INTRODUCTION TO NEUROLOGICAL DISEASE

LiR – Session #2

PART I: Communication in the Brain

PART II: Hormones and Stress
PART I

LiR – Session #2

Communication in the Brain
Lesson Overview

• By the end of this lecture, you should be able to answer the following questions:
  
  • How do signals travel *within* a neuron?
  • How do signals travel *between* neurons?
  • How do neural circuits work together to produce behaviour?
Life & energy

• A general rule of nature is that if you separate things, or move them out of equilibrium, they will tend to re-equilibrate.
• It doesn’t really matter what type of force is involved. The tendency toward equilibrium applies to the effects of gravity, heat, electricity, and more.
• As things move toward equilibrium, their movement can be used to do work or carry a message.

- If two buckets of water are connected, the water will tend to flow from the fuller bucket to the emptier bucket until both are equal.
- Until you open the barrier, this is merely a difference in potential energy – a potential difference.
Reminder…

• Dendrites receive

• Cell body integrates

• Axon transmits

• Let’s take a closer look at the cell body
Neurons and Batteries

- Neurons are like batteries
  - Instead of poles, neurons maintain an electric charge across their membrane
  - Neuronal membranes have gates that can open and close, allowing the movement of ions (back to equilibrium)

- The tendency of electrons to move represents their ability to do work and is called electric potential (measured in volts)
  - Until the barrier is opened (gates in membrane), there is merely a difference in potential energy across the membrane – a potential difference
Neurons and Batteries

- Voltmeter: measures potential energy
- Battery: +1.5V
- Neuron: -70mV

This is called the neuron’s resting potential (-70mV)

What does it mean that the resting potential of the neuron is negative?
Despite its name (resting potential), the neuron must actually do work to maintain it (using both passive and active mechanisms).

This consumes energy.

When neurons die, this process stops, and ions quickly scatter in order to re-equilibrate (even out).
The discovery of bioelectricity (late 1700s)

Galvani VS Volta

Alessandro Volta replicated and elaborated upon Galvani’s experiments, and identified that it was due to a small electric current created by the metal probes.

Luigi Galvani discovered the connection between electricity and life.
Electrophysiology of a Neuron

- So...the inside of the neuron is negative when compared to the outside
- How does this help it quickly send signals from one end to the other?
- To understand this, we need to take a closer look at the membrane... and think about what nature wants to do with that potential difference across the membrane
- The reason we have a membrane potential at all is because the positive and negative charges are separated **unevenly** by a barrier.
Electrophysiology of a Neuron

- Neuron’s resting potential is -70mV
  - Not ‘firing’, just resting here...
  - In resting state, neuron is polarized
- IF a stimulus causes this potential to rise (move toward 0), this is called a depolarization
- IF a stimulus causes this potential to fall (become more negative, move further from 0), this is called a hyperpolarization

A = ______________________
B = ______________________
Electrophysiology of a Neuron

- If membrane is depolarized to -60mV, it will just return to -70mV
  - Similarly, if membrane is hyperpolarized to -80mV, it will also find its way back to -70mV

- Events like this are happening all the time in neurons

- The magic happens when the stimulus is strong enough to cause the membrane to be depolarized to -55mV

- This change in membrane polarity triggers an **action potential** – a neuron’s way of sending a signal
The Magic Happens at -55mV
The Action Potential

- Before we take a closer look at what happens during an action potential, some things you need to know about them:
  - They are fast
  - They are localized (but spreading)
  - They are all-or-nothing
  - They involve a large reversal of membrane polarity (from -70mV to about +30mV)
The Action Potential: The Players

• Four types of charged particles are involved in creating the resting potential of a neuron
  • $A^{-}$ = negatively charged proteins
  • $K^{+}$ = positively charged potassium ions
  • $Na^{+}$ = positively charged sodium ions
  • $Cl^{-}$ = negatively charged chloride ions
The Action Potential: A Closer Look

• In order for the membrane potential to **change at all** (including maintaining the resting potential of -70mV), ions have to pass through the membrane... Options?

Voltage-gated channels open at specific **voltages**. Sodium channels open at -55mV... Does this sound familiar?
The Action Potential

• Voltage-gated sodium ($Na^+$) channels open at -55mV and close at +30mV

Step 1: Depolarization

a) Threshold reached (-55mV), and $Na^+$ channels open.

b) Positively charged $Na^+$ rushes into the cell. The membrane potential rises from ~-55mV up to +30mV
The Action Potential

• Voltage-gated potassium (K⁺) channels open at +30mV and close at -70mV

Step 2: Repolarization

c) At +30mV, the Na⁺ channel closes and K⁺ (potassium) channel opens

d) K⁺ rushes OUT of the cell. → positive ions leaving, therefore inside of cell is getting more negative; resetting to resting
The Action Potential

- Voltage-gated potassium (K⁺) channels open at +30mV and close at -70mV

Step 3: Hyperpolarization

e) The amount of K⁺ that leaves is slightly excessive, and the cell is more negative than resting – ‘hyperpolarized’

f) Na⁺/K⁺ pumps reset the ion concentrations and things return to resting
The Action Potential

-55mV: Na⁺ channels open

+30mV: Na⁺ channels close; K⁺ channels open

Refractory period – neuron is busy, cannot process other stimuli (absolute = no way, relative = unlikely)
The Action Potential

• How does an action potential move?

• **Depolarization can propagate**, because depolarization in one region can **stimulate adjacent areas to depolarize** as well

• This leads to a domino effect, and this is how action potentials travel down the neuron’s axon
**Action Potentials**

Neuron at rest

Inside of neuron is 70mV less than outside

Cell body integrates:

\[ +\text{VE}: 12\text{mV} + 13\text{mV} = 25\text{mV} \]
\[ -\text{VE}: 2\text{mV} + 8\text{mV} = 10\text{mV} \]

At rest: \(-70\text{mV} + 25\text{mV} - 10\text{mV} = -55\text{mV} \rightarrow \text{GO}!!\)

NT = Glutamate

NT = Glycine

NT = GABA

= Na\(^+\) channel

= K\(^+\) channel
The Action Potential

- Action potentials travel at a speed of 30-120m/s. **Myelinated** axons have a faster rate of conduction.

- Information always flows in the same direction in **neurons**:
  - Dendrites > Cell body > Axon > Axon terminal

- **Action potentials** are fast, directional, and can travel virtually limitless distances.
  - They therefore satisfy our first question: “How do signals travel within a neuron?”
The Action Potential

- Action potentials aren’t very exciting... they are always the same magnitude (A) – all behaviour from this?!

- But, they can alter in **frequency** (B and C)
  - This might help us distinguish between two stimuli

B – omg a bear! XO

C – OMG a BEAR

-55mV
The Synapse

- Next question: How do signals travel between neurons?
- Answer: The **synapse** (*to clasp, G.*)

- There is a small gap between neurons (usually between terminal button of one and dendrite of another)

- So an action potential travels down the axon to the terminal buttons of the neuron... Then what?
  - What happens at the synapse?

- The synapse is the site of **chemical transmission** in the cell
The Synapse

• The chemical synapse is the junction where chemical messengers are released from one neuron (the pre-synaptic neuron) to excite or inhibit the next neuron (the post-synaptic neuron)

• These chemical messengers = neurotransmitters (NTs)

• PNS parallel to neurotransmitters?
  • Hormones in the bloodstream
    • Slower, more distant targets than NTs

• First published scanning electron micrograph of a synapse (1956)
Neurotransmitters

- More than 50 kinds identified
  - More than one NT may be active at a synapse
  - No simple 1:1 relationship between single NT and single behaviour
- 3 principle categories of NTs (small molecules, peptides, transmitter gasses)
  - Small molecules further divided into:
    - Amines: dopamine (DA), norepinephrine (NE), epinephrine (E), serotonin (5-HT)
    - Amino acids: glutamate (Glu), gamma-aminobutyric acid (GABA)
    - Other: Acetylcholine

Identification Criteria

1. Chemical must be synthesized or present in neuron.
2. When released, chemical must produce response in target cell.
3. Same receptor action must be obtained when chemical is experimentally placed on target.
4. There must be a mechanism for removal after chemical's work is done.
The Synapse

• The synapse is where the **electrical** signal is converted to a **chemical** one.

• Each neuron can form synapses with thousands of other neurons.
  - Neuron sending signal = **pre-synaptic neuron**
  - Tiny gap between neurons (~20nm wide) = **synaptic cleft**
  - Neuron receiving signal = **post-synaptic neuron**

• Neurotransmitters are stored in **vesicles**
  - When stimulated by an action potential, the vesicles **fuse** with the pre-synaptic membrane and dump their contents into the **synaptic cleft**
  - NTs travel across the cleft to the post-synaptic membrane
    - Rich in **receptors** which can bind NTs (like locks, NTs = key)
Synaptic Transmission: 4 Steps

1. **Neurotransmitters** are synthesized and stored in the **presynaptic axon terminal**.

2. **Action potentials** stimulate the release of **NTs** into the synaptic cleft.

3. **NTs** bind to **receptors** – specialized proteins embedded into the **post-synaptic membrane**.

4. Receptors are often coupled to **ion channels** that open when bound to a **neurotransmitter**. The influx of ions changes the membrane potential of the **post-synaptic neuron**, causing a **post-synaptic potential (PSP)**.
Excitatory Post-Synaptic Potentials (EPSP)

Post-Synaptic Potentials: 2 Types

Neurotransmitters such as glutamate are classified as “excitatory” because their receptors allow the influx of cations (positive ions like Na⁺, Ca²⁺, K⁺).

Excitatory NTs depolarize the post-synaptic membrane, increasing the likelihood of another action potential.

Inhibitory Post-Synaptic Potentials (IPSP)

Neurotransmitters such as GABA and glycine are classified as “inhibitory” because their receptors allow the influx of anions (negative ions like Cl⁻).

Inhibitory NTs hyperpolarize the post-synaptic membrane, decreasing the likelihood of another action potential.
PSPs and the Action Potential

- Neurons receive hundreds of inputs. On their own, each input has a relatively small impact on the probability of an action potential.
  - The neuron integrates the combined input from all of its synapses.

- Each EPSP moves the neuron a little closer to the threshold potential of -55mv.

- If there is a sufficient number of EPSPs happening close together in time or space, then an action potential is triggered.
  - If EPSPs are too far apart, then the neuron may have time to return to its resting potential, cancelling out the effect of the EPSP.

- In a sense, the hundreds of inputs “vote” on whether an action potential will take place.
Triggering an Action Potential

- Dendrites receive
- Cell body INTEGRATES
- Axon transmits

The PSPs are the ‘signals’ or ‘information’ that the cell body integrates.

Two EPSPs in a row create a larger positive charge (depolarization).

Two IPSPs in a row create a larger negative charge (hyperpolarization).
Neural Signalling

1. PSPs are elicited on the cell body and dendrites (dendrites receive).

2. PSPs are conducted decrementally to the axon hillock (cell body integrates).

3. If the threshold potential (-55mv) is reached at the axon hillock, an action potential is triggered.

4. The action potential is conducted in an “all-or-none” fashion down the axon (axon transmits).

5. The action potential arrives at the terminal buttons and triggers the release of neurotransmitters into the synapse.

NTs bind to receptors on the post-synaptic membrane, which triggers ion channels to open, and….
How do neurotransmitters effect change?

- NTs are ligands for a specific receptor
  - Interaction resembles ‘lock and key’
  - The ligand-receptor interaction is common to many biological processes outside of the brain (e.g. hormones)

- Drugs and poisons often work by exploiting this interaction... how?
Where do the NTs go?

- One more piece to the puzzle...what happens after NTs bind to receptors?
- They must be **inactivated**, or they will continue to work indefinitely

**FOUR ways to deactivate NTs:**
- **1 – Diffusion**: Some of the NT diffuses away from the synaptic cleft
- **2 – Degradation**: Specialized enzymes break NTs down into inactive molecules
- **3 – Reuptake**: Specialized proteins recycle NTs back into the pre-synaptic terminal
- **4 – Glial cells**: Neighbouring glial cells may take up stray NTs

Back to our Questions...

• How do signals travel within a neuron?
  • Electricity – ACTION POTENTIALS

• How do signals travel between neurons?
  • Chemicals – NEUROTRANSMITTERS

• The final question... How do neural circuits work together to create behaviour?
  • We know that the brain and neurotransmission is far more complex than linking a chain of neurons
  • The simplest case = monosynaptic reflex loop

A monosynaptic reflex loop. Information from receptors in the knee are transferred, via a single synapse in the spinal cord, to muscles in the leg. The result is a 1:1 correspondence between stimulus and response. But real human behavior is never so direct...
The final question

- Since synapses can be either excitatory or inhibitory, neurons can control each other’s firing. This allows for the formation of more complex circuits. Messages do not always get passed along, and may involve the coordinated action of >1 neuron.

![Diagram 1](image1.png)


![Diagram 2](image2.png)

Scenario 2: Neuron A active, neuron B silent. Output neuron silent.

![Diagram 3](image3.png)

Scenario 3: Neurons A & B both active. B is cancelled out by A, so the output neuron remains silent.

This scenario considers only two inputs to a single neuron... Neurons can have thousands of inputs... Good thing the cell body integrates, so that we don’t have to!
PART II

LiR – Session #2
Hormones and Stress
Lesson Overview

- **Hormones**
  - Types/Categories
  - Principles of Action
  - Brain Regulation of Hormones
  - Feedback Systems

- **Stress**
  - What is stress?
  - Physiological response to stress
  - Stress Pathways
  - Consequences of Stress
    - Acute
    - Chronic

"The testes acts upon the blood, and the blood acts upon the whole organism."

A.A. Berthold, rooster
testicle expert and
1800s portrait stud
Hormones

THE AVERAGE TEENAGE BRAIN

Pregnancy hormones: the tragedy-maker

I DO NOT

HAVE PMS!

5 Amazing Fruits That Keep Away Hormonal Imbalance
Hormones

- Chemical messengers that are released by one cell group and travel through the bloodstream to act on targets
- Nearly all processes in the body controlled by either:

**THE NERVOUS SYSTEM**

**Synaptic signalling** – chemical release/diffusion across synaptic cleft
  - Fast, point-to-point, local
  - Electrical and chemical signalling

**OR**

**THE ENDOCRINE SYSTEM**

**Hormone signalling** – chemical release/diffusion into bloodstream
  - Slow, long distance, widespread
  - Secreted chemical signalling
Hormones

- Chemical messengers that are released by one cell group and travel through the bloodstream to act on targets

<table>
<thead>
<tr>
<th>Gland Type</th>
<th>Role</th>
<th>Examples</th>
</tr>
</thead>
</table>
| Endocrine  | Releases hormones throughout the body | 1. Testes (T)  
2. Thyroid (T3 and T4)  
3. Adrenal glands (epinephrine) |
| Exocrine   | Uses ducts to secrete fluids outside of the body | 1. Sweat  
2. Lacrimal (tears)  
3. Mammary (milk) |
Endocrine Glands/Hormones

**Hypothalamus**
Makes hormones that control the pituitary gland (also makes ones that are stored in pituitary)

**Pituitary gland**
Produces hormones that regulate many of the other endocrine glands

**Thyroid gland**
Produces *thyroxine*, which regulates metabolism

**Adrenal glands**
Release epinephrine and norepinephrine in response to stress

**Parathyroid glands (4)**
Release *parathyroid hormone*, which regulates level of calcium in the blood

**Pancreas**
Produces *insulin* and *glucagon*, which regulate blood glucose levels

**Ovaries**
Produce *estrogen* (required for development of secondary sex characteristics and eggs) and *progesterone* (prepares uterus for a fertilized egg)

**Testes**
Produce *testosterone*, responsible for sperm production and development of male secondary sex characteristics
Neurons can be Endocrine Glands!

• Called **neuroendocrine cells** in this case

• Release NTs into the bloodstream via **axosecretory synapses**
  • When terminal buttons synapse on blood vessel, and NT is released directly into the bloodstream

• Hypothalamus and pituitary gland are major locus of neuroendocrine integration in the body
  • Hypothalamic-pituitary-adrenal (HPA) axis
  • Hypothalamic-pituitary-thyroid (HPT) axis
  • Hypothalamic-pituitary-gonadal (HPG) axis
Hormones: 5 Principles of Action

Hormones:

1. Act in a gradual fashion
2. Change probability or intensity of a behaviour (not ON/OFF)
3. Have a reciprocal relationship with behaviour
4. May have multiple effects; one hormone may influence multiple behaviours
5. Often show pulsatile pattern of release; are released in specific temporal pattern (developmental, time of day and/or over lifespan)
   Ex. melatonin (diurnal rhythm), follicular stimulating hormone (FSH) (monthly patterns), growth hormone (pulsatile release during day/higher release at night/max levels during puberty)
Hormonal and Neural Signalling

• **Similarities**
  - Neurons and endocrine glands produce and store chemicals (NTs and hormones, respectively) and release them upon stimulation
  - Both bind to receptors to stimulate target cells
  - Some chemicals can act as either hormones or NTs, depending on site of release

<table>
<thead>
<tr>
<th>Example</th>
<th>Role in CNS</th>
<th>Role in PNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>Alertness/arousal</td>
<td>Stress response</td>
</tr>
</tbody>
</table>

• **Differences (neural VS hormonal)**

<table>
<thead>
<tr>
<th>1. Local VS Distant</th>
<th>3. Voluntary VS Involuntary</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Fast VS Slow</td>
<td>4. Precise VS Imprecise</td>
</tr>
</tbody>
</table>
The Brain is Boss

**Hypothalamus** produces neurohormones to stimulate the **Pituitary gland**, which secretes releasing hormones to influence **Target endocrine glands**, which release appropriate hormones into the blood to act on **Target tissues/organs** (and also almost every neuron in the brain!)
The Brain is Boss: Pituitary Gland

- AKA the **master gland**
  - Located at base of brain
  - Connected to hypothalamus via **pituitary stalk**

- Split into 2 parts: anterior and posterior pituitary
  - Anterior connected to hypothalamus via blood vessels
  - Posterior connected to hypothalamus directly by axons from hypothalamic neurons

- Secretes many hormones that affect the function of glands and organs throughout the body
  - Anterior: Releases stimulating hormones (e.g. TSH, ACTH, Prolactin)
  - Posterior: Stores/releases **vasopressin** and **oxytocin** synthesized in hypothalamus
The Brain is Boss: Hypothalamus

- Located at the base of the brain, just above the pituitary
- Nuclei synthesize hormones to either inhibit or stimulate release of hormones from the pituitary
- Called releasing hormones or tropic hormones
  - Ex. Growth hormone releasing hormone (GHRH), thyrotropin-releasing hormone (TRH)
- Also synthesizes oxytocin and vasopressin for direct release from posterior pituitary into bloodstream
- The true master gland??

Kolb & Whishaw. An Introduction to Brain and Behavior, Fourth Edition - Chapter 12
Feedback Systems: Self-regulation

- Endocrine systems can self-regulate via feedback loops
- Feedback involves a cycle where the output loops back to act as input to regulate system

Life examples?
Feedback Systems

- Some systems may have both **positive** and **negative** feedback components.
Hormones: Negative Feedback (General)

- Most hormones are regulated via negative feedback
Hypothalamic-Pituitary-Adrenal (HPA) Axis

• 1 – Stress stimulates hypothalamus to release corticotropin releasing factor/hormone (CRF or CRH, same thing)

• 2 – CRF stimulates ant pit to release adrenocorticotropic hormone (ACTH)

• 3 – ACTH stimulates adrenal glands to release glucocorticoids (e.g. cortisol)

• 4 – Cortisol induces metabolic changes related to stress (e.g. ↑ heart rate)

• 5 – Metabolic changes help us cope with stressor, and signalling to hypothalamus is shut off

What might happen if hypothalamus was not inhibited (i.e. shut off)?
How would you define stress?

- **Stressor**: *Stimuli that challenge the body’s homeostasis and trigger a response*
  - *Physical, psychological; may be real, perceived or imagined*
  - *If a stimulus causes a stress response, it can be considered a stressor*

- Stress response, then, is the body’s response to that challenge

- Stress is an everyday event
  - Minor stressors:
  - Major stressors:
Stress as an Adaptation

• Since most stressors in the wild are short-lived, life-or-death type scenarios, our stress response is actually set up quite well... It accomplishes 2 things:

1) Temporarily puts the brain and body into ‘overdrive’ in order to deal with the stressor.

2) Suspends bodily repair and growth in order to conserve energy.
Stress: The physiological response

• Two pathways:
  • 1 – FAST – Sympatho-adrenomedullary (SAM) Axis
    • This pathway sounds the alarm in response to surprise (i.e. acute) stressors
      • Ex.
  • 2 – SLOW – Hypothalamic-pituitary (HPA) Axis
    • This pathway deals with longer lasting (i.e. chronic) stressors
      • Ex.
Adrenal Glands

- The adrenal glands sit above the kidneys – key for hormonal release during stress response (both pathways)

- **2 for 1!** → Actually 2 glands (well, 4 I guess)

- Inner core = **Medulla** – secretes *epinephrine* (aka adrenaline) and *norepinephrine* (aka noradrenaline)
  - Medulla secretes mostly E (80%) and some NE (20%)

- Outer layer = **Cortex** – secretes cortisol
The FAST pathway – SAM Axis

• Sympatho-adrenomedullary Axis:
• TWO steps:

• 1 – **Hypothalamus** sends neural message to **spinal cord**; hypothalamic neurons synapse onto neurons of the sympathetic nervous system (**SNS**; fight or flight!!)
• 2 – Neurons of the **SNS** send projections to the **adrenal medulla**, which **releases E and NE** into circulation (mostly E)
Epinephrine and norepinephrine are peptide hormones of the catecholamine family.

- Their receptors are called adrenergic receptors.
- They produce diverse physiological effects, including:
  - ↑ Heart rate
  - ↓ Digestion
  - Bronchodilation
  - Vasoconstriction (↑ BP)

**Therapeutic Uses: Why do these work?**

- **EpiPen** – used to treat severe allergic reactions
- **High Blood Pressure** – drugs for hypertension block β-adrenergic receptors
The SLOW pathway – HPA Axis

Hypothalamus releases CRF/CRH, which acts upon the anterior pituitary gland.

Anterior pituitary releases ACTH, which travels through the bloodstream to act upon the adrenal glands.

Adrenals glands release cortisol and epinephrine/norepinephrine.
Shutting Down the Stress Response

- Cortisol is regulated by negative feedback
  - This ensures that CORT levels never stay too high/too long

- Certain brain areas are sensitive to circulating CORT
  - Hypothalamus
  - Anterior Pituitary
  - Hippocampus* (involved in memory)

- With ↓ secretion of releasing factors, what happens next?
  - Adrenal glands stop releasing hormones
  - This **shuts down** the stress response
Stress: The Consequences

**Acute Stress**

- Stress impairs cognition
  - PFC shuts down, older/more primitive regions of the brain take control
  - Does this make sense? Why?
  *Hint: The pre-frontal cortex is involved in planning, concentration, decision making, impulse control (executive functions)*

- Eustress VS distress – stress can be **GOOD**
  - Psychological resilience – ability to cope with stressors improved by regularly overcoming them
    - Especially true in children – highlights importance of setting realistic challenges for children to improve their resilience

---

This is your brain

This is your brain on drugs - STRESS

PFC

Dopamine

Norepinephrine

The Yerkes-Dodson law

Performance

low

medium

Arousal

high

The eternal struggle.

Getting stuff from here

To here.
Stress: The Consequences

Chronic Stress

• In the wild, stressors are short-lived (get away...or not)
• It’s OK to temporarily suspend tasks like growth, tissue repair, immunity – but damage ensues when these tasks are suspended for long periods of time

<table>
<thead>
<tr>
<th>PREDICTABLE</th>
<th>ACUTE</th>
<th>CHRONIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Which type of stressor do you think is the most damaging?
Chronic Stress: Consequences

- Changes in HPA axis
  - Changes in basal and stress-induced levels of GCs
  - Increased CRH expression
  - Hypertrophy of adrenal cortex (where CORT is made)
  - ↓ GRs in PFC and hippocampus – less opportunity for
    - *Overall, a greater capacity to mount a stress response*

- Hippocampal changes
  - ↓ spine density and # dendrites
  - ↓ neurogenesis in hippocampus
  - Impaired negative feedback (hence changes in HPA axis)
Contrasting Acute and Chronic Stress

• While acute stress sharpens cognition, chronic stress impairs it (and can cause neuronal damage and death)
• While acute stress mobilizes energy, chronic stress results in chronic fatigue

Take-home message: While acute stress keeps us healthy, chronic stress is damaging.