

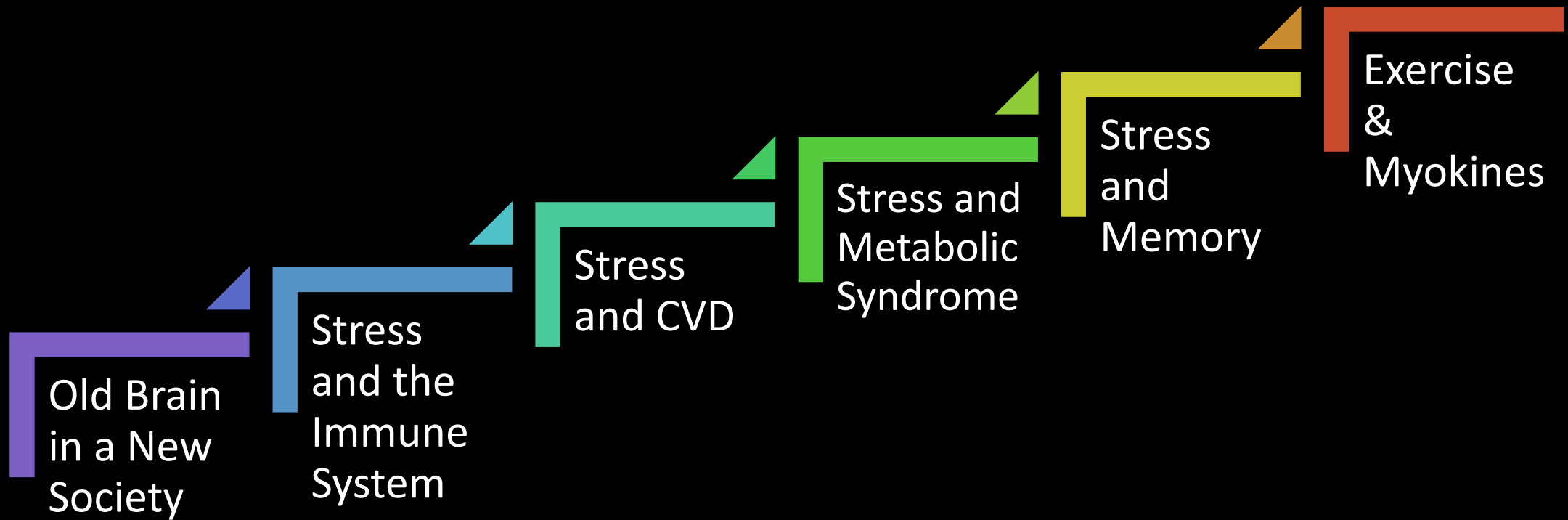


Stress & The Neuroprotective Factors of Exercise

Week 9: Thursday, November 29

Sonia Romo

Today's Agenda



Old Brain in a New Society

Stress & the Immune System

Exercise

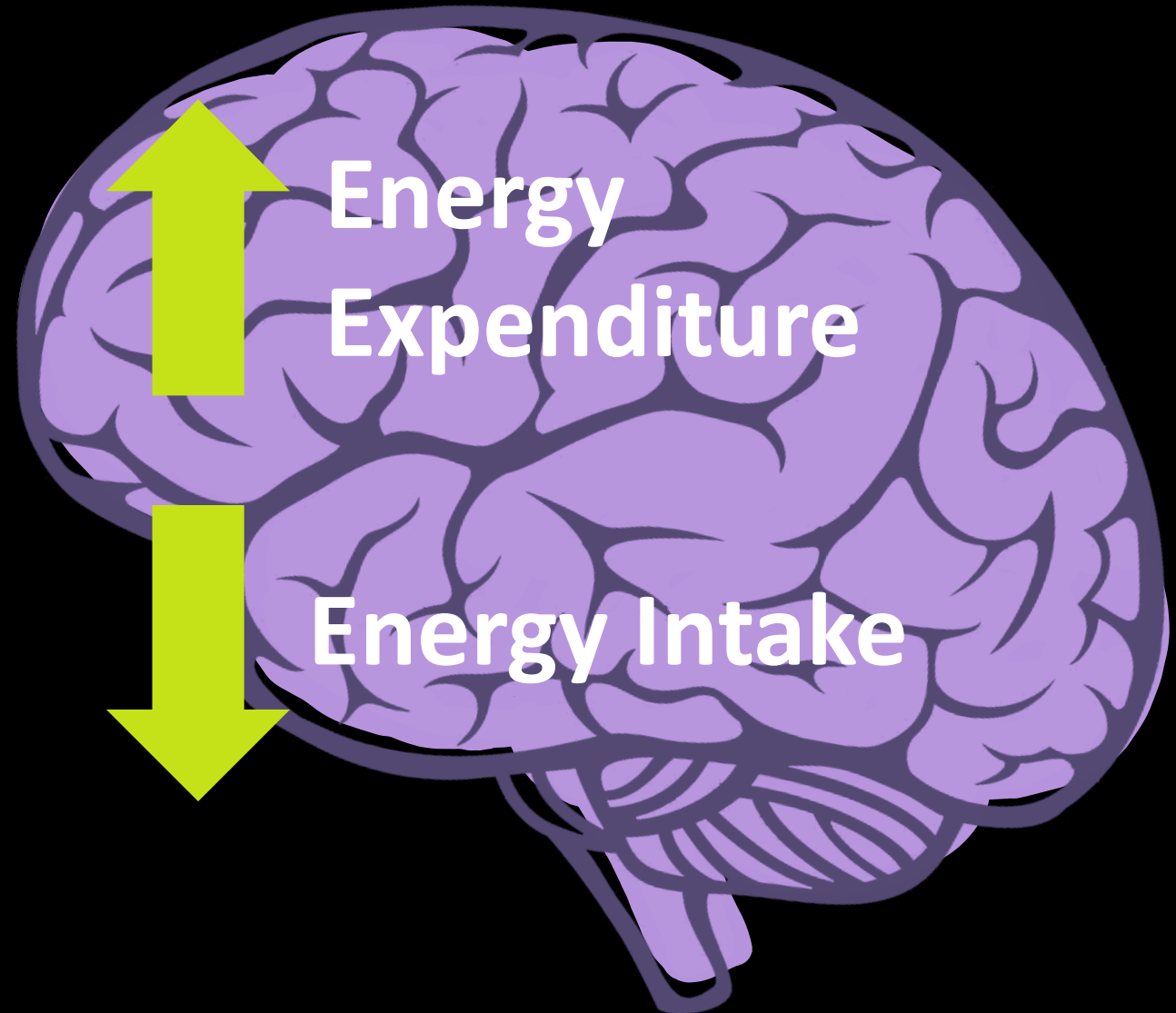
Myokines

Old Brain in a New Society

Evolutionary Perspective

Ancestors

- ❖ Hunter gatherer lifestyle
 - ◆ Travel long distances
- ❖ Limited food supply
- ❖ High competition for food
 - ◆ Competition within species (amongst ourselves) & other animals



Current Predicament

Recent technological advancements



Sedentary (Inactive) Lifestyle



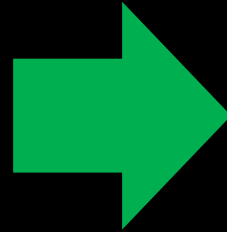
Various Diseases: Metabolic Disease, Type 2 Diabetes, Cardiovascular Disease, neurological disorders

Obesity Epidemic

Sedentary Lifestyle



Excessive Caloric
Intake



Obesity

- ❖ Obesity is a disease that is associated with an increased risk for many detrimental health issues
- ❖ Two out of every five adult Americans are obese
- ❖ Obesity is a leading cause of death and it is preventable
- ❖ The link between T2D & obesity is inflammation

Stress & the Immune System

Immune System & Stress

Stress

- ❖ **In physics:** stress describes the force that puts strain on a physical body
- ❖ A *stressor* is broadly defined as anything that causes the release of stress hormones (glucocorticoids)
- ❖ May be either physiological and/or psychological
- ❖ **Acute stress:** immediate transient stress response

Chronic Stress

- ❖ Prolonged stress which negatively impacts overall health
- ❖ Chronic stress suppresses the immune system
- ❖ Is linked with increase risk for Cardiovascular Disease, depression, anxiety etc

Immune System & Stress

Immune System

- ❖ The body's security system
- ❖ Made up of a network of cells, tissues, and organs that work together to protect the body
- ❖ Produces the inflammatory response

Inflammatory Response

- ❖ Normal levels of inflammation protect the body
- ❖ Too much inflammation has negative effects on the body
- ❖ Inflammation hinders the actions of insulin
- ❖ Obesity exacerbates these conditions

Cytokine

- ❖ Bloodborne chemical messengers that communicate between cells
- ❖ Myriad of cytokines produced and secreted throughout the body
- ❖ Carry out many functions

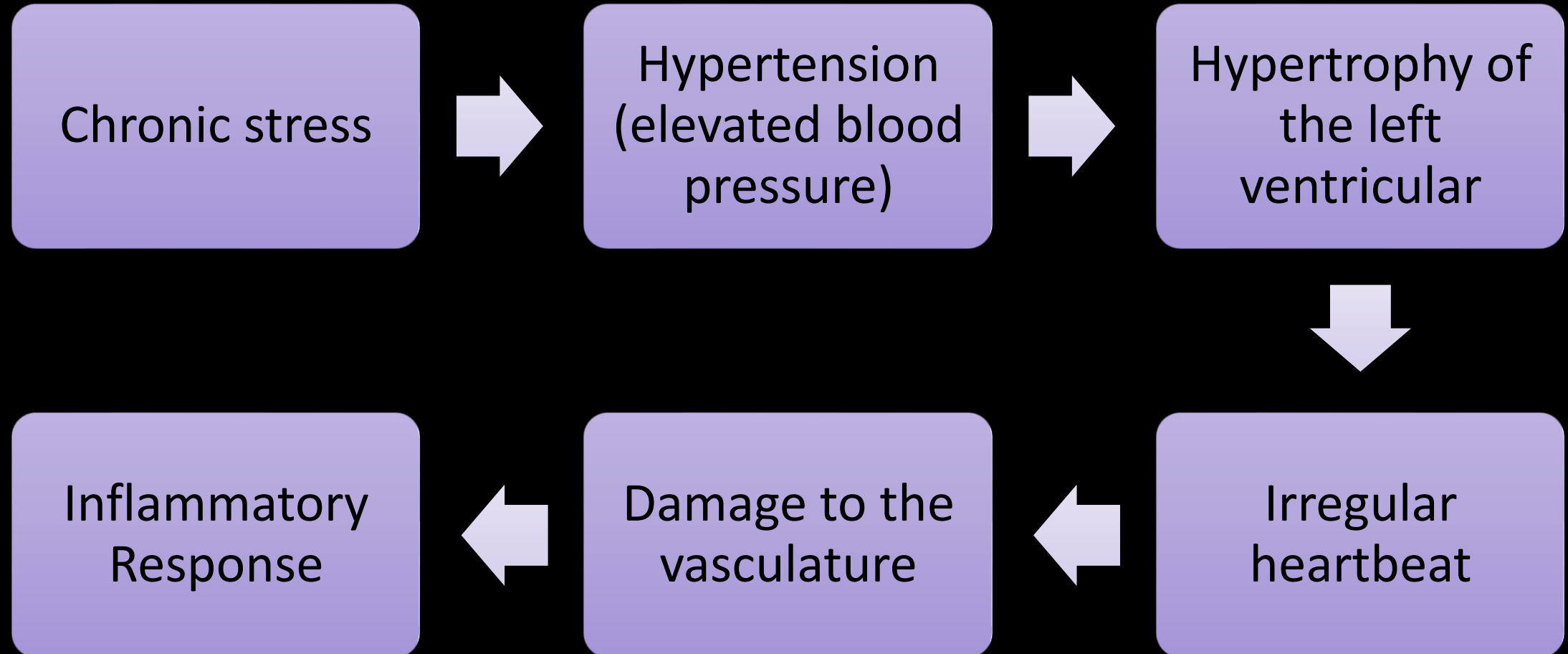
Chronic Stress & Cardiovascular Disease

CVD is the #1 leading cause of death in the USA & the developed world

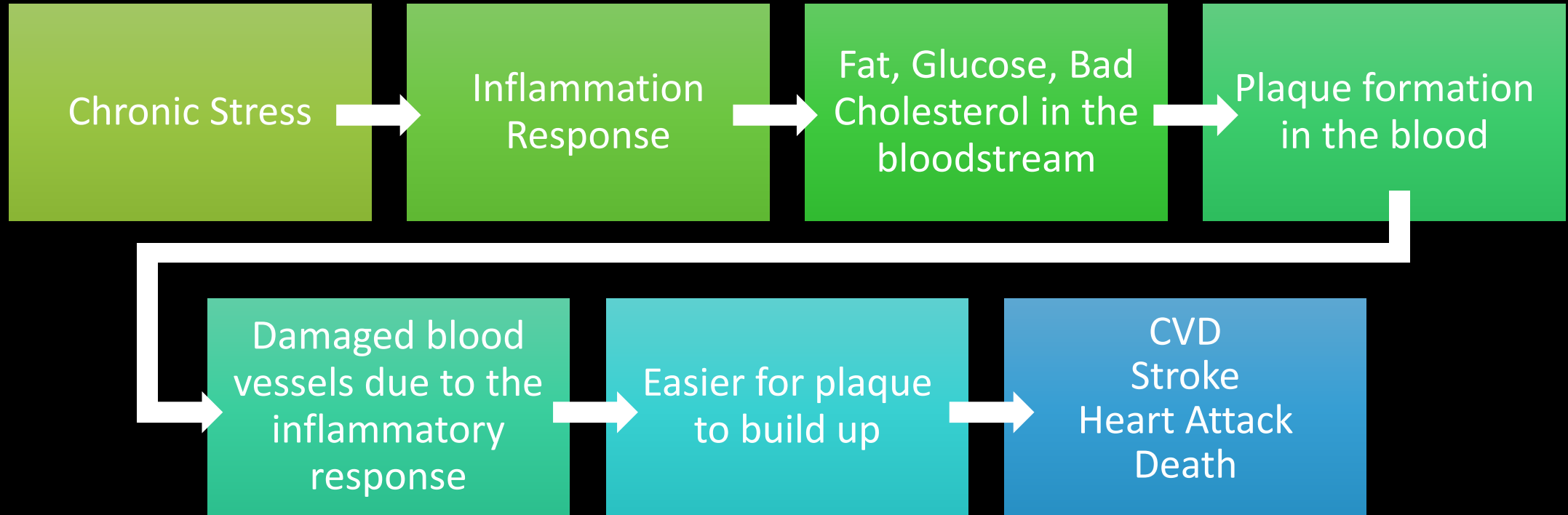
A risk factor of CVD is *chronic stress*

During stress the body mobilizes energy into the bloodstream in the form of fat, glucose (sugar), & bad cholesterol

Chronic Stress & Cardiovascular Disease



Chronic Stress & Cardiovascular Disease



Stress & Metabolic Diseases

Food



Glucose
Amino Acids
Glycerol
Free Fatty Acids



Energy

Glucose

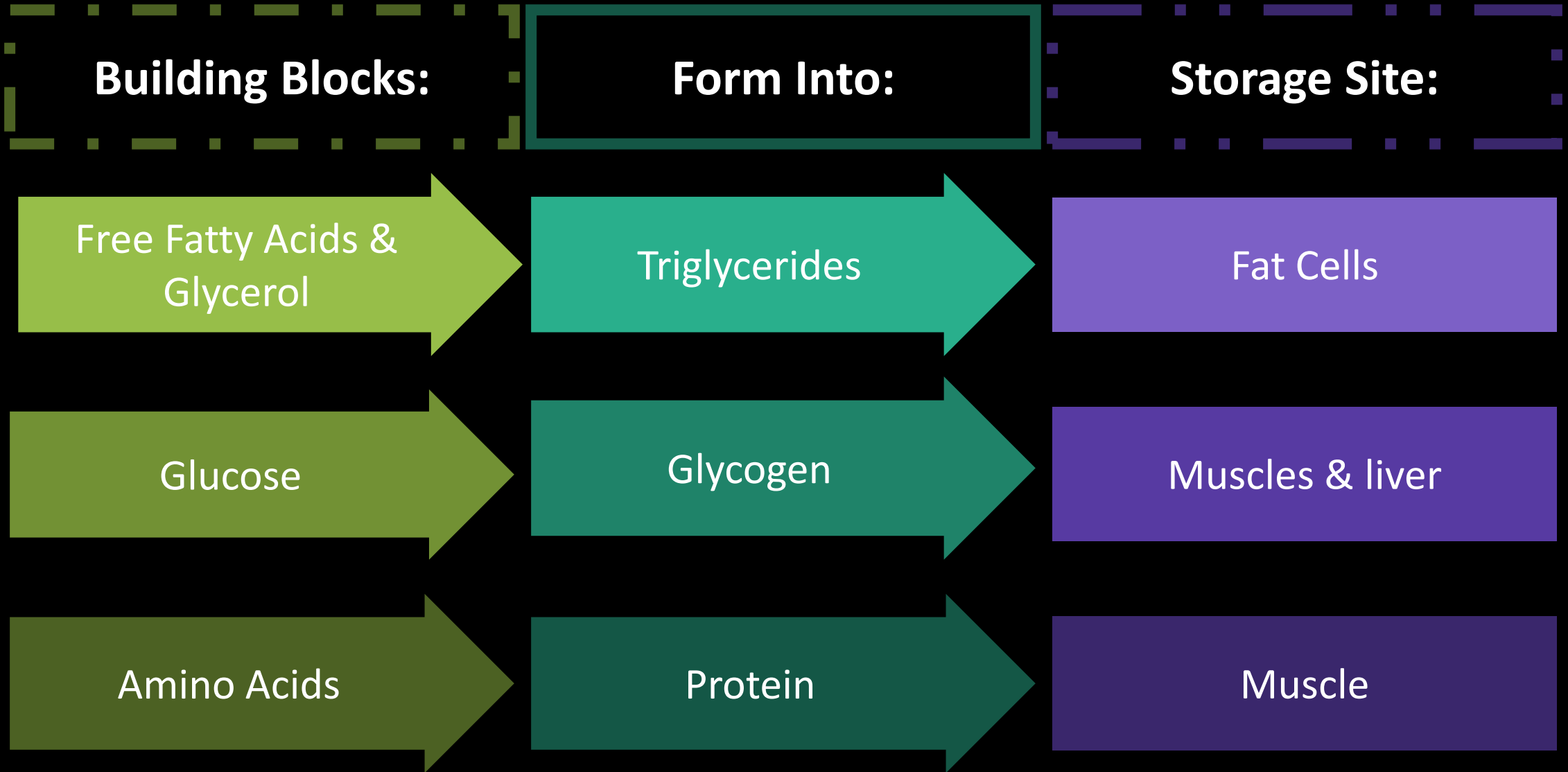
Amino Acids



Glycerol

Free Fatty Acids

Stress & Metabolic Disease



Stress & Metabolic Disease

Insulin

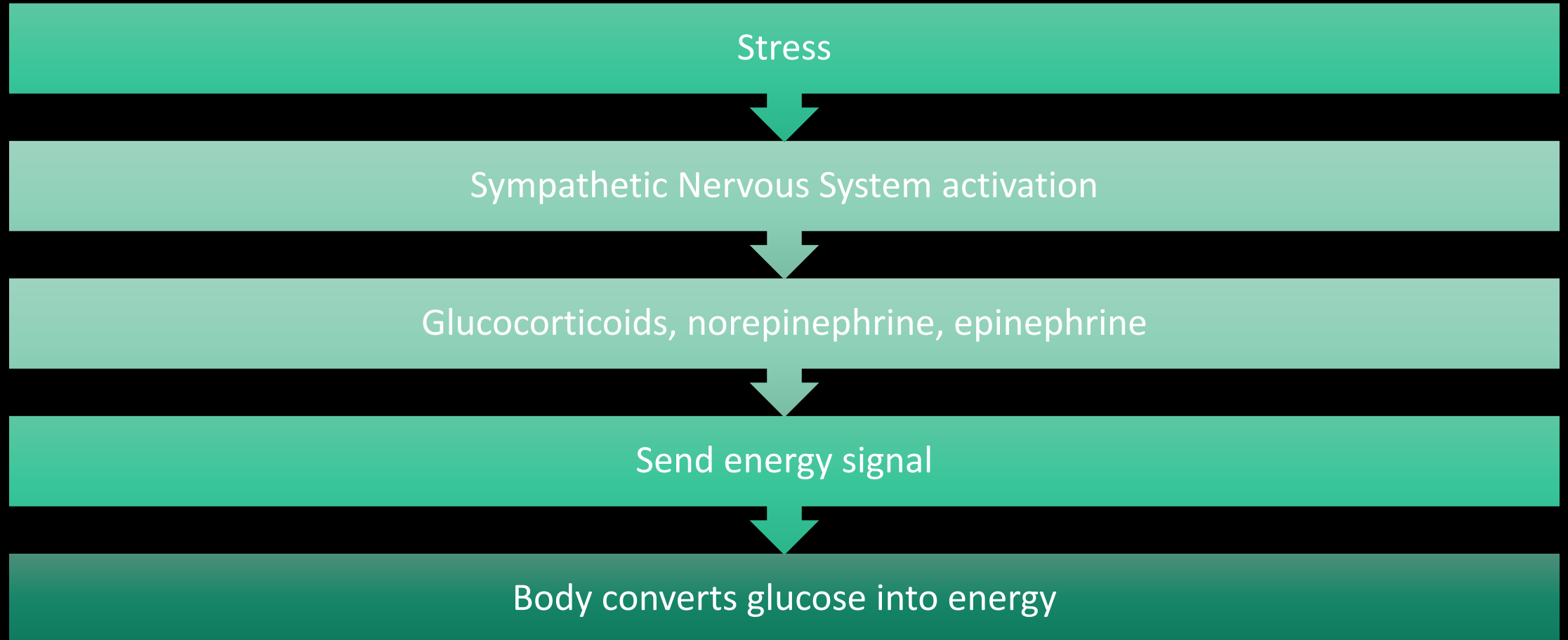
Secreted from the
pancreas

Stimulates the
transport of free
fatty acids into fat
cells

Stimulates
glycogen & protein
synthesis

Important in the
regulation of
cellular glucose
uptake

Stress & Metabolic Disease



Stress & Metabolic Disease

Metabolic Syndrome

- Elevated blood pressure
- Elevated insulin
- Elevated circulating glucose levels (hyperglycemia)
- Insulin resistance

Prolonged Stress promotes insulin resistance (Type 2 diabetes)

- Cells fail to respond to insulin → less glucose uptake
- The body thinks it needs more insulin → pancreas secretes more insulin → leading to further insulin resistance and so on & so forth

Stress & Memory

Long Term Potentiation (LTP)

- ❖ A persistent strengthening of synapses
- ❖ A long lasting increase in signal transmission between two neurons
- ❖ A way in which the brain changes with experience and is thus a proposed mechanism for learning and memory

Long Term Depression (LTD)

- ❖ A long-lasting decrease of synaptic transmission
- ❖ Weakens synaptic connections
- ❖ Function not yet well understood
 - ❖ Thought to be important for memory formation by resetting synaptic changes
 - ❖ Underlying mechanism posited to be involved in the process of forgetting

Chronic Stress & Memory

Stress disrupts LTP in the hippocampus

- Stress → ↑ glucocorticoids → ↓ LTP and ↑ LTD

Stress inhibits the birth of new neurons

- Stress → ↑ glucocorticoids → ↓ neurogenesis

Stress activates the amygdala

- Activation of this pathway causes a disruption of hippocampal function

Prolonged exposure to stress

- Atrophied neuronal projections
- Hippocampal neuronal death

Exercise

Exercise

Skeletal muscle

Muscle

the most abundant organ of the human body, in terms of weight

Roles of the skeletal muscle

Important in energy metabolism

Oxidative metabolism & insulin stimulated glucose uptake

maintenance of posture

power/force of voluntary movement

breathing, thermoregulation

Exercise

Neurobiological Effects of Exercise

- ❖ Reduces anxiety & depression
- ❖ Reduces risk of age-related cognitive impairment & AD
- ❖ Improves social skills & self esteem
- ❖ Improves mood & cognitive abilities
- ❖ Stimulates hippocampal neurogenesis
- ❖ Enhances memory

Types of exercise



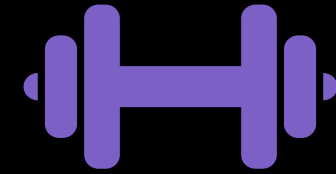
Acute

a single bout of physical activity



Aerobic

Endurance exercise
Jogging, swimming, cycling,
brisk walking



Resistance

Any exercise that strengthens
or builds muscle
Lifting weights, squats, push
ups etc

Myokines

Myokines vs Adipokines

Myokine

- ❖ A type of cytokine with myo simply meaning muscle
- ❖ Cytokine: proteins that are important for cell signaling
- ❖ Exercise causes skeletal muscles to produce and secrete myokines

Adipokine

- ❖ Proinflammatory proteins
- ❖ Secreted from adipose tissue aka “fat” during periods of inactivity
- ❖ Negative effects may be mitigated by myokines

PGC-1 α

In skeletal muscle

- Exerts a detoxifying potential & regulates central functions such as memory & mood

Endurance Exercise

- Increases levels of energy substrates that influence neuronal activity, angiogenesis (formation of blood vessels), and memory formation
- Increases the amino acid glutamine (an essential metabolic fuel), which is important for regulating multiple signaling pathways related to inflammation, cell integrity & metabolism

Acute Exercise

- Increases the production of ATP (via AMPK)
- Promotes glucose transport & fatty acid oxidation

Irisin & FNDC-5

FNDC-5

- Exercise cleaves FNDC-5, a membrane protein, which then secretes irisin
- FNDC-5 overexpression decreases lipid levels in the blood

Irisin

- In the bloodstream, irisin stimulates a process that yields energy for skeletal muscles
- Stimulates glucose uptake via glycogenesis and decreases gluconeogenesis in the liver
- Crosses the BBB & induces the release of BDNF in the hippocampus

Brain Derived Neurotropic Factor: BDNF

Promotes synaptic plasticity involved in learning & memory

Stimulates neurogenesis and promotes overall neuronal survival

Reduces production of neurotoxic peptide (amyloid beta protein seen in Alzheimer's)

Reduces insulin resistance (Insulin resistance leads to T2D & other metabolic disorders)

Protects neurons against both metabolic and oxidative stress

BDNF activity is increased by Aerobic exercise (brisk walking)

Interleukin- 6 (IL-6)

IL (Interleukin) 6: the “prototypical” myokine involved in many of the different effects of myokines

Produced by the contraction of muscles

Functions of IL-6

- Inhibits the production of both TNF alpha & IL-1 beta (proinflammatory cytokines)
- Regulates muscle growth & local muscle metabolism
- Regulates muscle cells glucose uptake and fatty acid oxidation
- Induces breakdown of glycogen & breakdown of lipids

In Summary

Acute Exercise	Irisin	PGC-1α	IL-6
	Regulates energy metabolism	Increases ATP (energy)	Glucose Homeostasis Breaks down FFA
Endurance Exercise	BDNF & PGC-1α	BDNF	Irisin
	Neuroprotection & memory	Reduces insulin resistance	Crosses the BBB to increase BDNF expression

Climb up the steps to better health

Why I choose to take the stairs: The beneficial effects of exercise on the brain and body

By: Sonia Romo

We have long turned away from the hunter-gatherer lifestyles of our ancestors as it is no longer necessary to travel long distances and compete for food. Our ancestors evolved prepared for periods of food scarcity; therefore, *our* brains and *our* bodies evolved to favor lower energy intake and higher energy expenditure. But, why does this matter?

Many Americans are eating more and exercising less which contributes to a cascade of metabolic events that are bad for one's health. Moreover, sedentary lifestyle behaviors are becoming more commonplace in this technologically

Read my blog
post that
summarizes
this lecture!

<https://medium.com/@dopeaminecogs163/why-i-choose-to-take-the-stairs-823b7fc90b21>

“Exercise gives you
endorphins. Endorphins
make you happy.
Happy people just don't
shoot their husbands, they
just don't.”

~ Elle Woods



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