Stress & The Neuroprotective Factors of Exercise

Week 9: Thursday, November 29
Sonia Romo
Today’s Agenda

- Old Brain in a New Society
- Stress and the Immune System
- Stress and CVD
- Stress and Metabolic Syndrome
- Stress and Memory
- 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

Energy Expenditure

Energy Intake
Current Predicament

Recent technological advancements

Sedentary (Inactive) Lifestyle

Various Diseases: Metabolic Disease, Type 2 Diabetes, Cardiovascular Disease, neurological disorders
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 → Hypertension (elevated blood pressure) → Hypertrophy of the left ventricular

Inflammatory Response ← Damage to the vasculature ← Irregular heartbeat
Chronic Stress & Cardiovascular Disease

Chronic Stress

Inflammation Response

Fat, Glucose, Bad Cholesterol in the bloodstream

Plaque formation in the blood

Damaged blood vessels due to the inflammatory response

Easier for plaque to build up

CVD Stroke Heart Attack Death

Death
Stress & Metabolic Diseases

Food → Glucose → Energy
Food → Amino Acids
Food → Glycerol
Food → Free Fatty Acids

Glucose
Amino Acids
Glycerol
Free Fatty Acids
Stress & Metabolic Disease

Building Blocks:
- Free Fatty Acids & Glycerol
- Glucose
- Amino Acids

Form Into:
- Triglycerides
- Glycogen
- Protein

Storage Site:
- Fat Cells
- Muscles & liver
- Muscle
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

1. Stress
2. Sympathetic Nervous System activation
3. Glucocorticoids, norepinephrine, epinephrine
4. Send energy signal
5. Body converts glucose into energy
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 $\rightarrow$ less glucose uptake
- The body thinks it needs more insulin $\rightarrow$ pancreas secretes more insulin $\rightarrow$ 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

<table>
<thead>
<tr>
<th>Effect</th>
<th>Description</th>
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<tbody>
<tr>
<td>Stress disrupts LTP in the hippocampus</td>
<td>Stress → ↑ glucocorticoids → ↓ LTP and ↑ LTD</td>
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<td>Stress inhibits the birth of new neurons</td>
<td>Stress → ↑ glucocorticoids → ↓ neurogenesis</td>
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<td>Stress activates the amygdala</td>
<td>Activation of this pathway causes a disruption of hippocampal function</td>
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<td>Prolonged exposure to stress</td>
<td>Atrophied neuronal projections</td>
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Chronic stress disrupts LTP in the hippocampus, inhibits the birth of new neurons, activates the amygdala, and leads to prolonged exposure to stress, resulting in atrophied neuronal projections and hippocampal neuronal death.
Exercise
Exercise

Skeletal muscle
- the most abundant organ of the human body, in terms of weight
- Roles of the skeletal muscle
  - maintenance of posture
  - power/force of voluntary movement
  - breathing, thermoregulation
- Important in energy metabolism
- Oxidative metabolism & insulin stimulated glucose uptake

Muscle
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-1α

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

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<td>Glucose Homeostasis</td>
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<td>Breaks down FFA</td>
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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
“Exercise gives you endorphins. Endorphins make you happy. Happy people just don't shoot their husbands, they just don’t.”

~ Elle Woods
Sources


