol

When your cortisol levels remain consistently high:

- Body craves carbohydrates/sugars for energy, and high fats
- Your sleep is not as optimal- even if you are sleeping the same amount of time; quality is less
- Your energy expenditure becomes less
- Your appetite changes (timing of eating/type of food eaten)

Putting It All Together

- **Sustained HIGH levels of Cortisol**

→ need for comfort foods: high fats, high glycemic index (your brain runs better on glucose/sucrose for energy)

→ with poor diurnal regulation, hormone signaling becomes imbalanced (ghrelin, leptin, adiponectin) and timing of food intake is different. Your body distributes these calories differently

→ this combination causes your WAT to redistribute to the abdominal region of the body and you now have increased (adipokine) activity from WAT

→ this abdominal WAT decreases the activity of BAT

Putting It All Together

→ Cortisol reduces the ability to focus and think clearly

When this occurs, we do not make smart food choices

Rather, we follow our cravings for high glycemic carbohydrates and fats

And we may not consider the timing of when we eat

→ When we are stressed, we don't create space for physical activity which also creates metabolic imbalance

Our bodies are thrown out of routine

And our bodies really like routine!

Putting It All Together

It’s not just about

CALORIES IN = CALORIES OUT

Putting It All Together

It’s not just about

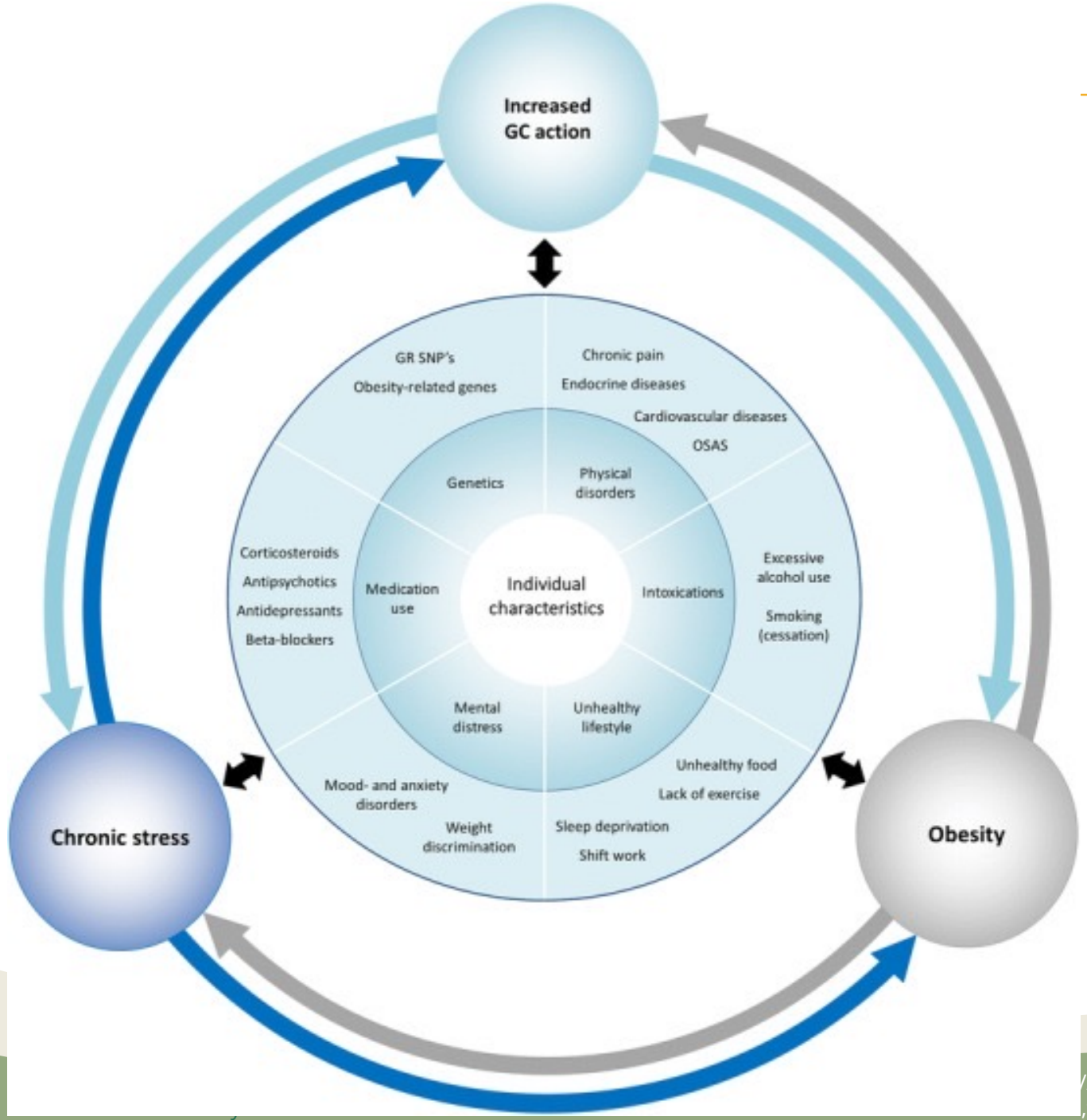
CALORIES IN  CALORIES OUT

Putting It All Together

- Multiple studies show that sustained high levels of cortisol correlate with a high BMI
- Elevated cortisol metabolites (THF/THE) correlate with high BMI
- Still other studies have shown that sustained high levels of cortisol predict obesity in multiple populations (children and adults)

- Newman, M. Smeaton, J. Endocrine and Metabolic Science. Dec 2023.
- Rossum, E. Obesity. Feb 2017.

The Vicious Cycle



Circle of Stress

Obesity

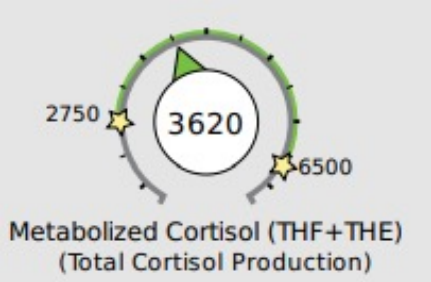
GC reactivity

*dependent on GC receptor activity: over or under reactive

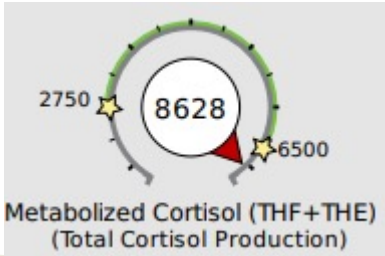
Cortisol and Weight Gain: Considerations

NOT all cases of weight gain have high cortisol levels

- Normocortisolistic obesity – normal cortisol levels
  - There are likely other factors influencing metabolism



- Hypercortisolistic obesity – elevated cortisol levels
  - Many times, this is also associated with abnormal body composition, poor diurnal pattern, insulin dysregulation and inflammatory states.



https://onlinelibrary.wiley.com/doi/full/10.1002/oby.21774

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Cortisol and Weight Gain: Considerations

- People who are overweight or obese and are mentally stressed about weight discrimination show higher cortisol levels

- This correlates to ongoing elevated cortisol levels that perpetuate cortisol with weight gain

https://onlinelibrary.wiley.com/doi/full/10.1002/oby.21774

Cortisol and Weight Gain: Treatment Considerations

When elevated cortisol is involved, it is important to consider:

- Stress Management

  (yes! Even the studies say: mindfulness!)

- Adopting an appropriate sleep routine

- Stabilizing blood sugar:
  - Timing and quality of nutrients is key
  - Protein and balanced foods every 2-4 hrs when stressed can help to maintain stable blood sugar and reduce cravings for high glycemic foods

Cortisol and Weight Gain: Treatment Considerations

When elevated cortisol is involved, it is important to consider:

- Physical Activity:
  - Walking for 20 min (especially post meal)
  - Weight-lifting to support healthy muscle metabolism

- Food Planning:
  - This reduces the stress of having to decide on foods in the moment of stress
  - This is proven to reduce snacking, poor food choices, craving frenzies!

Cortisol and Weight Gain: Treatment Considerations

Addressing the root cause:

What is contributing to stress and elevated cortisol?

- Mood
- Immune function
  - Virus
- Inflammation
  - Environmental
  - Food
  - Exposures

Cortisol and Weight Gain: Treatment Considerations

AND…TEST, Don’t guess!

- It is important to have information to approach your treatment appropriately

Serum testing:

- Leptin
- Adiponectin
- Inflammatory markers (cytokines)

Cortisol and Weight Gain: Treatment Considerations

AND…TEST, Don’t guess!

DUTCH testing:

- Metabolized Cortisol (cortisol metabolites: THF/THE)
- Diurnal pattern of free cortisol to evaluate appropriate circadian rhythm
- 8-OH marker to evaluate oxidative stress (cellular stress)
- Inflammatory markers:
  - Kynurenate
  - Xanthurenate
  - Quinolinate

QUESTIONS?

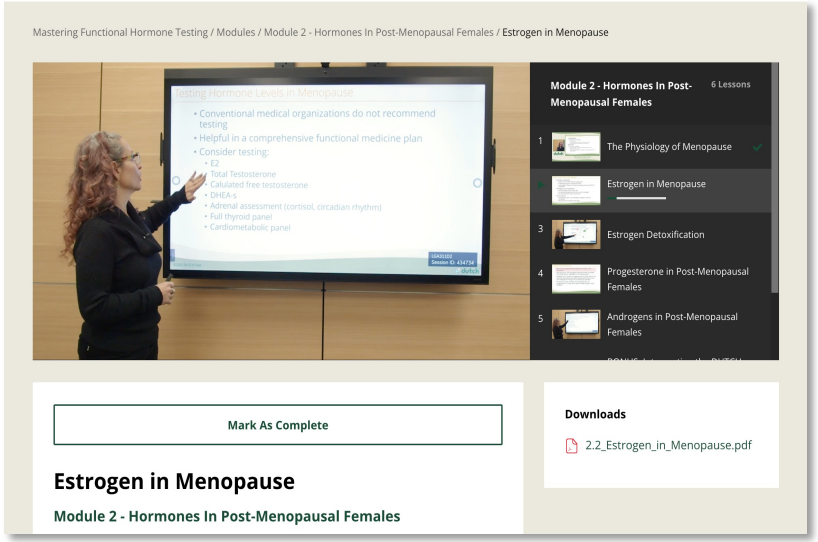
THANK YOU FOR LEARNING WITH ME TODAY!

Become a Provider

Exclusive Hormone Education for DUTCH Providers

DUTCH Interpretive Guide

Mastering Functional Hormone Testing Course



Group Mentorship Sessions

Click the Link Below to

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Thank You!

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