# The Anatomy of Stress

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#### Outline

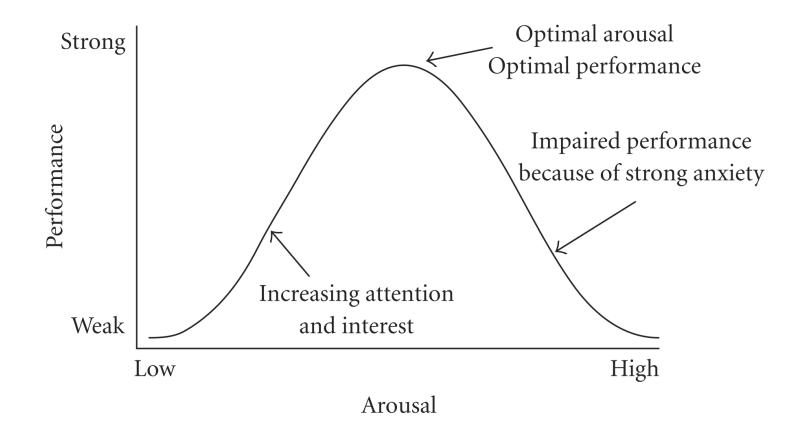
- What is stress? What is a stressor?
- What happens in our brains when we are stressed?
- How does stress impact chronic diseases?
- What can we do to cope?

#### What is stress vs a stressor?

- Stress: any stimulus that disrupts the body's internal balance
- "a real or perceived threat to homeostasis" (balance)
- Stress can be positive (eustress) or negative (distress)

Eustress	Distress
Motivates, focuses energy	Causes anxiety or concern
Short term	Can be short or long term
Perceived as within coping abilities	Perceived as outside one's ability to cope
Feels exciting	Feels unpleasant
Improves performance	Decreases performance
Often no long term effects	Can lead to mental and physical problems

#### Stress can be helpful



Yerkes-Dodson Law: performance increases with psychological stimulation but only to a certain point

# Stressor: Typically, negative

- Hazardous or demanding work environment
- Legal stress
- Family/relationship stress
- Low income
- Retirement
- Global pandemic
- A stressor can become a stress to the body if
  - It is persistent
  - Coping strategies are not healthy

# Physical vs. Psychological Stressors

- Physical
  - Infection
  - Pregnancy
  - Surgery
  - Acute/serious illness
- Psychological
  - Loss/grief
  - Socioeconomic: food insecurity, housing crisis, financial hardship
  - Relationship tension
  - Anxiety
  - Situational

# Responding to Stress

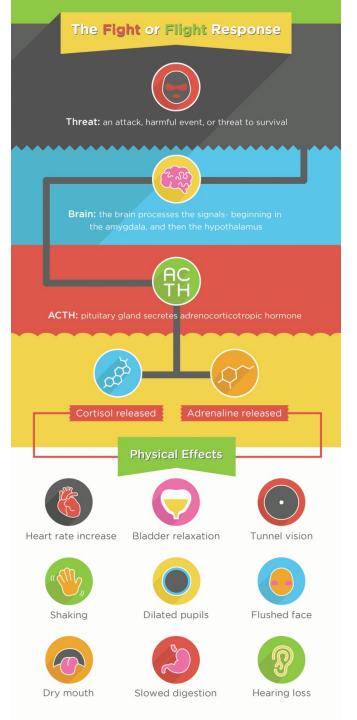
- Physical response: autonomic via the neuroendocrine system
- Psychological response
  - Depends on the individual perception of predictability and controllability
- Time course is dictated by whether the stressful stimulus is manageable or not
  - stimuli that elicit strong neuroendocrine responses become real stressors if they overcome the individual's ability to change and adapt

# Fight or Flight Response



# Fight or Flight Response: Sympathetic

- Adrenaline is the first hormone released from the adrenal glands
- Cortisol is released second and longer acting
- This is a normal response
  - Ensures safety
  - Attempts to return the body's systems to normal through negative feedback loop – "homeostasis"

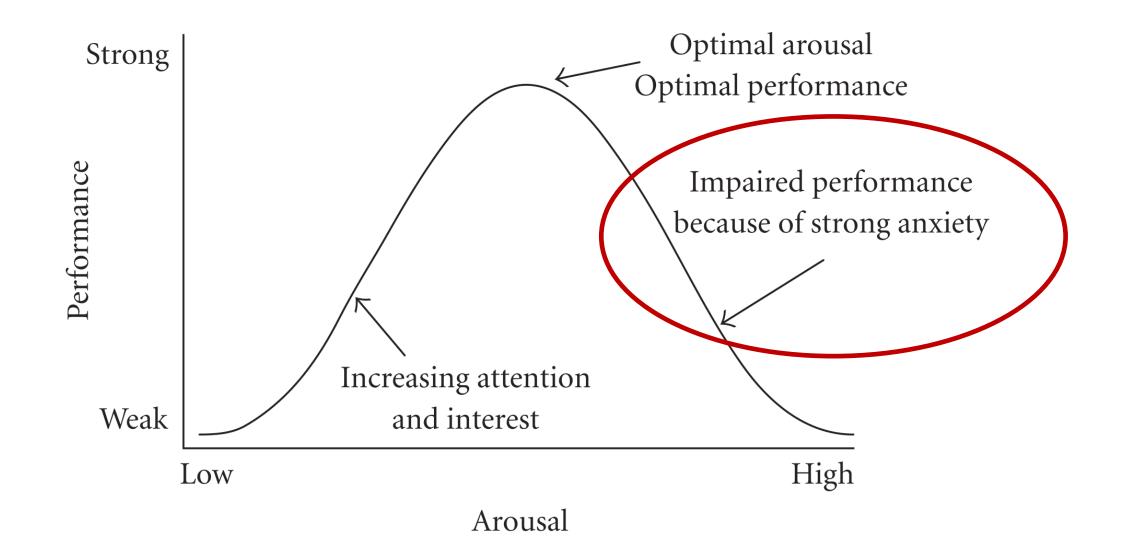


#### What does acute stress do?

Nervous system	<ul> <li>Increased cardiovascular and respiratory tone</li> </ul>
Endocrine system	<ul> <li>Decreased digestion</li> <li>Decreased growth and reproduction</li> </ul>
Immune system	• Lowered immunity
Behavioural system	<ul> <li>Increased awareness and cognition</li> <li>Euphoria and analgesia</li> </ul>

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- When cortisol levels are chronically high, the receptors in the body become resistant
  - High levels of glucocorticoids, stress peptides, and pro-inflammatory cytokines
  - Acute stress response is blunted
  - The body takes a longer time to return cortisol levels to normal

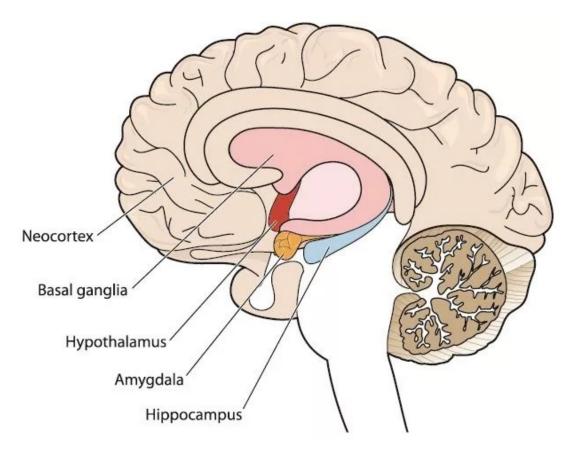


#### Rest and Digest Response: Parasympathetic

- This system makes us calm after a stimulus
- Pupils constrict
- Heartbeat slows
- Airways relax
- Digestion is stimulated
- Alertness decreases
- Muscle tone decreases

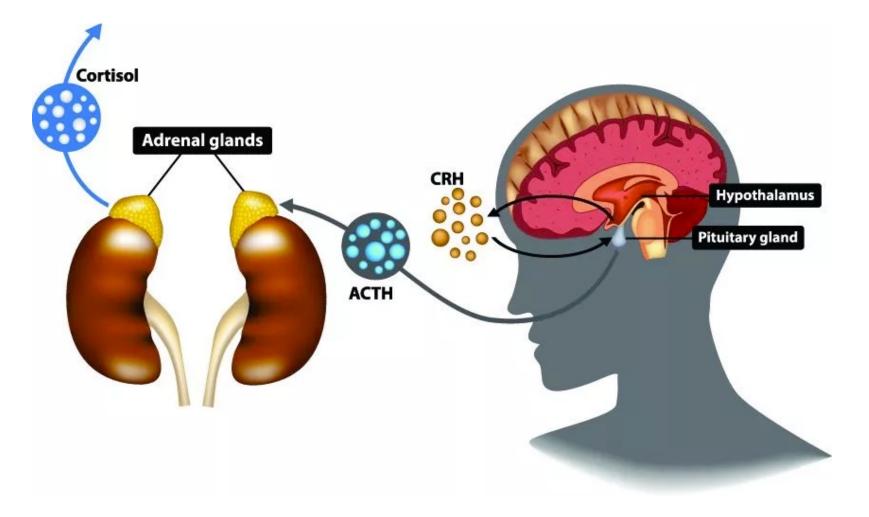
#### How our brains deal with stress

- Limbic system
  - Hippocampus helps consolidate memory
  - Amygdala drives emotional responses (fear, anxiety, etc.)
- Has many glucocorticoid receptors
- Impacts of higher glucocorticoid levels:
  - Altered neurochemistry
  - Excitability
  - Less neuronal branches
  - Cell death



#### HPA Axis and Glucocorticoids

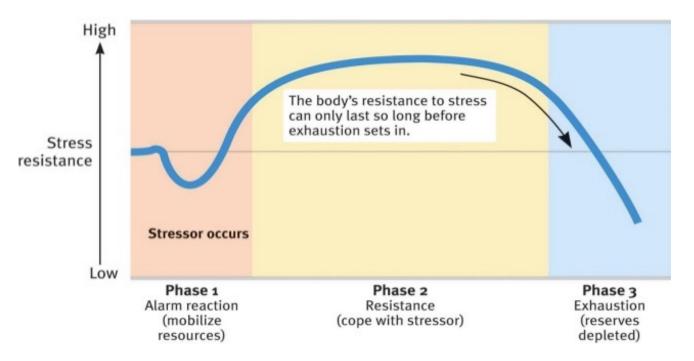
- Stress causes the hypothalamus to release hormones that in turn result in cortisol production
- Cortisol receptors:
  - Sympathetic nerves
  - Brain regions
  - Immune cells



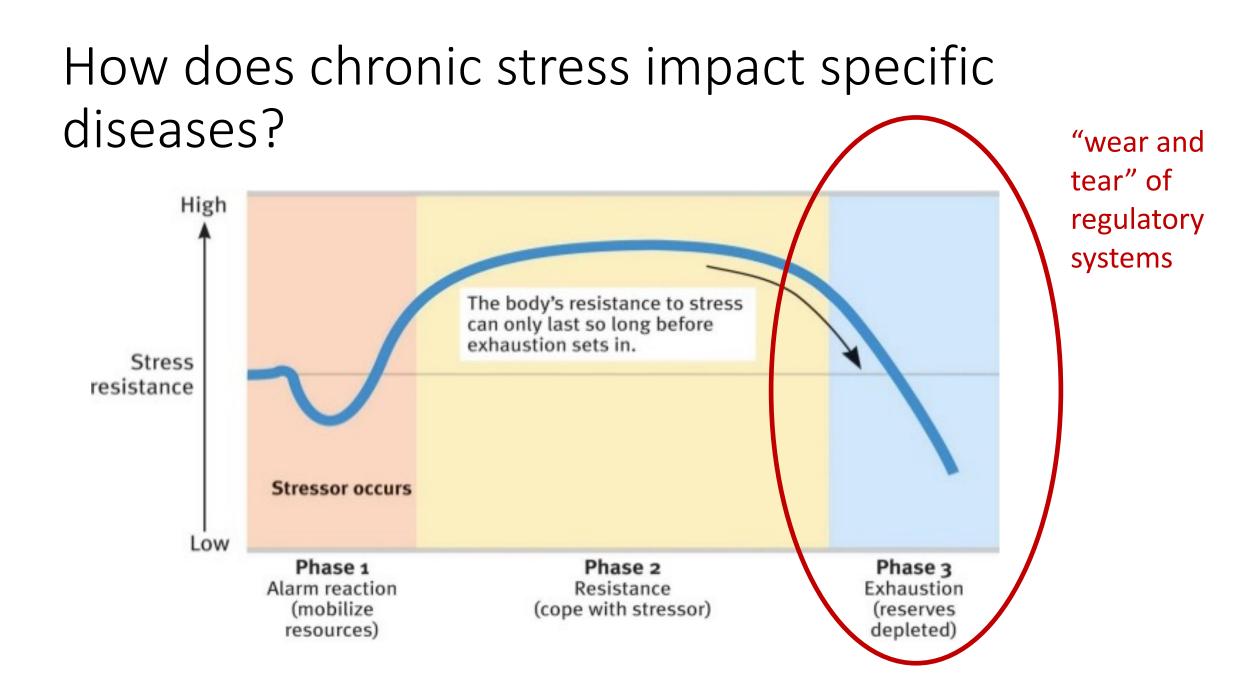
# What impacts regulation of the HPA Axis?

- Genetics
- Early life environment (exposures during pregnancy, childhood trauma/abuse)
- Current life stress
  - Family or work-related problems
  - Combat exposure
  - Community violence
  - Chronic illness
  - Neuropsychiatric disorders
- Alcohol use/dependence
- Post-traumatic stress disorder
- High fat/high sugar diets dampen HPA activity

### General Adaptation Syndrome

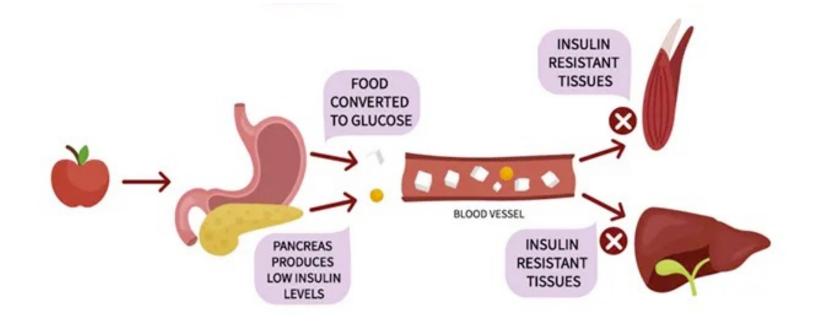


- Alarm phase: fight or flight response takes over
- Resistance phase: body stays activated at a higher metabolic level to offset the persistent stress
- Exhaustion phase: body loses ability to cope, becomes burnt out



# Glycemic control/Diabetes

- Increases glucose production in the liver
- Causes muscles to break down proteins
- Lowers insulin production in the pancreas

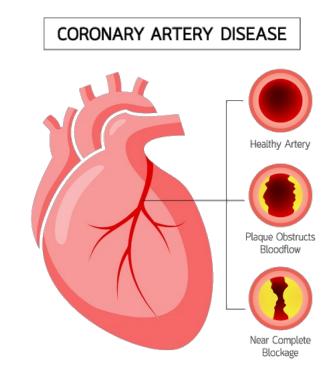


# Coping Technique: Exercise

- Consistency over 3-4 weeks will start to decrease insulin resistance
- Benefit continues for 24 hours habits are important to form!
- Moderate to vigorous exercise (10 minutes minimum)
  - Reduced cardiovascular risks
  - Reduced microvascular risks
  - Lowers blood glucose
- Exercise causes the muscles to take up glucose (similar to how insulin works) – allows the cells to be more sensitive to insulin
- Muscle cells are the main target strength and cardio are both important
- Stick with it changes are slow!

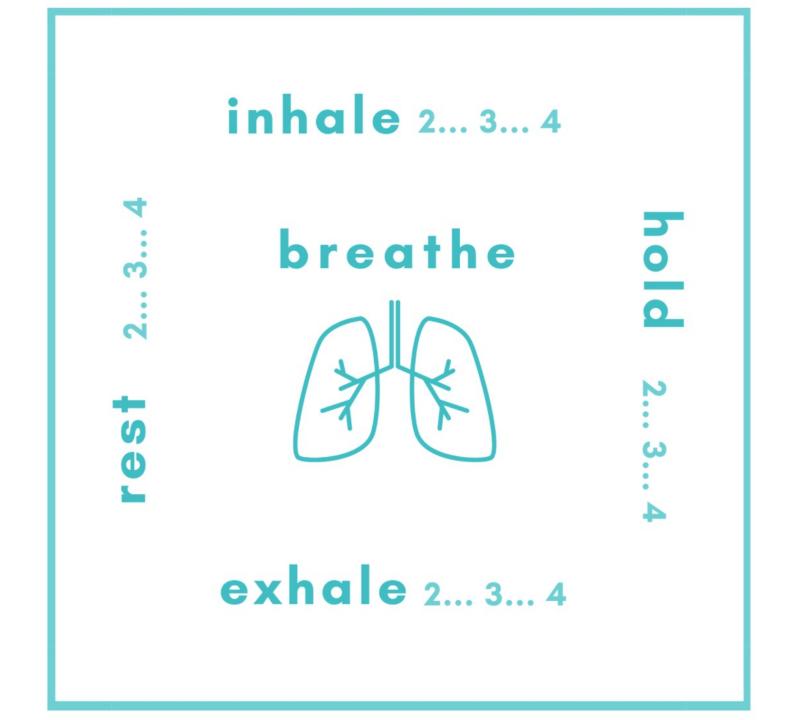
# Heart disease/Hypertension

- Increases heart rate
- Contracts (narrows) arteries, increased blood pressure
- Stimulate plaque and platelet aggregation in small arteries
- Alpha-adrenergic stimulation of the heart increases oxygen demand – may make heart attacks more likely
- Estrogen is protective women often develop heart disease later



# Coping technique: breathing

- Deep breathing dilates blood vessels and decreases the heart rate
- Options:
  - Diaphragm breathing (lying down with hand on chest and abdomen, in through nose, out through mouth)
  - Equal breathing (4 seconds in through nose, 4 seconds out through nose)
  - Square breathing (4 seconds in through nose, hold for 4 seconds, 4 seconds out through mouth, hold for 4 seconds)
  - 4-7-8 breathing (inhale through the nose for 4 seconds, hold for 7 seconds, out for 8 seconds through mouth)



# Using a device

- 5-Minute breathing workout (Inspiratory Muscle Strength Training)
  - 6 week treatment
  - Lowers blood pressure as much as exercise or medications (9 point reduction)
  - Helped dilate arteries and prevent plaque buildup
  - Reduces inflammation
- Search for "inspiratory muscle trainer"





# Sleep Deprivation



- Recommendation is 7-9 hours per night
- Stress increases when length and quality of sleep decreases
- Cortisol tries to keep us awake
- Higher stress can further decrease sleep; more likely to cause:
  - Mind racing
  - Sluggish/low energy
  - Irritability
  - Poor concentration
  - Feelings of sadness or depression
- Sleep deprivation can lead to: insulin resistance, high blood pressure, heart disease, obesity

# Coping Technique: Sleep Hygiene

- Consistent sleep/wake times
- No caffeine after 2pm
- No eating after 7pm
- No screen time for 2 hours before bed
- Avoid alcohol before bed
- Exercise during the day
- Keep your room dark, quiet, comfortable temperature
- Reduce fluid intake before bed

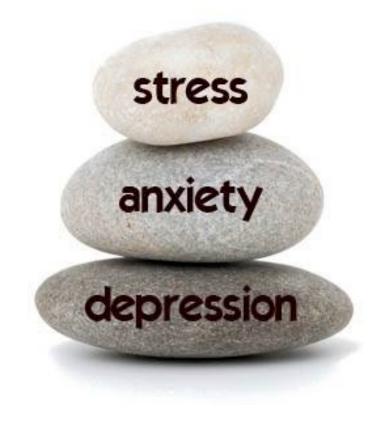
#### Meditation

- More effective than medication in improving sleep symptoms and daytime sleepiness
- Increases melatonin (sleep hormone)
- Increases serotonin
- Reduces heart rate and blood pressure
- Activates the sleep centers of the brain
- Try out:
  - YouTube
  - Spotify
  - Headspace



#### Depression/Anxiety

- Stress can cause chronic cognitive, emotional, and behavioural dysfunction
  - Adjustment disorder
  - Acute stress disorder



#### Adjustment Disorder

- The development of emotional or behavioral symptoms in response to an identifiable stressor(s) occurring within 3 months of the onset of the stressor(s).
  - Marked distress that is out of proportion to the severity or intensity of the stressor, taking into account the external context and the cultural factors that might influence symptom severity and presentation.
  - Significant impairment in social, occupational, or other important areas of functioning.
- The symptoms do not represent normal bereavement.

#### Acute Stress Disorder

- Exposure to actual or threatened death, serious injury, or sexual violation
- Presence of symptoms of intrusion (negative mood, dissociation, avoidance, and arousal)
- 3 days to one month after exposure
- May turn into PTSD if lasts longer than one month

#### Depression/Anxiety

- Stress can cause chronic cognitive, emotional, and behavioural dysfunction
  - Adjustment disorder
  - Acute stress disorder
- Changes in brain structure can increase vulnerability to mental health disorders
- Depressed individuals show reduced hippocampal size
  - Improves when on anti-depressant therapy and/or in remission

# Coping technique: Mental and physical health care

- Physical exercise produces neurotransmitters that can
  - Enhance cognitive abilities
  - Lessen depression
  - Reduce risk of neurodegenerative disease
- Mental health care
  - Counselling/therapy
  - Social supports
- Kelty's Key: <u>https://www.keltyskey.com/</u>
  - Free, online self-guided therapy from Vancouver Coastal Health
  - Anxiety, chronic pain, grief, depression, insomnia, providing family support, panic, substance use

#### Stress and Gastrointestinal health

- Can promote inflammation
- Increases gastric acid production
- Increases cell permeability, reduces water removal from the colon
- Increases risk of colitis
- Increases gastric motility
- Irritable bowel syndrome is strongly linked to stress



- Avoid trigger foods
  - High acid
  - High fat
  - High sugar
  - Alcohol
  - Caffeine
- Understand the link between mental health and IBS
  - Treatment of stress/anxiety often improves GI health
- Low FODMAP diet
  - fermentable oligo-, di-, mono-saccharides and polyols
  - Often lead to pain, bloating, gas

FOOD	EAT	AVOID
Vegetables	lettuce, carrot, cucumber & more	garlic, beans, onion & more
Fruits	strawberries, pineapple, grapes & more	blackberries, watermelon, peaches & more
Proteins	chicken, eggs, tofu & more	sausages, battered fish, breaded meats & more
Fats	oils, butter, peanuts & more	almonds, avocado, pistachios & more
Starches, cereals & grains	potatoes, tortilla chips, popcorn & more	beans, gluten-based bread, muffins & more

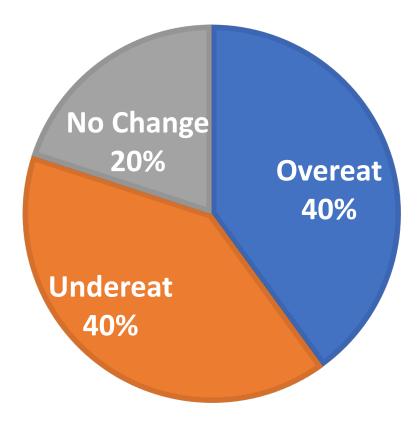
## Appetite/weight management

- Short term (fight or flight) appetite is suppressed
- Chronic stress
  - cortisol promotes appetite
  - Increases insulin resistance worsened in those with diabetes
  - Influences appetite-related hormones
  - Promotes abdominal fat deposition
- Tendency to seek out high-calorie/high-fat foods when stressed
  - Strengthens "hedonic" (pleasurable) networks involved in over-eating
    - Similar pathways in drugs of abuse
    - Can increase the compulsive nature of over-eating
  - Counter-acts stress-related responses and emotions (only short term)

#### Not everyone turns to food

**DURING STRESS** 

- The stressed brain has a strong desire to eat and an inability to inhibit eating
- Women tend to turn more to food, men to smoking and alcohol
- Stress can lead to skipped meals as well
  - Causes the body to preferentially store remaining calories



# Stress and eating

- Why?
  - Distraction
  - Habit
  - Emotional eating
- What promotes stress eating?
  - Obesity more adipose tissue means less negative feedback to your body to stop eating, and blunts the HPA axis response
  - Emotions anxiety, depression, anger, apathy, alienation activates the emotional "fight or flight" response
  - Restriction can work against you
    - May make your body less attentive to the physiological cues of hunger and satiety
    - May deplete your cognitive resources, leaving you less able to deal with the stressor, which increases the likelihood of binge or over-eating

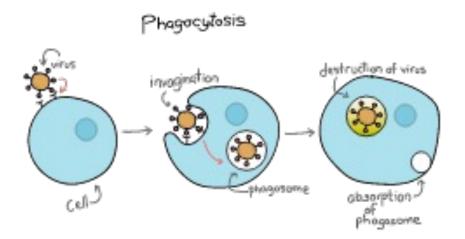


Yau, 2013. Harvard, 2021

- Keep "comfort foods" out of your house
- Stay involved with your care team
  - Follow up appointments
  - Group sessions
  - Social motivation/supports
- Medications might help
  - Ozempic (semaglutide)
    - Decreases appetite hormones in the stomach/intestines
  - Contrave (Bupropion/Naltrexone)
    - Blocks the 'reward' pathway in the brain that gets stimulated in food addiction

#### Immunity

- Stress-mediated proteins pass through the blood-brain barrier
- Cortisol suppresses macrophages

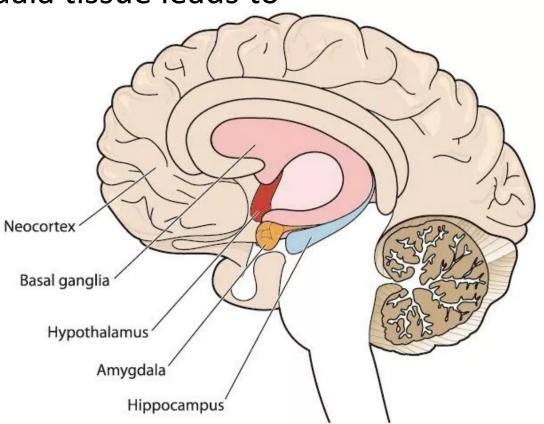


- Can lead to decreased T cell lymphocytes genetic instability, malignant cells, cancer
- Lowers antibody production

- Vaccinations
  - COVID, influenza, pneumococcal
  - Shingles (Varicella Zoster)
- Public/personal health guidelines
- Good nutrition
  - Canada food guide
  - Emphasis on whole non-processed foods
- Activity/exercise
- Age- and sex-appropriate cancer screening
  - Pap smear, mammogram, rectal examination, colonoscopy

## Memory/cognitive function

- Loss of hippocampus and amygdala tissue leads to
  - Memory disorders
    - Spatial memory
    - Verbal memory
    - Declarative memory
  - Cognitive dysfunction
    - Reduced cognition
    - Behaviour changes
    - Mood disorders
    - Decreased reaction time
    - Impaired learning



- Reading
- Puzzles
- Socializing
- Board games





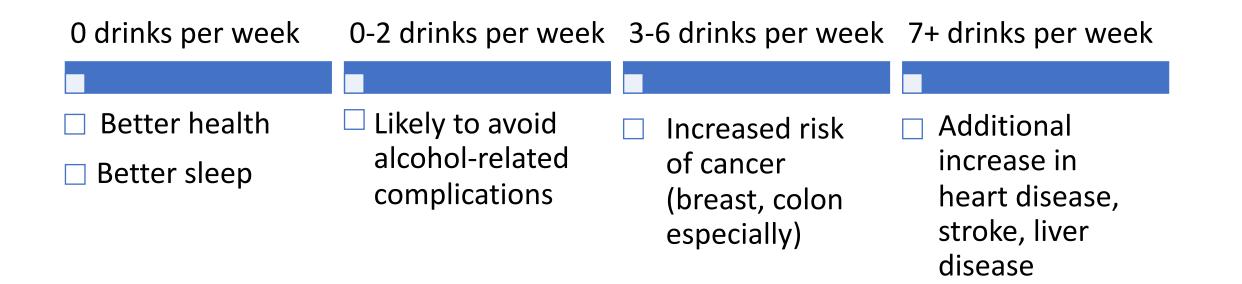


## Stress can lead to more unhealthy behaviours

- Smoking
- Alcohol consumption
- Harmful drug use
- Medication reliance
- Poor sleep

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### NEW Canadian Guidance on Alcohol and Health





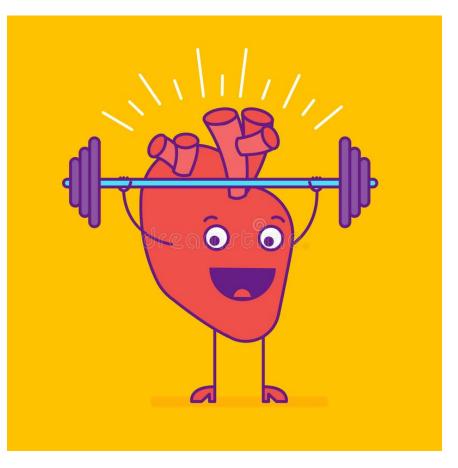
#### How to cope with unavoidable stress

- Healthy, acute stress responses can turn into pathogenic chronic responses
- Try to use the coping mechanisms
- Control what you can, try to adapt to what you can't
- Build up your support systems and resilience



## When all else fails... dance (and exercise!)

- Lower blood pressure
- Important for weight maintenance
- Increased level of good cholesterol (HDL)
- Reduce fatty liver
- Leaner, stronger muscles
- Stronger bones
- More energy
- Improved mood
- Better sleep
- Stress management



### References

- Conrad, C. A critical review of chronic stress effects on spatial learning and memory. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2010. 34(5): 742-755.
- 2. Yaribeygi, H. et al. The impact of stress on body function: A review. EXCLI J. 2017. 16:1057-72.
- 3. Craighead, D. et al. Time-Efficient Inspiratory Muscle Strength Training lowers blood pressure and improves endothelial function, NO bioavailability, and oxidative stress in midlife/older adults with above-normal blood pressure. Journal of the AHA. 2021.
- 4. Stephens, M. et al. Stress and the HPA Axis. Alcohol Research. 2012. 34(4):468-483.
- 5. Mariotti, A. The effects of chronic stress on health: new insights into the molecular mechanisms of brain–body communication. Future Sci OA. 2015. 1(3): FSO23.
- 6. Stress and Sleep. American Psychological Association. Available <u>https://www.apa.org/news/press/releases/stress/2013/sleep</u>
- 7. Harvard Health Publishing. Why stress causes people to overeat. Feb 15, 2021. Available <u>https://www.health.harvard.edu/staying-healthy/why-stress-causes-people-to-overeat</u>.
- 8. Yau, H. Stress and eating behaviors. Minerva Endocrinology. 2013. 38(3):255-267.