the hypothalamus
Types of behavior

• Unconscious reflexes and voluntary movements

Voluntary movement—motivation

• Driving force on behavior
  • Analogy: like ionic driving force, motivation depends on many factors
  • Probability and direction of behavior
  • Vary with the driving force needed to perform the behavior

Patterns of communication in the nervous system:

Point to point: restricted synaptic activation of target cells and signals of brief duration.
Patterns of communication in the nervous system:

Neurons of the secretory hypothalamus release hormones directly into the bloodstream.
Patterns of communication in the nervous system:

Networks of interconnected neurons of the Autonomic Nervous System work together to activate tissues all over the body.

The ANS simultaneously controls the responses of many internal organs, blood vessels and glands.
Diffuse modulatory systems extend their reach with widely divergent axonal projections.
The Secretory Hypothalamus

- Hypothalamus integrates somatic and visceral responses.
- Hypothalamus has enormous influence on the brain and body.
- A lesion in the hypothalamus can produce significant damage.

Hypothalamus sits below the thalamus along the walls of the 3rd ventricle.
• Three components of nervous system with great reach of influences:
  • Secretory hypothalamus (all over the body)
  • Autonomic nervous system (all over the body)
  • Diffuse modulatory systems (all over the brain)

• At detailed level
  • Each system performs different functions.

• At general level
  • All work maintain brain homeostasis.
The Hypothalamus, Homeostasis, and Motivated Behavior

• Homeostasis
  • Maintains internal environment within a narrow physiological range

• Role of hypothalamus
  • Regulates homeostasis

• Three components of neuronal response
  • Humoral response
  • Visceromotor response
  • Somatic motor response
The Hypothalamus, Homeostasis, and Motivated Behavior

• Response when body is cold
  • Body shivers, blood shunted away from the body surface, urine production inhibited, body fat reserves—mobilized

• Lateral hypothalamus
  • Initiates motivation to actively seek or generate warmth—maintain homeostasis
Homeostasis: is the regulatory process that maintains the body’s physiological needs.

Example: Temperature Regulation
- The hypothalamus has temperature sensitive cells.
  - The hypothalamus orchestrates the body to shiver, turn blue and get goose bumps when cold and turn red and sweat when you are hot.
Temperature Regulation

• Cells fine-tuned for constant temperature—37°C (98.6°F)
• Neurons for temperature homeostasis
  • Clustered in anterior hypothalamus
  • Humoral and visceromotor responses
    • Neurons in the medial preoptic area of the hypothalamus
• Somatic motor (behavioral) responses
  • Neurons of lateral hypothalamic area
Temperature Regulation—(cont.)

• Process during a fall in temperature

  TSH released by anterior pituitary $\rightarrow$ TSH stimulates release of thyroxin from thyroid gland $\rightarrow$ Increase in cellular metabolism

  • Visceromotor response: constricted blood vessels in the skin
  • Involuntary somatic motor responses
    • Shivering, seeking warmth
  • Rise in temperature: metabolism slowed by reducing TSH release, somatic responses

# Temperature Regulation

## Table 16.1 Hypothalamic Responses to Stimuli That Motivate Behavior

<table>
<thead>
<tr>
<th>Bloodborne Stimulus</th>
<th>Site of Transduction</th>
<th>Humoral Response</th>
<th>Visceromotor Response</th>
<th>Somatic Motor Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating signals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↓ Leptin</td>
<td>Arcuate nucleus</td>
<td>↓ ACTH</td>
<td>↑ Parasympathetic activity</td>
<td>Feeding</td>
</tr>
<tr>
<td>↓ Insulin</td>
<td>Arcuate nucleus</td>
<td>↓ ACTH</td>
<td>↑ Parasympathetic activity</td>
<td>Feeding</td>
</tr>
<tr>
<td>Drinking signals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ Angiotensin II</td>
<td>Subfornical organ</td>
<td>↑ Vasopressin</td>
<td>↑ Sympathetic activity</td>
<td>Drinking</td>
</tr>
<tr>
<td>↑ Blood tonicity</td>
<td>OVLT</td>
<td>↑ Vasopressin</td>
<td></td>
<td>Drinking</td>
</tr>
<tr>
<td>Thermal signals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ Temperature</td>
<td>Medial preoptic area</td>
<td>↓ TSH</td>
<td>↑ Parasympathetic activity</td>
<td>Sweating, seeking cold</td>
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<td>↓ Temperature</td>
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<td>↑ TSH</td>
<td>↑ Sympathetic activity</td>
<td>Shivering, seeking warmth</td>
</tr>
</tbody>
</table>

The 3 Functional Zones of the Hypothalamus

LATERAL, MEDIAL AND PERIVENTRICULAR
The cells in the periventricular zone are adjacent to the 3rd ventricle.
Magnocellular cells secrete oxytocin and vasopressin directly into the capillaries of the posterior lobe.

The magnocellular neurosecretory neurons, extend axons down towards the stalk of the posterior lobe of the pituitary.
Love, Lactation, Trust, & Bonding

Vasopressin acts on the kidney as an anti-diuretic. When the body is deprived of water, the blood volume decreases and blood salt concentration increases. There are salt sensitive cells in the hypothalamus.
Other Motivated Behaviors: Drinking

- Pathways triggering volumetric thirst
- Hypovolemia: decrease in blood volume
Drinking: Pathway Triggering Osmotic Thirst

• Hypertonicity: increased concentration of dissolved substances in blood (solutions)
Drinking: Role of Vasopressin

- Vasopressin—antidiuretic hormone, or ADH
  - Acts on kidneys to increase water retention
  - Inhibits urine production
- Loss of vasopressin-secreting neurons of hypothalamus
  - Causes diabetes insipidus
    - Strong motivation to drink water

Image: https://www.medicalnewstoday.com/articles/312628.php
Kidney drives your thirst.

1. Lowered blood volume
2. Kidney secretes renin into blood
3. Renin promotes synthesis of angiotensin II
4. Angiotensin II excites neurons in the subfornical organ
5. Subfornical neurons stimulate the hypothalamus to release vasopressin (ADH)
6. Feeling of thirst
Kidney drives your thirst.

1. Lowered blood volume
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Diagram:
- Subfornical organ
- Hypothalamus
- Pituitary
- Angiotensin II
- Blood vessels, kidney
- ADH
- Angiotensin I
- Renin
- Angiotensinogen
- Lowered blood pressure
- Kidney
- Liver
Regulation of plasma volume - ADH

Thirst

Plasma volume
Plasma osmolality

Osmotic pressure

Detected by osmoreceptors in _________ is released

Plasma volume ________ reabsorption Urine
Hypothalamus is the Master Gland of the Endocrine System

- Controlled by parvocellular neurosecretory cells
  - Secrete hypophysiotropic hormones
  - Hypothalamo-pituitary portal circulation
    - Pituitary cells secrete or stop secreting hormones.
Secretory Hypothalamus controls the Anterior Pituitary

The cells of the anterior lobe synthesize and secrete a wide range of hormones that regulate secretions from other glands throughout the body.


Image: https://me-pedia.org/wiki/File:Pituitary_diagram.jpg
<table>
<thead>
<tr>
<th>Hormone</th>
<th>Target</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicle-stimulating hormone (FSH)</td>
<td>Gonads</td>
<td>Ovulation, spermatogenesis</td>
</tr>
<tr>
<td>Luteinizing hormone (LH)</td>
<td>Gonads</td>
<td>Ovarian and sperm maturation</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone (TSH); also called thyrotropin</td>
<td>Thyroid</td>
<td>Thyroxin secretion (increases metabolic rate)</td>
</tr>
<tr>
<td>Adrenocorticotropic hormone (ACTH); also called corticotropin</td>
<td>Adrenal cortex</td>
<td>Cortisol secretion (mobilizes energy stores, inhibits immune system, other actions)</td>
</tr>
<tr>
<td>Growth hormone (GH)</td>
<td>All cells</td>
<td>Stimulation of protein synthesis</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Mammary glands</td>
<td>Growth and milk secretion</td>
</tr>
</tbody>
</table>

TABLE 15.1 **Hormones of the Anterior Pituitary**
Hypothalamus communicates with the anterior lobe of the pituitary gland by:

- Neurons secrete hypophysiotropic hormones
- Into the bed at the floor of the III ventricle
- The tiny blood vessels run down into the stalk of the pituitary and branch into the anterior lobe.
- The network of blood vessels is called the hypothalamo-pituitary portal circulation
- Hormones bind to the receptors on the cells in the pituitary
- The activation of the receptors control the hormone release activity.
Neurons secrete hypophysiotropic hormones. They travel into the bed at the floor of the III ventricle. The tiny blood vessels run down into the stalk of the pituitary and branch into the anterior lobe. The network of blood vessels is called the hypothalamo-pituitary portal circulation. Hormones bind to the receptors on the cells in the pituitary. The activation of the receptors controls the hormone release activity.
To stress or not stress – it’s up to the parvocellular neurosecretory cells.

CRH (corticotropin releasing hormone)
ACTH (adrenocorticotropic hormone)
BBB (blood brain barrier)
Stress Response

- Periventricular hypothalamus secretes CRH into portal circulation.
- ACTH (adrenocorticotropic hormone) released into circulation
- ACTH stimulates cortisol release from adrenal cortex.
- Cortisol inhibits CRH release
Recall:
Divisions of Autonomic Nervous System

Sympathetic division: “fight or flight”
- Increased heart rate and blood pressure
- Depressed digestive function
- Mobilized glucose reserves

Parasympathetic division: “rest and digest”
- Slower heart rate, fall in blood pressure
- Increased digestive functions
- Stop sweating
Recall:
ANS Circuits versus Somatic Motor System
Effector organs:
- Cardiac muscle
- Smooth muscle
- Glands
- Adipose tissue
Sympathetic and Parasympathetic Divisions
Mammillary Bodies

Parasympathetic

Anterior Hypothalamus

Pituitary

Sympathetic
Your gut, your second brain.

image: https://exploringyourmind.com/enteric-nervous-system-second-brain/
The Enteric Division

- Location: lining of esophagus, stomach, intestines, pancreas, and gallbladder
- Two complicated networks: myenteric (Auerbach's) plexus and submucous (Meissner's) plexus
- Function: control physiological processes involved in transport, digestion of food
- Input indirectly from brain via axons of the sympathetic and parasympathetic divisions

Central Control of the ANS

Connections for autonomic control

- Periventricular zone connections to brain stem and spinal cord nuclei
- Nucleus of solitary tract

Function of solitary nucleus

- Integrates sensory information from internal organs and coordinates output to autonomic brain stem nuclei
Autonomic Neurotransmitters
The peripheral nervous system uses two neurotransmitters:
1. **Acetylcholine** is the most common.
2. **Norepinephrine** the other neurotransmitter.

(a) Sympathetic nervous system

Image: http://droualb.faculty.mjc.edu/Course%20Materials/Physiology%20101/Chapter%20Notes/Fall%202007/chapter_11%20Fall%202007.htm
(b) Parasympathetic nervous system
The Noradrenergic Locus Coeruleus

Norepinephrine system

- Neocortex
- Thalamus
- Hypothalamus
- Temporal lobe
- Locus coeruleus
- Cerebellum
- To spinal cord
Path: Axons innervate cerebral cortex, thalamus, hypothalamus, olfactory bulb, cerebellum, midbrain, and spinal cord.

Function: regulation of attention, arousal, sleep–wake cycles, learning and memory, anxiety and pain, mood, brain metabolism

Activation: new, unexpected, nonpainful sensory stimuli
Neurotransmitters and the pharmacology of autonomic function

• ANS better understood than the CNS—e.g., drug mechanisms influencing synaptic transmission

Preganglionic neurotransmitters

• ACh binds to nAChR, evokes fast EPSP.
• Ganglionic ACh activates mAChR, causes slow EPSPs and IPSPs.
• Some preganglionic terminals release NPY, VIP—trigger small EPSPs.
Postganglionic Neurotransmitters

- **Parasympathetic: release Ach**
  - Local effect

- **Sympathetic: most release NE**
  - Far-reaching effects

- **Parasympathomimetic**: mimic or promote muscarinic actions of ACh or inhibit actions of NE

- **Sympathomimetic**: mimic or promote NE actions or inhibit muscarinic actions of ACh
Loading and Emptying the Body's Energy Reserves

(a) Anabolism during the prandial state

(b) Catabolism during the postabsorptive state

Energy balance

(a) Intake = expenditure  
Body fat: Normal

(b) Intake > expenditure  
Body fat: Obesity

(c) Intake < expenditure  
Body fat: Starvation

Body Fat and Food Consumption

- Lipostatic hypothesis
- Experiments with parabiosis
- Leptin
  - Regulates body mass
    - Decreases appetite
    - Increases energy expenditure
- Leptin depletion
  - Incites adaptive responses to fight starvation

---

Energy Balance

- Prandial state— anabolism: energy storage as glycogen and triglycerides

- Postabsorptive state— catabolism: breaking down complex macromolecules for energy
The Hypothalamus and Feeding

- Anorexia from lateral hypothalamic syndrome
- Obesity from ventromedial hypothalamic syndrome
- Both related to leptin signaling
Arcuate nucleus of hypothalamus important for the control of feeding.
Response to Elevated Leptin Levels

- Activation of arcuate neurons that release αMSH and CART peptides
  - Anorectic peptides—diminish appetite
- Project to regions that orchestrate coordinated response of humoral, visceromotor, and somatic responses
  - Paraventricular nucleus (humoral response)
  - Intermediolateral gray matter of spinal cord
  - Lateral hypothalamus
Response to Decreased Leptin Levels

Activation of arcuate neurons that release NPY and AgRP

Effects on energy balance: opposite the effects of αMSH and CART

Orexigenic peptides—increase appetite

NPY and AgRP inhibit secretion of TSH and ACTH
Activate parasympathetic division of ANS
Stimulate feeding behavior
Response to Decreased Leptin Levels

Inhibit secretion of hypophysiotropic hormones controlling ACTH and TSH

Stimulate feeding behavior

NPY/AgRP neurons of arcuate nucleus

Lateral hypothalamic area

Paraventricular nucleus

Third ventricle
Control of Feeding by Lateral Hypothalamic Peptides

- LH neurons stimulating feeding behavior contain:
  - Melanin-concentrating hormone (MCH)
    - Widespread connections in the brain
    - Prolongs consumption
  - Orexin
    - Also with widespread cortical connections
    - Promotes meal initiation
Summary of Responses to Increased and Decreased Adiposity

<table>
<thead>
<tr>
<th></th>
<th>Fat</th>
<th>Lean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood leptin level</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>αMSH/CART neuron activity</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>NPY/AgRP neuron activity</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>TSH and ACTH release</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Sympathetic NS activity</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Parasympathetic NS activity</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Feeding behavior</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

- Arcuate nucleus response
- Humoral response
- Visceromotor response
- Somatic motor response
Competition for Activation of the MC4 Receptor

Model for Short-Term Regulation of Feeding

Three phases: cephalic, gastric, substrate
• Cephalic: hunger
  • Ghrelin released when stomach is empty
  • Activates NPY/AgRP-containing neurons in arcuate nucleus
  • Removal of ghrelin-secreting cells of stomach thought to cause loss of appetite

Image: https://www.olyaschmidt.com/hangry-printable/
Model for Short-Term Regulation of Feeding

- Gastric: feeling full
  - Gastric distension signals brain via vagus nerve.
  - Works synergistically with CCK released in intestines in response to certain foods
  - Insulin also released by β cells of the pancreas—important in anabolism
• Changes in blood insulin levels before, during, and after a meal
• Highest during substrate phase
The Diffuse Modulatory Systems of the Brain

• Anatomy and functions differ:
  • Four systems with common principles
    • Small set of neurons at core
    • Neurons arise from brain stem.
    • One neuron influences many others.
  • Synapses release transmitter molecules into extracellular fluid.
• Reinforcement and reward
  • Liking: hedonic
  • Wanting: drive reduction
• Electrical self-stimulation experiments—identify brain sites of reinforcement
• Effective sites for self-stimulation
  • Trajectory of dopaminergic axons in the ventral tegmental area projecting to the forebrain
• Drugs that block dopamine receptors: reduce self-stimulation
Dopaminergic Substantia Nigra and Ventral Tegmental Area
Axons project to the striatum.
Facilitates the initiation of voluntary movements (degeneration causes Parkinson’s disease)

Innervates circumscribed region of telencephalon

• Mesocorticolimbic dopamine system: dopaminergic projection from midbrain

The Cholinergic Diffuse Modulatory Systems
Cholinergic System

**Basal forebrain complex**
- Core of telencephalon, medial and ventral to basal ganglia
- Function: mostly unknown, participates in learning and memory

**Pontomesencephalotegmental complex**
- Utilizes ACh
- Function: regulates excitability of thalamic sensory relay nuclei
Stimulant Drug Action on Catecholamine Axon Terminal

- Stimulants: block catecholamine reuptake
  - Cocaine targets DA reuptake.
  - Amphetamine blocks NE and DA reuptake and stimulates DA release.
  - Alpha-methyltyrosine will block the effects of cocaine or amphetamine
Mesocorticolimbic Dopamine System
The Role of Dopamine in Motivation

Former belief: dopamine projection served hedonic reward

New understanding

Dopamine-depleted animals “like” food but do not “want” food.
Lack motivation to seek food but enjoy it when available

Stimulation of the dopamine axons

Produces craving for food without increasing the hedonic impact
The Serotonergic Raphe Nuclei
Serotonergic system

Path: innervate many of the same areas as noradrenergic system

Function: together with noradrenergic system, comprise the ascending reticular activating system

Particularly involved in sleep–wake cycles, mood
Other transmitters involved in coordination

Raphe Nuclei

Most active during wakefulness, when aroused and active
Changes in Hypothalamic Serotonin Levels Before and During a Meal

- Low in postabsorptive period
- Rise in anticipation of food
- Spike during meal
  - Mood elevation—rise in blood tryptophan and brain serotonin
• Serotonin, food, and mood
  • Drugs that elevate serotonin suppress appetite.
    • Example: dexfenfluramine (Redux)

• Disorders in serotonin regulation: anorexia nervosa, bulimia nervosa—both often accompanied by depression

• Treatment
  • Antidepressant drugs that elevate brain serotonin levels
    • Example: fluoxetine (Prozac)
Drugs and the Diffuse Modulatory Systems

Psychoactive drugs act on CNS.

Interfere with chemical synaptic transmission

Many drugs of abuse act on modulatory systems.

LSD, *Psilocybe* mushrooms, and peyote are close to the structure of serotonin.

Cocaine and amphetamine affect dopaminergic and noradrenergic systems - sympathomimetic
Concluding Remarks

Overview of motor systems
- The “how” questions of behavior
  - Example: How is movement initiated?

Overview of motivation systems
- The “why” questions of behavior
  - Example: Why do we drink when dehydrated?

Important discovery of neural basis for feeding behavior
- Allows us to frame new questions that will impact how we view our own behaviors