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1.1 Prehistoric

- A million years or more, people have been interested in the brain. Archaeological evidence shows that skulls are bashed in (jagged, not precise). As a result, the person dies, and therefore the brain is vital to life.

1.2 7000 Years Ago

- New holes in the brain, but these holes show signs of healing. Therefore, these new holes are intended to help the person who is suffering. The fancy name is trephination.
- The theory for these holes is that they were drilled to cure the person. In other words, to relieve a person of a wicked spirit.

1.3 5000 Years Ago

- Egyptian physicians show that they were aware of brain damage through their writings.
- Complications arise because they thought the heart contained the soul—you need it to live and emotions effect it.

1.4 Ancient Greece—Hippocrates 4th Century, BC

- Ponder the correlation between structure and function. Now, extend this thought to the brain/head.
- The brain is the place where sensation and intelligence reside. Not the heart.

1.5 Ancient Greece—Aristotle

- Clung to the idea of the heart being the one in charge.
- Figured the brain was a radiator. That is, we would send heated blood to the brain for it to be cooled off. This “heated blood” arose from our emotions. Thus, humans are more rational because we have a lot of cooling when compared to other animals.



1.6 Roman Empire–Galen 2nd Century, AD

- Galen is a physician to gladiators.
- Thought the cerebellum was for motor control (because the cerebellum is hard, like muscles) and the cerebrum is for memory because it is soft, and you can "write on it."
- Noticed there were large spaces (called "ventricles" literally translated to spaces) that were filled with fluid.
- From here, we get the four humors (literally translated to fluids).
- Galen thought that these fluids are what control the brain, NOT the brain structure itself. Think of the purpose of canned vegetables. The tin container does not actively contribute to the liquid / vegetables; rather, it is disposable.
- These ideas were jumpstarted by the invention of aqueducts. The movement of water was so important from aqueducts, so the idea this idea was extended to the brain.

1.7 Analysis by Analogy–17th Century

- French developed hydraulically controlled machines.
- Again, this is adding to the idea that water (which can flow through things and cause movements).

1.8 Rene Descartes–1596-1650

- Believed that non-humans–what he called animals–are controlled by fluid.
- From this, he posited that the human body is a material entity functioning as a machine (like animals)–these are known as reflexes.
- But, the mind is nonmaterial and free from the laws of the universe and was uniquely human.
- Question: How does the nonmaterial part of the body (the mind) communicate with the material part of the body? Through the pineal gland! This gland would move around like a joystick and would manipulate the fluid that came from the third ventricle.

1.9 The Mind/Body Problem

- What is the basic relationship between mental events and physical events?
- Dualism–The mind exists independently of the brain and exerts some control over it. Strengths: Commonsense view.



- Weaknesses: The universe is composed of matter or energy.
- Modern neuroscientific explanation: Everything the body does rests on the events taking place in specific, definable parts of the nervous system—the “mind” is the product of the nervous system activity.

1.10 Recall and Overview

- Prehistorically: People knew you needed the brain to live.
- 7000 years ago: trephination
- Egyptians: mixed but mostly supported the heart
- Greeks: mixed between Hippocrates and Aristotle
- Roman Empire: Galen—Shift from brain structure to fluid
- Descartes: backed the fluid model
- What’s next? The scientific method

1.11 The Scientific Method—17th and 18th Century

- A new world view at the end of the Renaissance.
 - Replace Rationalism with Scientific Method.
- Closer look at the substance of the brain:
 - Gray and white matter change the way we look at the brain. That is, why would these parts of the brain that are clearly different, be different if the brain is used just to move fluids around.
 - Also, everyone has the same brain structure, so these bumps and groves must mean something.

1.12 Electricity

- Isaac Newton showed it is possible to electrically stimulate nerves.
- Then, Luigi Galvani and Emil du Bois-Reymond showed that electricity can make muscles contract.
- Later on, Hermann von Helmholtz showed that the speed of nerve conduction is not instantaneous.



- This important distinction shows that these nerves are not like wires—such as Luigi Galvani and Emil du Bois-Reymond thought.
- Bell and Magendie showed that the dorsal nerve root and the ventral nerve root are different.
- The dorsal nerve root is for sensory information, and the ventral nerve root is for motor information.
- Thus, dorsal = sensory and ventral = muscle.
- Johannes Müller came up with the doctrine of Specific Nerve Energies.
- This doctrine states that the nature of a sensation depends on which nerve is stimulated, not on how the nerve is stimulated.
- For example, if you stimulate the optic nerve, you will see something. If you stimulate the auditory nerve, you will hear something.
- Spawned the Great Debate: Is the brain a homogenous mass or is it made up of different parts?

1.13 The Great Debate

- Franz Joseph Gall and Johann Spurzheim thought the brain was made up of different parts.
- They thought that the bumps and groves in the brain were due to the size of the brain parts.
- They also thought that the size of the brain parts was due to the amount of use of that part.
- This is known as phrenology.
 - Phrenology was a pseudoscience because it was not based on empirical evidence. However, it did lead to the idea that the brain is made up of different parts.
- Localization of Functions—brain function can be localized to regions, pathways, or neurons.
 - Basically, if you cut out a piece of brain, and the animal (a pigeon) is no longer able to do a specific task, then that part of the brain is responsible for that task.
 - However, it turns out that these pigeons were able to relearn the task, so the brain is not as localized as we thought.
- Aggregate Field Theory



- Complex brain functions emerge from the collective interactions of numerous simple neuronal activities
- Unlike localizationist models, this theory emphasizes the distributed nature of cognitive processes across neural networks
- Pierre Flourens thought the brain was a homogenous mass.
 - He believed in Localization of Function, until his results nullified his beliefs.
- Paul Broca
 - Found a patient who could understand language but could not speak.
 - After the patient died, Broca found a lesion in the left frontal lobe.
 - This area is now known as Broca's area.
 - This area is responsible for speech production.
 - These results put us back into the realm of Localization of Function.
- In comes Carl Wernicke (1874)
 - Found a patient who could speak but could not understand language.
 - After the patient died, Wernicke found a lesion in the left temporal lobe.
 - This area is now known as Wernicke's area.
 - This area is responsible for language comprehension.
- Then, we have Gustav Fritsch and Eduard Hitzig (1870)
 - Similarly to Luigi Galvani and Emil du Bois-Reymond, they electrically stimulated the brain.
 - They found that the motor cortex is responsible for movement.
- Shepherd Ivory Franz (in D.C. from 1907-1924)
 - Found that people are able to relearn tasks after brain damage.

1.14 Same Resolution?

- Modified Aggregate Field Theory
 - Karl S. Lashley (1890-1958)
 - The Principles of Mass Action
 - Complex behavior—such as learning—is dependent on the total mass of the brain.
 - Equipotentiality
 - Specialization of function is not tied to specific brain regions.



- All parts of the cortex contribute equally to complex behavior.
- Vicarious functioning
- If one part of the brain is damaged, another part can take over.

1.15 Analysis

1. **Prehistoric:** Recognition of the brain's vital role in life through skull injuries. No scientific theories yet.
2. **7000 Years Ago:** Trephination (skull drilling) practiced to release "evil spirits," indicating early medical intervention.
3. **5000 Years Ago:** Egyptians documented brain damage but prioritized the heart as the seat of the soul.
4. **Ancient Greece—Hippocrates (4th Century BCE):** Proposed the brain as the center of sensation/intelligence, countering heart-centric views.
5. **Ancient Greece—Aristotle:** Defended the heart as the command center, viewing the brain as a blood-cooling "radiator."
6. **Roman Empire—Galen (2nd Century CE):** Linked cerebellum to motor control and cerebrum to memory; emphasized ventricular fluids (humors) over brain structure.
7. **17th Century (Analysis by Analogy):** Hydraulic systems inspired fluid-based brain theories.
8. **Rene Descartes (1596–1650):** Dualism (mind vs. body); proposed pineal gland as the mind-body interface.
9. **17th–18th Century (Scientific Method):** Shift to empirical study; recognition of gray/white matter differences.
10. **Electricity Discoveries:** Newton (nerve stimulation), Galvani/du Bois-Reymond (muscle contraction via electricity), Helmholtz (nerve conduction speed), Bell/Maggendie (sensory/motor nerve roots), Müller (specific nerve energies).
11. **The Great Debate:**
 - Gall/Spurzheim: Phrenology (localization via brain bumps).
 - Flourens: Shifted to aggregate theory after experiments.
 - Broca/Wernicke: Localized language areas.
 - Fritsch/Hitzig: Mapped motor cortex.
 - Franz: Relearning post-injury supported aggregate theory.
12. **Modified Aggregate Theory:** Karl Lashley emphasized mass action and equipotentiality.

Table 1.1: Key Scientists and Contributions

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Scientist	Contributions	Relation to Others
Hippocrates	Brain as seat of sensation/intelligence	Opposed Aristotle
Aristotle	Heart as command center; brain as radiator	Opposed Hippocrates
Galen	Cerebellum (motor), cerebrum (memory); humors	Influenced by Roman aqueducts
Rene Descartes	Mind-body dualism; pineal gland	—
Isaac Newton	Early nerve stimulation via electricity	—
Luigi Galvani	Electricity-induced muscle contraction	Collaborated with du Bois-Reymond
Emil du Bois-Reymond	Same as Galvani	Collaborated with Galvani
Hermann von Helmholtz	Measured nerve conduction speed	—
Charles Bell & François Magendie	Sensory/motor nerve roots (Bell-Magendie Law)	Collaborators
Johannes Müller	Doctrine of specific nerve energies	—
Franz Joseph Gall	Phrenology (brain localization)	Collaborated with Spurzheim
Johann Spurzheim	Promoted phrenology	Collaborated with Gall
Pierre Flourens	Shifted to aggregate theory	Opposed Gall/Spurzheim
Paul Broca	Localized speech production (Broca's area)	—
Carl Wernicke	Localized language comprehension (Wernicke's area)	Complementary to Broca
Gustav Fritsch & Eduard Hitzig	Mapped motor cortex	Collaborators
Shepherd Ivory Franz	Relearning post-brain damage	Influenced Lashley
Karl S. Lashley	Mass action, equipotentiality	Built on Franz's work

3.1 Neuroanatomy

3.1.1 Nervous System Structure

Structural Nervous System

How are neurons organized into systems?

- Central Nervous System (CNS)
 - Brain
 - Spinal Cord
- Peripheral Nervous System (PNS)

Functional Nervous System

What are the ‘jobs’ of the nervous system?

- Somatic Nervous System
 - Skeletal Muscles (Striated)
 - Sensory information in
 - Voluntary motion out
- Autonomic Nervous System
 - Uses smooth muscles
 - Glands
 - Sympathetic Nervous System
 - Fight or Flight
 - Heart rate, blood pressure, respiration, and alertness.
 - Parasympathetic Nervous System
 - Rest and Digest
 - Enteric Nervous System
 - A mesh-like system of neurons that governs the function of the gastrointestinal system.
 - AKA: ‘Second Brain’
 - GI problems are correlated with psychological disorders.



- The GI track houses a lot of our microbiota.
- Fecal Microbiota Transplant
 - Rat studies showed that when a skinny rat has a fecal transplant from a fat rat, the skinny rat becomes fat. This works in reverse too.
 - Therefore, the microbiota change the *behavior* of the rat.
- Elevated Plus Maze
 - A test to measure anxiety in rats.
 - The rats with the fecal transplant from the anxious rats were more anxious.
 - **This is huge!** This shows that the microbiota can change if a rat is anxious or not!

Starting a new list because I don't know where to put this. But we are starting with Meninges.

3.2 Meninges

- Cover the outside of the nervous system.
 - Three for the CNS and two for the PNS.
 - The PNS does not use the arachnoid mater.
- **Dura Mater**
 - “Hard Mother”
 - The outermost layer.
 - Tough and fibrous.
 - Contains blood vessels.
 - Early anatomists called it “pachymeninges” because similar to elephant skin.
- **Arachnoid Mater**
 - “Spider Mother”
 - Middle layer.
 - Web-like structure.
 - Contains blood vessels.
 - Subarachnoid Space
 - Between the arachnoid and Pia mater.
 - Contains cerebrospinal fluid (CSF).
 - Arachnoid trabeculae
 - Web-like structures that connect the arachnoid mater to the Pia mater.



- **Pia Mater**
 - “Soft Mother”
 - Innermost layer.
 - Thin and delicate.
 - Follows over every sulci (grooves), fissure (deep indentations), and gyri (bumps).
 - Follows the contours of the brain and spinal cord.
- **Meningitis**
 - Inflammation of the meninges.
 - Can cause symptoms such as headache, fever, a stiff neck, or hallucinations.

3.3 Cerebrospinal Fluid (CSF)

- Similar to blood plasma.
- Functions of CSF
 - Protection
 - Failures:
 - Brain is injured.
 - AND even Contrecoup—when the brain is injured on the opposite side of the impact—injuries.
 - Chronic Traumatic Encephalopathy (CTE)
 - Old name: Dementia Pugilistica (boxer’s dementia).
 - Symptoms (not exhaustive): Memory loss, confusion, impaired judgment, impulse control problems, aggression, depression, Parkinson’s-like symptoms, insomnia, and progressive dementia.
 - Causes ventricular enlargement. In other words, the larger your ventricles, the less brain matter you have.
 - Also causes atrophy of the fornix. The fornix is a C-shaped bundle of nerve fibers in the brain that acts as the major output tract of the hippocampus.
 - Tau are abnormally phosphorylated aggregate into tangles. They accumulate both inside neurons and even released into extracellular space.