Nervous Systems

Chen, J. H., 030106

- Human nervous system might be the most intricately organized aggregate on Earth - over 50 million nerve cells in one cubic centimeter: Each of which may communicate with thousands of other neurons in information-processing networks that make the most elaborate computer look primitive.

- Three main differences in the roles of the nervous and endocrine systems.
  1. The nervous system reacts much more quickly:
     - Nervous system: >100 m/sec.
     - Endocrine system: several minutes.
  2. The nervous system is of **pinpoint** control:
     - Nerve cells transmit signals directly to individual target cells.
     - Endocrine dispatches its messages to target cells via the bloodstream: Hormones may reach all parts of the body, but only certain types of cells, the **target cell**s, are equipped to respond.
  3. The nervous system has an incomparable structural complexity that enables it to integrate more kinds of information and to elicit a broader range of responses than the endocrine system.

An Overview of Nervous Systems

Nervous systems perform the three overlapping functions of sensory input, integration, and motor output

- **Central nervous system** (**CNS**): **brain** and **spinal cord**.
- **Peripheral nervous system** (**PNS**): communication between the central nervous system and the rest of the body.

Networks of neurons with intricate connections from nervous systems

- **Neuron**s: The functional units of the nervous system.
  1. Relatively large **cell body**.
  2. Fiber like extensions increase the ability of the cells to conduct messages
     - **Dendrite**s are numerous and short fibers, which increase the surface area of the receiving end of the neuron - convey signals toward the cell body.
     - **Axon**: usually a single and very long fiber, which extends from **axon hillock**, can conduct messages away from the cell body.
       - The axons may have branched ends, **synaptic terminal**s.
     - **Synapse**: the site of contact between a synaptic terminal and a target cell.
       - Neurotransmitters release from the **presynaptic** cell (transmitting cell) to **postsynaptic** cell (receiving cell)

<u>A simple nerve circuit – the reflex arc</u>

- **Sensory neuron**s transmit information about the external and internal environments from sensory receptors to the central nervous system.
- **Motor neuron**s convey impulses from brain or other processing center of the nervous system to effector cells, such as muscle cells or gland cells.
- **Interneuron**s located within the central nervous system integrate sensory input and motor output of the nervous system.
- Neurons are arranged in circuits made of two or more functional types:
  - **Reflex**: a simple automatic nervous (sensory/motor) response
    - **Knee-jerk reflex**: more than one sensory/motor circuits are involved.
- **Ganglion (Ganglia)**: a cluster of nerve cell bodies in the PNS.
- **Nuclei**: Similar functional clusters in the brain.

Type of nerve circuits

- Neurons are arranged in circuits to carry information along specific pathways: **convergent circuit**, **divergent circuit**, or **reverberating circuit**.

Supporting Cells (Glia):

- Not for nerve conduction, but for protection, and insulation.
- **Glial cell**s (glue cells): the supporting cells in the central nervous system.
- **Astrocyte**s line the capillaries in the brain to form the **blood-brain barrier**.
- **Myelination**: **Schwann cell**s (in many vertebrate axons of the PNS) or **oligodendrocyte**s (in CNS) grow around axons in such a way that their plasma membranes form many concentric layers - **myelin sheath**.
  - The lipid membrane is electrical insulation.
  - **Multiple sclerosis**: myelin sheaths gradually deteriorate and progressive loss of coordination results.

The Nature of Nerve Signals

Every cell has a voltage, or membrane potential, across its plasma membrane

- All living cells have a charge difference across their plasma membranes - **membrane potential**.

Measuring membrane potentials

- The membrane potential in animal cell is **-50 ~ -100 mV**: the minus sign indicates that the inside of the cell is negative compared to the outside.
- **Resting potential**: the membrane potential of an unexcited cell (in resting state) is around **-70 mV**.

How a cell maintain a membrane potential

- **Membrane potential** is due to differences in ionic composition of the solutions on opposite sides of the membrane and to the selective permeability of the membrane to these ions.
  - Inside cells: cation - potassium (K^+); anion - proteins, a.a., sulfate, and phosphate, etc.
  - Outside cells: cation - sodium (Na^+); anion - chloride (Cl^-)
  - Most cells, including neurons, have much greater permeability to K^+ than to Na^+.
  - Because the internal anions are primarily large organic molecules, they cannot cross the membrane and thus are a pool of internal negative charge that remain in the cell.
  - **Sodium-potassium pump**s are ATP-driven proteins, which can transport Na^+ out and K^+ into the cells to maintain the gradient of Na^+ and K^+.

Changes in the membrane potential of a neuron give rise to nerve impulses

- Chemical-gated ion channels and voltage-gated ion channels: Na^+ and K^+

Graded potentials: hyperpolarization and depolarization

- **Graded potential**s: the membrane potential changes, which last only about a millisecond is proportional to the strength of the stimulus.
- **Hyperpolarization**: K^+ channels were opened (**efflux of K^+**) to drop membrane potential from -70 mV to -90 mV.
- **Depolarization**: Na^+ channels were opened (**influx of Na^+**) to raise membrane potential from -70 mV to -50 mV.

The action potential: all or nothing depolarization

- **Threshold potential**: a minimum depolarization to achieve action potential.
  - Many neurons have threshold of about -50 mV.
- **Action potential** most generated at the **axon hillock**, is due to ion fluxes through specific **voltage-gated ion channel**s in the membrane.
  - The voltage change corresponding to the action spike is of the same magnitude each time, regardless of the nature or strength of the stimulus.
  1. Resting stage:
  2. Depolarizing phase (from - 70 mV to near O mV): Na^+ cross the membrane and enter the cell, driven by the concentration gradient and by the attraction of the cations for the electrically negative interior of the cell.
  3. Repolarizing phase: voltages-sensitive K^+ gates open, and the Na^+ gates close initiates **repolarization**, which results in a rapid **efflux** of K^+ ion.
  4. **Undershoot**: This increased permeability to K^+ helps to restore the resting potential and may even temporarily hyperpolarize the membrane.
     - **Refractory period**: the Na^+ gates are insensitive in the short time period until the membrane potential returns to the resting potential.

Nerve impulses propagate themselves along an axon

- An action potential is a localized electrical event, which does not actually travel but is regenerated anew in a sequence along the axon: like **dominoes**.
  1. The sodium ions that rush into a stimulated neuron at the point where the action potential is first triggered diffuse laterally from their point of entry.
  2. This positive charge depolarizes a neighboring region of the membrane to the threshold potential, causing voltage-sensitive Na^+ gates in this adjacent region to open and another action potential to occur.

3. Lateral diffusion of the incoming Na^+ at this point incites an action potential still farther along the axon.

- **One way impulse**: Due to a spike of an action potential is followed by a refractory period, a wave of depolarization passing a point along the axon can not induce new action potential behind it, but only in the forward direction.

- Factors affect the speed of nerve impulses:
  - The larger the diameter of the axon, the faster the rate of transmission.
  - Myelin sheath has small gaps, **nodes of Ranvier**.
    1. The voltage-sensitive ion channels that function in the action potential are concentrated in the node regions of the axon.
    2. Extracellular fluid contacts with the neuron only at these nodes.
    3. **Saltatory conduction**: the action potential does not propagate in a continuum over the length of the axon, but rather "jump" from node to node, skipping the insulated regions of membrane between the nodes - results in faster transmission of the nerve impulse.

Chemical or electrical communication between cells occurs at synapse

<u>Electrical Synapses</u>

- **Gap junction**: action potentials spread directly without delay and with no loss of sign strength.
  - Giant axons of crustaceans: several short, thick neurons connect end-to-end and couple by electrical synapses.
  - Intercalated discs in cardiac muscle:

<u>Chemical Synapses</u>: more common than electrical synapses

- **Synaptic cleft**, a narrow gap, separates the presynaptic cell from the postsynaptic cell.
- **Synaptic vesicle**s: the numerous sacs within the cytoplasm of the **synaptic knob** contain **neurotransmitter**. When the action potential being propagated along the axon arrives at the synaptic knob and depolarizes the presynaptic membrane, the neurotransmitter is secreted into the synapse cleft.
  - Most neurons secret only one kind of neurotransmitter. However, a single neuron may receive various chemical signals.
- **Calcium ion**s play a central role in this conversion of the electrical impulse into a chemical signal.
  1. Depolarization of the presynaptic membrane causes Ca^{++} to rush into the cell through voltage-sensitive channels.
  2. The sudden rise in the cytoplasmic concentration of Ca^{++} stimulates the synaptic vesicles to fuse with the presynaptic membrane and spill the neurotransmitter into the synaptic cleft by exocytosis.

Neural integration occurs at the cellular level

- The **axon hillock** is the neuron's integrating center:
  - **Inhibitory postsynaptic potential** (**IPSP**) making membrane more permeable to K^+: Such ion fluxes push the membrane potential to a voltage even more negative the resting potential.
  - **Excitatory postsynaptic potential** (**EPSP**):
- Several synaptic knobs act simultaneously on the same postsynaptic cell or synaptic knobs discharge neurotransmitters repeatedly in rapid-fire succession: the **additive effect** of postsynaptic potentials.

- **Temporal summation**: new chemical transmissions from one or more synaptic knobs occur so close before the voltage has returned to the resting potential after the previous stimulation.
- **Spatial summation**: several different presynaptic neurons stimulate a postsynaptic cell at the same time.

The same neurotransmitter can produce different effects on different types of cells

- **Neurotransmitter**:
  1. Neurotransmitters affect the membrane potential of the postsynaptic cell.
  2. Neurotransmitters are removed rapidly from the synapse, either enzymatic degradation or uptake by a cell.
- **Acetylcholine**: one of the most common neurotransmitters in animals.
- **Biogenic amine**s derived from a.a. perform most functions within CNS. Some psychoactive drugs, such as LSD and mescaline, can induce **hallucination**.
  1) **Catecholamine**s like epinephrine, norepinephrine, and dopamine.
  2) **Serotonin** is synthesized from **tryptophan**:
- **Amino acid**s: glycine, glutamate, aspartate, and gamma aminobutyric acid:
  - Gamma aminobutyric acid (**GABA**) produces IPSPs in brain.
- **Neuropeptide**s:
  - endorphins and enkephalins as natural analgesics.
  - substance P is a key excitatory signal to mediate our perception of pain.
- Acetylcholine and amino acid transmitters alter the permeability of the postsynaptic membrane to specific ions. The biogenic amines and the neuropeptides usually have a long-lasting impact because they affect metabolism within the postsynaptic cell.

Gaseous Signals of the Nervous System

- Some neurons of the PNS or CNS utilize NO and CO as local regulators.
  - **Acetylcholine** released by neurons into the walls of blood vessels stimulates the endothelial cells of the vessels to synthesize and release **NO**.
  - **Nitroglycerine** is used to treat chest pain: NO can dilate blood vessels.

Evolution and Diversity of Nervous Systems

Nervous systems show diverse patterns of organization

- **Nerve net**: the simplest type of nerve system - no central control; e.g., hydra
- **Cephalization**: brain or cephalic ganglia
  - Flatworm, the simplest animals show cephalization: ladder-like nervous system.
  - Annelids and arthropods: well-defined ventral **nerve cord** with a prominent brain.
  - Sessile or slow-moving mollusks have little or no cephalization and relatively simple sense organs: how the nervous system organization of animals interacts with their environments
  - The cephalopods have the most sophisticated nervous systems at any invertebrates: large brain, giant axon, and image-forming eyes.

Vertebrate Nervous Systems

Vertebrate nervous systems have central and peripheral components

- The vertebrate CNS is derived from the dorsal hollow nerve cord of the embryo – chordate.

- The narrow **central canal** of the spinal cord is continuous with the fluid-filled space, called **ventricle**s, of the brain.
- **Cerebrospinal fluid**, the filtration of blood, conveys nutrients, hormones, and WBCs across the **blood-brain barrier**, and act as shock absorber: circulating through central canal and ventricles and then draining back into the veins.
- **White matter** and **gray matter** (mainly nerve cell bodies, dendrites, and unmyelinated axons):

The divisions of the peripheral nervous system interact in maintaining homeostasis

- Most of the **cranial nerve**s and all the **spinal nerve**s contain both **sensory** (afferent) and **motor** (efferent) neurons.
  - **Cranial nerve**s originate in the brain and innervate organs of the head and upper body: 12 pairs in mammals.
  - **Spinal nerve**s innervate the entire body: 31 pairs in mammals.
- Motor division of PNS:
  - **Somatic nervous system voluntarily** carries signals to skeletal muscles mainly in response to external stimuli, but a substantial proportion of skeletal muscle movement is determined by reflexes.
  - **Autonomic nervous system**: **involuntary**
    - **Sympathetic nervous system** (increasing energy expenditures and prepares for action) and **parasympathetic nervous system** (enhancing to gain and conserve energy)

Embryonic development of the vertebrate brain reflects its evolution from three anterior bulges of the neural tube

- There are three regions presented in all embryonic vertebrates: **forebrain** (**telencephalon** and **diencephalon**), **midbrain** (**mesencephalon**), and **hindbrain** (**metencephalon** and **myelencephalon**).
- In adult: telencephalon (**cerebrum**), diencephalon (**thalamus**, **hypothalamus**, and **epithalamus**), and metencephalon (**cerebellum**).

Evolutionarily older structures of the vertebrate brain regulate essential automatic and integrative functions

The Brainstem

- The brainstem (lower brain), a stalk and cap-like swellings at the anterior end of the spinal cord, consists **mesencephalon** (**mid brain**), part of **metencephalon** (**pons**), and **myelencephalon** (**medulla oblongata**): homeostasis, coordination of movement (large-scale like walking), and conduction of information to higher brain center.
- **Medulla oblongata** and **pons** controls breathing, heart and blood vessel activity, swallowing, vomiting, and digestion: The right side of the brain controls much of the movement of the left side of the body, and vice versa.
- The **midbrain** contains centers for the receipt and integration of several types of sensory information. It also serves as a projection center, sending coded sensory information along neurons to specific regions of the forebrain.
  - **Inferior** and **superior colliculi**, prominent nuclei of the midbrain are part of the auditory and visual system, respectively.

The Reticular System, Arousal and Sleep

- Arousal and sleep are controlled by several centers in the bainstem and cerebrum:

- **Reticular activating system** (**RAS**), part of the **reticular formation**, as a sensory filter can selectively send information to the cortex: the more input the cortex receives, the more alert and aware a person is.
- The **pons** and **medulla** contain ganglia that cause sleep when stimulated.
- **Serotonin** may be the neurotransmitter of the sleep-producing centers: Drinking milk before bedtime might induce sleep because milk contains large amounts of the initiator of serotonin, **tryptophan**.

- Sleep and wakefulness produce different patterns in the electrical activity of the brain, which can be recorded by **electroencephalogram** (**EEG**): the less mental activity taking place, the more synchronous the brain waves.
  - Wakefulness:
    - **Alpha wave**s, the slow synchronous waves predominate when a normal person is lying quietly with closed eyes.
    - **Beta wave**s, the faster waves occur when the eyes are opened or the person solves a complex problem: desynchronization.
  - Sleeping:
    - **Theta wave**s: the more irregular waves in the early stage of sleep.
    - Deeper sleep can be divided into two patterns that alternate during a night: a 90-minute cycle.
      1. **Delta wave**s are quite slow and highly synchronized.
      2. **REM** (rapid eye movement) sleep: a desynchronized EEG reminiscent of wakefulness occurs – Most dreaming occurs during REM sleep.

- All birds and mammals sleep and show a characteristic **sleep-wake cycle** - One hypothesis: sleep is involved in the consolidation of learning and memory.

The Cerebellum

- The **cerebellum** receives sensory information about the position of the joints and the length of the muscles, as well as information from the auditory and visual systems: when part of the body is moved, the cerebellum coordinates other parts to ensure smooth action and maintenance of equilibrium.

The Thalamus and Hypothalamus

- **Thalamus**, a major integrating center is also the main input center for sensory information and the main output center for motor information.
- **Epithalamus** includes the **pineal gland** and a **choroid plexus**, one of several clusters of capillaries that produce cerebrospinal fluid.
- The hypothalamus and **circadian rhythm**s: daily rhythm
  - **Biological clock**: The **suprachiasmatic nuclei** (**SCN**) in hypothalamus of rodents produce specific proteins in response to changing light-dark cycle.
  - The clock can continuously run without external cues. However, external cues (like day length) can adjust the clock, so that the rhythmic behavior can be synchronized with the outside world.

The cerebrum is the most highly evolved structure of the mammalian brain

- The cerebrum is divided into right and left **cerebral hemisphere**. Each hemisphere consists of an outer covering of gray matter, **cerebral cortex**, internal white matter, and a cluster of nuclei, **basal nuclei**.
  - The **basal nuclei** are the important centers for planning and learning movement sequences:
    - **Parkinson's disease** or **Huntington's disease**: degeneration of cells entering the basal nuclei.

- The **cerebral cortex** is the largest and most complex part of the mammalian brain: The part has changed the most during vertebrate evolution.
  - An additional outer layer of cortex, **neocortex** consists of six sheets of neurons running tangential to the brain surface.
  - Mammal's greater cognitive abilities and more sophisticated behavior are associated with the relative size of the cerebral cortex and the presence of convolutions that increase its surface area of the neocortex.

- **Corpus callosum**: a thick band of fibers connect the two hemispheres.
  - Without the **corpus callosum**, knowledge of the size, texture, and function of the object cannot be transferred from the right to the left hemisphere.

Regions of the cerebrum are specialized for different functions

- Each side of the cerebral cortex has four lobes including **frontal, temporal, occipital,** and **parietal lobe**s: Each lobe has a number of functional area, such as **primary sensory area**s for input of different kinds of sensory information (visual information to the occipital; auditory input to the temporal lobe; somatosensory information about touch, pain, pressure, temperature, and the position of muscles and limbs to the parietal lobe; olfactory information to the frontal lobe) and **association area**s that integrate the input with information from other parts of the brain.
- Two functional cortical areas, the **primary motor cortex** and the **primary somatosensory cortex**: the boundary between the frontal and parietal lobe.
  - The proportion of motor or somatosensory cortex devoted to a particular part of the body is correlated with the relative importance of sensory or motor information for that part of the body.

Integrative Function of the Association Area

- Sensory information → **cortex** → **thalamus** → **primary sensory area**s within the lobes → adjacent association areas → more association areas → frontal lobe → primary motor cortex

- The major increase in the size of the neocortex that occurred during mammalian evolution expanded the association areas that integrate higher cognitive functions that make more complex behavior and learning possible.

Lateralization of Brain Function

- The right and left **cerebral hemisphere**s, which control different functions:
  - Noble Prizewinner Roger Sperry: "**split-brain**".
  - Right hemisphere: pattern recognition, face recognition, spatial relation, emotional processing
  - Left hemisphere: language. Math, logic, operation
- When one person lost one of cerebral hemisphere, the remaining hemisphere might take over most of the functions normally provided by two hemispheres.

Language and Speech

- Language is processed by multiple areas in the cortex: read, meaning, …
  - Broca’s area (a frontal lobe area) damage could understand but not speak.
  - Wernick’s area (a posterior portion of the temporal lobe) damage could abolish the ability to comprehend speech but leave speech generation intact.
  - Damage to parts off the left hemisphere can cause different sorts of **aphasia**.
- A principle of brain function: novel stimuli or instructions cause the greatest mobilization of brain areas and resources. Once a situation or procedure has become familiar, it is accommodated by a much lower level of brain activity

Emotions

- Human emotion (feeling) is generated by **limbic system**: parts of the hypothalamus, thalamus, and two nuclei, **amygdala** and **hippocampus** in the cerebral cortex form a ring structure.
  - **Amygdala** is central in recognizing the emotional content of facial expression and laying down emotional memories.
  - **Hippocampus** is involved in explicit memory.
  - As children develop, primary emotions such as pleasure and fear are associated with different situations in a process that requires the frontal lobes.
    - **Frontal lobotomy**: destruction of limbic structure or connections between the limbic system and cerebral cortex – to treat severe emotional disorder.
- Distinguishing mammals from other vertebrates: The limbic system mediates primary emotions that manifest in such behaviors as laughing and crying.

Memory and Learning

- To store and retrieve information related to previous experiences is essential for learning.
  1. **Short-term memory** reflects immediate sensory perception of an object or idea and occurs before the image is stored.
  2. **Long-term memory**:
     - **Fact memory** can be consciously and specifically retrieved from the data bank of your long-term memory.
     - **Skill memory** involves motor activities that are learned by repetition without remembering specific information: Once a skill memory is learned, it is difficult to unlearn.

  - The transfer of information from short-term to long-term memory is enhanced by rehearsal, favorable emotional state, and association of new information with information previously learned.
- **Memory pathway**: **Amygdala** may act as memory filter, and certain synapses in the **hippocampus** changes may relate to memory storage and learning.
  - **Long-term depression** (**LTD**): a decreasing responsiveness to an action potential by a postsynaptic cell is induced by repeated, weak stimulation.
  - **Long-term potentiation** (**LTP**): presynaptic cell bombards with repeated action potentials to postsynaptic cell. With LTP established, a single action potential from the presynaptic cell has a much greater effect than before.
    - LTP is associated with the release of the excitatory neurotransmitter **glutamate** by the presynaptic cell. Glutamate binds with specific receptors in the postsynaptic membrane to opens Ca^{++} channels that trigger a cascade reactions in the postsynaptic cells.

<u>Human Consciousness</u>

- Until relatively recently the study of human consciousness has been considered outside the province of hard science, more appropriate as a subject for philosophy and religion.

Research on neuron development and neural stem cells may lead to new approaches for treating CNS injuries and diseases

- Unlike the peripheral nervous system, the mammalian central nervous system cannot repair itself when damaged or assaulted by disease: Spinal cord injuries, stroke, brain injuries, and diseases that destroy brain cells, such as Parkinson's and Alzheimer's have devastating effect.

Nerve Cell Development

- However neurons find their way during development of the nervous system?
  - **Growth cone**: the responsive region at the leading edge of the growing axon
  - The response of the axon may be to grow toward the source of the signal molecules (attraction) or grow away from the source (repulsion)
  - Nerve growth factor released by Astrocytes and growth promoting proteins produced by the neurons themselves contribute to the process by stimulating growth of axons.
- The ultimate goal of repairing damaged neurological tissue: using the right combination of attractant, repellants hope to coax damaged axon to regrow, following the correct pathway and forming connections with the correct targets.

Neural Stem Cells

- Mice in cage with exercise wheel have more new brain cells in their hippocampus than those in standard cage: Perhaps people can improve their brain capacity by stimulating their minds and exercising their bodies, resulting in a greater capacity for learning.
- In adult human, newly divided cells were found in the hippocampus: the new brain cells must have come from **stem cell**s – relatively unspecialized cells that continually divide.
  - The **neural progenitor cell**s divided 30-70 times and differentiated into neurons and Astrocytes in vitro.
  - One of the goals of further research is to find a way to induce the body's own neural progenitor cells to differentiate into glia or specific type of neurons when and where they are needed.