Blindsight, Traumatic Brain Injuries, and the Brain

Blindsight, Traumatic Brain Injuries, and the Brain:

Thinking about Thinking

By

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Dedicated to Sanjay, Sandhya, & Dhruva

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INTRODUCTION

April 5 started out as a beautiful, California day. I was in love with my husband-to-be Sanjay, and getting great data for my Biophysics doctorate studying vertebrate vision at U. C. Berkeley with Professor W. Geoff Owen. I showed up at lab, and readied things for an experiment for the next day. Since my experiments ran about 12-18 hours, I left early in order to get a run in. Sanjay and I decided to jog around Lake Merritt by his apartment. The sun was still shining when we left. We almost turned around because he had forgotten his knee brace, but we decided to keep on jogging anyways. In order to get to Lake Merritt from his apartment we had to cross a 4-lane road with a crosswalk. Two cars had stopped for us in each of the directions so we thought it was safe to cross. But, a red van in a hurry came up behind one of the stopped cars and since he saw the car's blinker on for a turn, this new car sped up to pass him at about 40 mph. As a result, he hit first Sanjay and then me. We flew through the air thirty-five feet back to the other side of the road where we landed, destroying the car's windshield in the process and cracking open my head—a severe Traumatic Brain Injury (sTBI, left basilar). I was also bleeding from my nose and left ear when the ambulance came, and I was lucky to not have gone into a seizure and die then. I had anterograde amnesia for about two months as I couldn't make any new memories and it took about a year before I could really get back to work on my doctorate, which I then finished in June two years later. Since that time I have taught 3 semesters of the upper-undergraduate class, "Introduction to Neurobiology," 3 semesters of, "The Biology of Sensory Systems," many semesters of, "Thinking about Thinking: Blindsight, Phantom Limbs, and your Brain," and five years of "Human Anatomy & Physiology". I would now like to share with you what little I know and love about Neuroscience, and perhaps a bit of insight into Neuroscience that I have discovered from this injury and my recovery.

CHAPTER 1

INTRODUCTION TO THE NERVOUS SYSTEM

We have been trying to figure out the brain, the central part of the Nervous System, for a long time. Plato, c. 427-347 B. C., was on the right track as he based his Theory of Mind on Geometry. Since he felt (understandably) that the sphere was the most perfect geometrical figure, he reasoned that the head housed the brain-mind. However, his pupil Aristotle thought that the mind was located in the physical heart region. Although he might have been seeking more of a location of the soul, as brought to my attention by one of my students.

Today we divide the Nervous System into 2 main parts: the Central Nervous System and the Peripheral Nervous System. (Fig. 1-1) In this first chapter, I will briefly map the many things we will get to cover in this book.

First, the Central Nervous System (CNS). The CNS, unlike the Peripheral Nervous System (PNS), is encased in a suit of armor for protection made up of the skull bones and vertebral column bones, or vertebrae. The CNS is further protected by a series of thick membranes, called the cranial meninges (the dura mater, the arachnoid mater, and the pia mater). Inflammation of the meninges, or Meningitis, can be caused by bacteria or a virus. It can be deadly if it causes Encephalitis, or inflammation of the brain, as well. The meninges contain yet another CNS protection: the blood-brain barrier. This is a combination of specialized, so as not to be too leaky, blood capillaries surrounded in part by a supportive cell of the CNS called the astrocyte. The blood-brain barrier prevents many substances from leaking past the capillary wall cells, so that what does get past is basically filtered by the capillary wall cells and the astrocytes. Most macromolecules, like proteins, as well as some smaller ions like Chloride, can't enter or leave the CNS as a result. The blood-brain barrier makes it difficult to get many drugs into the CNS—although alcohol, caffeine, most anesthetics, and the gases O_2 and CO_2 can cross it. (Restak, 2000)

The CNS can conveniently be divided into 7 main parts: the spinal cord, medulla oblongata, pons, midbrain, cerebellum, diencephalon, and the cerebral

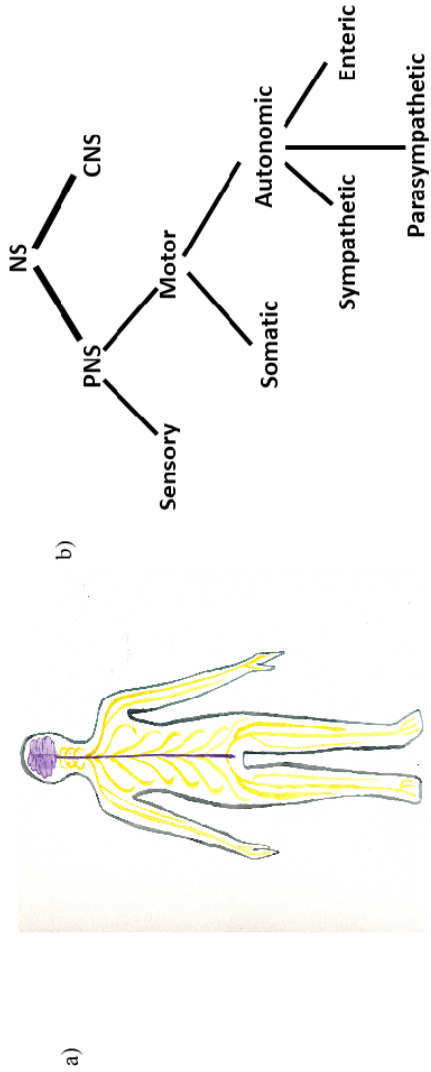

Fig. 1-1. a) In this representation of the Nervous system, the CNS is shown in purple and the PNS is shown in yellow. b) A map of the Nervous System.

hemispheres. (Fig. 1-2) Around and within these parts are the network of capillaries that supply blood to the brain as well as cerebrospinal fluid. Cerebrospinal fluid is a clear liquid that helps maintain a constant environment around cells of the CNS, and nourishes them. The cerebrospinal fluid also removes potentially harmful substances from the CNS and provides a cushion to protect the brain from impacts with the surrounding bones—yet another layer of protection!

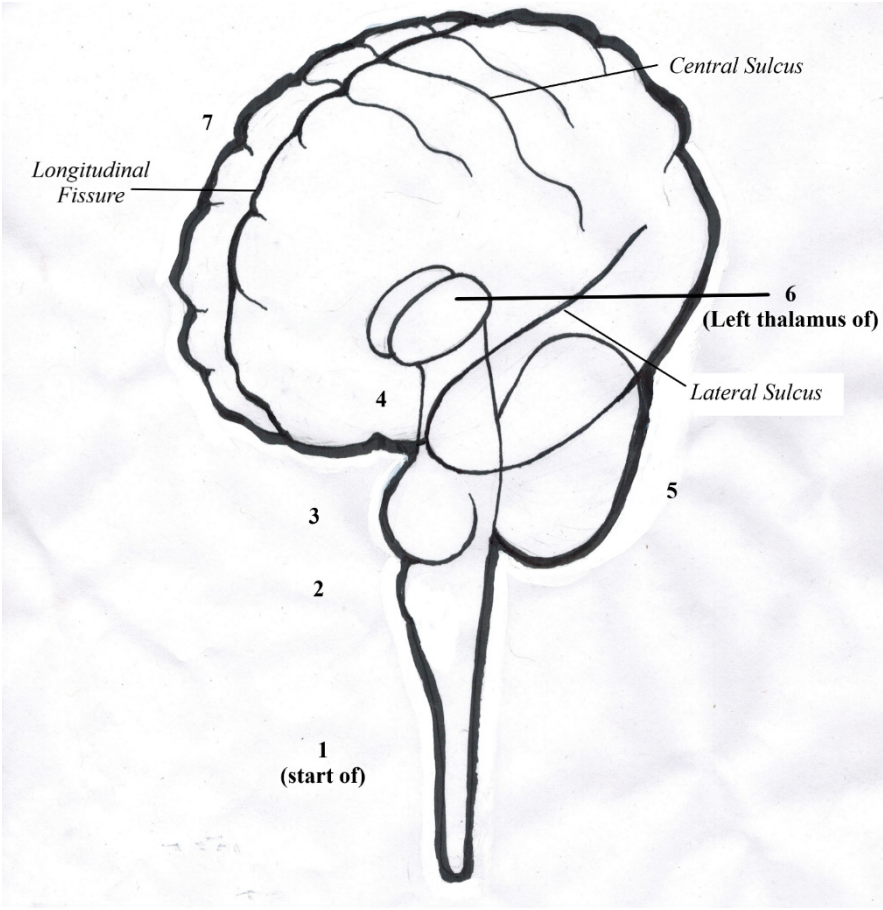

Fig. 1-2. The Central Nervous System: 1) start of the spinal cord 2) medulla 3) pons 4) midbrain 5) cerebellum 6) diencephalon (left and right thalamus of it shown) 7) cerebral hemispheres.

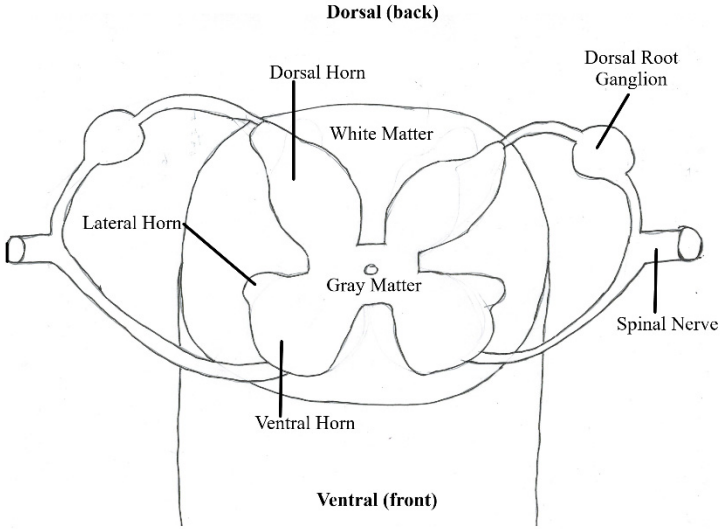

Fig. 1-3. A horizontal slice of the spinal cord.

The first part of the CNS we will consider is the spinal cord whose diameter is about that of your pinky finger (in some regions), and contains a central canal filled with cerebrospinal fluid. It gets sensory information from your skin, joints, and muscles and also contains the cells, called motor neurons, that are responsible for voluntary and many reflex movements. In general, a neuron is the specialized type of cell found in the Nervous System. Chapter 2 is devoted to them. In summary, the spinal cord deals primarily with sensation from and motor control of your trunk and limbs. The spinal cord can be divided into gray and white matter (Fig. 1-3). The white matter consists of long processes of neurons that are white because they are surrounded by white fat. These processes form ascending (afferent) pathways of mainly sensory information to the brain and descending (efferent) pathways that, in part, carry motor commands from the brain. Some of this white matter leaves between the vertebrae and so exits the CNS to innervate the body as the 31 pairs of spinal nerves of the PNS. The gray matter is where many nerve cell bodies are, and is also divided into 2-3 parts: the dorsal horns which receive sensory inputs of touch, pain, and temperature (and also body position information which we can delve into later in the book, called proprioception) coming from the periphery of the body, and the ventral horns which contain the motor neuron cell bodies that

innervate skeletal muscles. Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's Disease, destroys these ventral horn motor neurons causing paralysis. The Polio virus can also attack these ventral horn motor neurons. Some sections of the spinal cord contain a third horn, known as the lateral horns. These are found in the thoracic and upper lumbar sections of the spinal cord. The spinal cord is broken into 4 sections starting from the top: cervical, thoracic, lumbar, and finally the sacral division. These lateral horns contain the cell bodies of autonomic motor neurons which implement our stress response, the Sympathetic or fight-and-flight response.

The next 3 section of the CNS are collectively called the brainstem: the medulla oblongata, the pons, and the midbrain. Overall, the brainstem deals with sensation from and motor control of the head, neck, and face. It is also the entry site to the CNS for information from several specialized senses like hearing, balance, and taste, and it helps in breathing, blood circulation, and a person's level of consciousness. Specifically, the medulla is crucial in some basic, subconscious processes like breathing, blood pressure, and heart rate. It also has centers for vomiting, hiccupping, swallowing, coughing, and sneezing. The pons also plays a role in breathing and is important in determining your awake or asleep state and your level of consciousness. Consciousness can be defined as a state of wakefulness in which a person is fully alert and aware. Several groups of neurons that play a large role in setting whether you are awake or asleep make up what is called the Reticular activating system which are found in and around the pons. The Reticular activating system stimulates the brain to consciousness, and we inactivate it when we sleep. General anesthetics work by turning off consciousness via the Reticular activating system. This system of neurons also filters out insignificant information so that our CNS doesn't get a sensory overload. Lastly, the midbrain has components of your Auditory (hearing) and Visual systems in its posterior part, known as the tectum (superior colliculi for vision and inferior colliculi for hearing); and tracts of white matter, called the cerebral peduncles, which are important in linking different parts of your Motor system.

This brings us to CNS part number 5, the cerebellum. This subdivision of your CNS has more neurons than any other subdivision. There is still a lot of research to be done on it, but the cerebellum is important for learning motor skills and coordination—especially of the head, eye, and arm. For example, the cerebellum plays a large role in learning to ride a bike. It also is important in maintaining posture and may play a role in some cognitive processes as well. One major task that the cerebellum does is that it gets a copy of the Nervous System's motor commands and then compares them

with the actual movements occurring so that it can adjust ongoing movements if needed. Lack of a cerebellum doesn't result in paralysis, but rather a decrease in movement accuracy and coordination. For example, one young lady made it into her twenties before anyone realized she was entirely missing her cerebellum. (Yu, Jiang, Sun, & Zhang, 2015)

The diencephalon is towards the center of your skull, so medial. It consists of two to three parts: mainly the thalamus and the hypothalamus. Diencephalon means two-brain after all, but many now add a third part to them. First, the thalamus which is made up of two egg-shaped structures that are essential links in the transfer of sensory information from peripheral receptors to the sensory processing regions of the cerebral hemispheres. Motor information coming from the cerebral hemispheres also travels through the thalamus on its way to the rest of the body. In part, the thalamus could be considered a gateway for sensory information, allowing the sensory information from an environmental stimulus to reach conscious awareness, or not. For example, during Stage 2 of sleep, neurons of the thalamus and cerebral cortex fire rhythmically creating patterns of activity called sleep spindles in EEG recordings of brain activity. These sleep spindles help keep us from being woken up by sensory information. They do this by preventing sensory information from being transmitted to the cerebral cortex by the thalamus. Interestingly, Fatal Familial Insomnia, a rare disease that causes the inability to sleep leading to death after about a year, looks to be caused by prions (types of malformed proteins that spread their mis-structure) that attack the thalamus especially (as well as other brain regions).

Next, the hypothalamus controls homeostasis functions to maintain a stable, internal environment. Specifically, it has different clusters of neurons in it, or nuclei, that control: blood pressure as well as electrolyte composition via thirst and salt appetite and the release of certain hormones; energy metabolism via hunger and feeding behavior; reproductive behaviors; body temperature; protective behavior via our stress (Sympathetic) system; and our sleep-wake cycle that is driven by the light in our environment—a part of our circadian rhythms. The cluster of hypothalamic neurons responsible for setting our circadian rhythms and so tuning our body to the environment is called the suprachiasmatic nucleus. This is our master, biological clock. It gets information about the timing of daylight directly from neurons in the back of your eyeball in order to set its clock.

The hypothalamus is also the principal subdivision of the CNS that regulates the Autonomic Nervous System which is the involuntary part of our

Nervous System. The Autonomic Nervous System has 3 main branches. The Sympathetic branch which activates your stress response (fight-or-flight response) by increasing your heart rate and blood pressure, increasing your breathing rate, and slowing digestion, as well as dilating your pupils. These actions of the Sympathetic branch help prepare us to combat danger or handle stress better. Its neurons are connected through a chain of ganglia (collections of neurons) that parallels the spinal cord, a primitive looking structure. When these neurons are activated, one thing they do is to stimulate the adrenal glands to release the hormones epinephrine, also known as adrenaline, and norepinephrine, or noradrenalin. The Parasympathetic branch, on the other hand, restores the body back to equilibrium after a stress is over. It slows down the heart, slows our breathing rate, increases digestion activities, and constricts the pupils. Overall, it increases relaxation allowing us to conserve energy and gives this system the nickname of rest-and-digest. The third component of the Autonomic Nervous System is the Enteric branch which controls smooth muscle action, like the movement of the gut during digestion. One way the hypothalamus controls these states is through regulating hormonal secretions into the blood by the pituitary gland which lies just below it.

Lastly, the diencephalon also contains the epithalamus. The epithalamus consists of the pineal gland and the habenular nuclei primarily. The pineal gland releases melatonin in the dark, and the habenular nuclei contain a few parts, one of which is involved in some emotional aspects relating to smell.

The seventh part of your CNS is the cerebral hemispheres. The cerebrum is the name given to both cerebral hemispheres together. Each cerebral hemisphere consists of 5 parts. The cerebral cortex is the heavily wrinkled, gray outer layer. It weighs about three pounds, is 2-4 mm thick, and contains ~86 billion neurons, the specialized cell found in the Nervous System. Neurons are responsible for learning, remembering, our perceptions, and thoughts. In contrast, a mouse has about 75 million neurons in its cerebral cortex whereas an elephant has 257 billion neurons—perhaps to aid in controlling the millions of tiny muscles in its trunk. Underneath the cerebral cortex lies the white matter which connects different parts of the CNS and is made up of long processes coming from the neurons in the gray matter. These long processes are covered in insulating, white fat called myelin. The third part is the amygdala which is made up of a left and a right one as there is one in each hemisphere underneath the cerebral cortex (in Fig. 1-2 they would be lateral to, or to each side of, the thalamus). The amygdala is involved with the expression of emotions especially fear, so it is part of our danger and warning system. It also plays a role in our reward system. Then

there is the hippocampus, of which there are two equivalent parts to it again where one is in each hemisphere and each one ends just before the amygdala. The hippocampus plays a large role in making long term memories. The hippocampus, amygdala, hypothalamus, thalamus, cingulate gyrus, and the olfactory bulbs are part of the Limbic system whose definition is still evolving. The Limbic system is important in producing emotions and memory. Finally, there is the basal ganglia. This is a collection of small nuclei, so clusters of neurons, deep in the brain that are important for smooth and complex movements, reward-based learning, and may play a role in some higher thinking processes as well, like filtering out incorrect or inappropriate responses. There is still a lot of research to be done on it. Some texts are now referring to it as the basal nuclei which is anatomically correct, but historically not used as much. A cluster of neurons in the CNS is a nucleus usually, whereas a cluster of neurons in the PNS is a ganglion. Similarly, a grouping of white matter containing processes from neurons in the CNS is called a tract, but is called a nerve in the PNS.

Now that we have made a primary map of the CNS, let us look back at the fascinating cerebral cortex where, for example, sensory information can become part of our conscious experience. Its most obvious feature is that it is so wrinkly. This increases the amount of surface area available for processing and connections but still keeps everything in a finite volume, the skull. In some animals, the amount of wrinklinenss of the cerebral cortex might correlate with deeper thinking. The cerebral cortex of sheep is quite wrinkly whereas that of rabbits and koala bears not so much. The pattern of the wrinkles is not random within a species, so some of the wrinkles can be used as landmarks as you will discover. Firstly, a groove is called a sulcus and an elevated region is a gyrus. The two hemispheres are separated by the longitudinal fissure and are interconnected by the corpus callosum. The corpus callosum is a set of fibers, or long white neuron processes, that connect symmetrical regions of the two hemispheres.

Each cerebral cortex can be divided into roughly 4-5 main lobes. (Fig. 1-4) The frontal lobe deals with planning future actions, and really higher cognitive abilities—like knowing when it is good to be nice. When this lobe is injured, it can greatly affect ones' personality. It also contains the Primary motor cortex, called M1, where movement commands are finalized. M1 is located in the pre-central gyrus, because it lies just before the central sulcus landmark (also called the Rolandic fissure). Each point on the surface of M1 corresponds to the movement of a particular part of the body. Next is the parietal lobe which contains the Primary somatosensory cortex, or S1, where sensory information about touch, pain, temperature, and the location

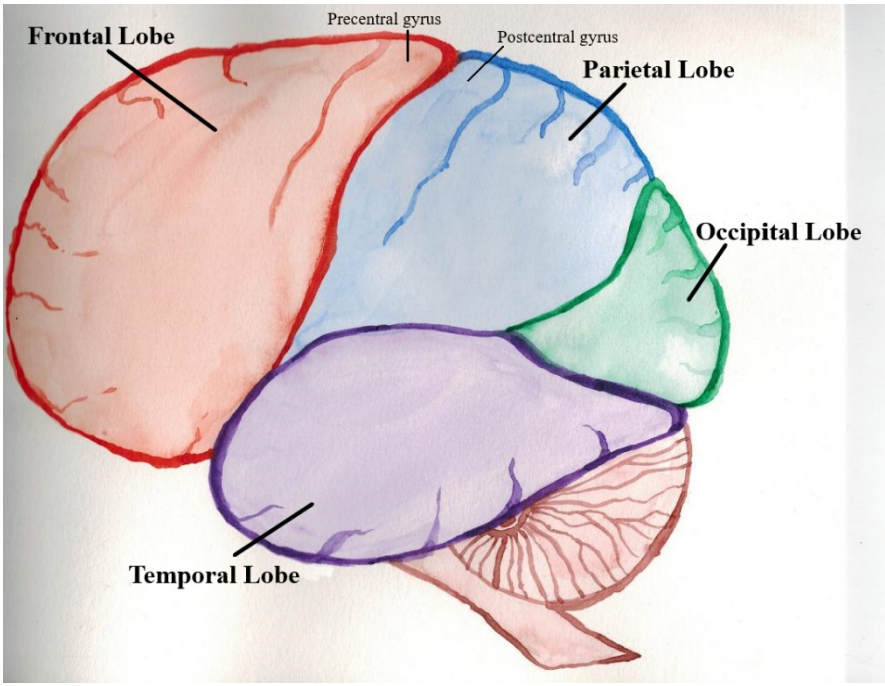

Fig. 1-4. Four of the lobes of the cerebral cortex. In this figure, the insula lobe is underneath the parietal and temporal lobes, although continuous with each of them as it is an invagination of the cerebral cortex at this point.

of the body starts to be processed in the cerebral cortex. This is located in the post-central gyrus. The parietal lobe is important in processing some other sensations too and in bringing information from the senses together into a coherent whole understanding. It is also important in forming a body image that is understood in space. For example, if you hold a pencil in your hand, then your parietal lobe helps you to understand that your hand continues to the fingertips, but not the pencil. This may seem obvious, but one can easily fool this sense. For example, there is an interactive display in the Baltimore Science Museum where you have a mirror that separates 2 rings hanging on a round, metal bar. First you grasp one ring with your left hand and the other ring with your right hand, and then look into the mirror which reflects back the left hand. Next, while looking at your left-hand reflection, you move the ring held by your right hand. Most people feel shock and dismay when this happens because the image they are looking at doesn't change—not surprising since it is an image of your left hand. Your

mind though assumes that you are looking at your right hand which at that moment appears to be disregarding the motor commands you just sent it!

In the back of the cerebral cortex lie the occipital lobes. These lobes process vision, and so contain the Primary visual cortex, V1. Next are the temporal lobes. The lateral sulcus (or Sylvian fissure) separates the temporal lobe from the frontal and parietal lobes. The temporal lobe plays a large role in memory functions, and contains the Primary auditory (hearing) cortex, A1, as well as the Primary olfactory (smell) cortex, O1. Lastly, there is a fifth lobe known as the insula. It contains the main part of the Primary gustatory (taste) cortex, G1, as well as the Primary vestibular cortex used for balance and equilibrium.

We are still learning about the functions of these lobes and how they are interconnected. One way to learn about different parts of the Nervous System is to study injuries or diseases people have had. Imaging studies can be useful too, like functional Magnetic Resonance Imaging (fMRI) studies. One example of an injury that helped us understand a little bit more about the frontal lobe, is the injury that Phineas Gage sustained on September 13, 1848. Mr. Gage was a railroad foreman in Vermont, and as such he was a capable worker in charge of others. On Sept. 13 there was an explosion which sent a thick, steel rod through his head. (Fig. 1-5). This severely injured his frontal lobe and took out an eye, but he miraculously survived. However, his personality went from being capable and organized to being more profane and disorganized. This injury aids in our understanding of the frontal lobes' role in controlling and expressing emotion, and in organizing abilities—especially the prefrontal area of it.

Broadening our scope to the entire cerebral hemispheres, there are five properties that are important to the understanding of the CNS. (Restak, 2000) The first idea is the Association cortex. This arises due to the connections of the ~86 billion neurons in the cerebral cortex. Each neuron makes on average 1000 synaptic connections with other neurons! As a result of these connections, there is a vast network of communicating fibers that synthesize our experiences. The corpus callosum, connecting the two hemispheres, is a part of this.

The second property is that each hemisphere is concerned primarily with sensory and motor experiences from the opposite side of the body. For example, the softness of kitten fur felt by your right hand is processed by the left hemisphere.

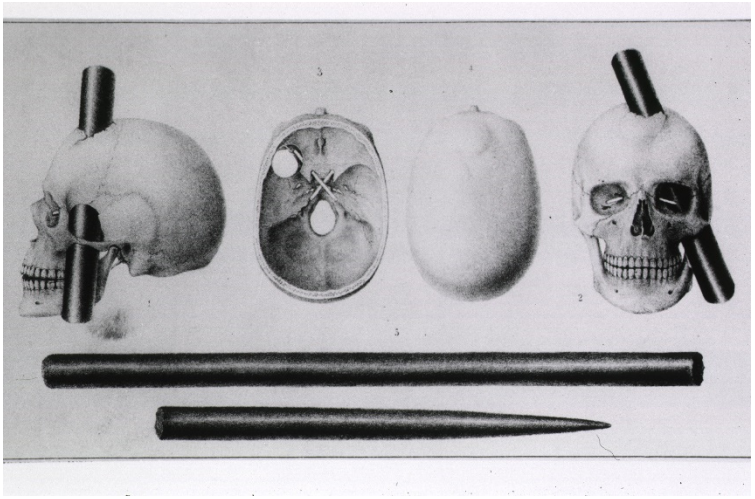

Fig. 1-5. Views of the skull wound sustained by Phineas Gage from the July, 1850 Am. Journal of the Med. Sci., "Dr. Harlow's Case of Recovery…an iron bar through the head." (Image in the Public Domain from //resource. nlm. nih. gov/101434515)

Third, there is a hierarchical organization to the brain. As information proceeds from sensation to subsequent higher brain areas, it becomes increasingly more abstracted. For instance, the back of your eye might observe spots of light coming towards you. Then your occipital lobes would interpret these spots of light to be a bar of light. That information perhaps races to your temporal lobe so that you interpret the bar of light as a spear, which could then trigger your amygdala to alert your whole system to the danger of a rapidly approaching spear.

The fourth property is the idea of topographical maps. For most of your sensory and motor systems, each part of the brain projects in an orderly fashion onto the next part which preserves spatial, or other, aspects of information. At each brain level, a map is thus formed of inputs that is identical to the map at the next level. These maps are called topographical maps, and are most easily understood in the Somatosensory system which deals primarily with touch, temperature, muscle and joint status, and pain. In the case of touch, different parts of the body, for example your right hand, are mapped to actual physical locations in the brain! This map is repeated at different processing stages of the brain until the information becomes too abstract, perhaps. However, not every part of your body gets the same number of neurons devoted to it. Regions where we are more sensitive, have

more neurons monitoring that area. This results in a distortion of your body map in the brain. The drawing of this map is known as a homunculus which has enlarged lips, fingers, and soles of the feet.

The final property of the cerebral hemispheres is that although the two are similar in appearance, they are not equivalent in function. This is more of an emphasis on certain qualities rather than complete differences. Usually, the left hemisphere is slightly better at processing information in a sequential fashion and is the dominant hemisphere for language processing and speech. The right hemisphere still has some aspects of comprehending language, but is more dominant usually in visual-spatial processing, like painting and face recognition. These slight differences between the hemispheres were further uncovered in the study of about twelve "split-brain" patients. These patients had their corpus callosum surgically cut between the 1940s and 1970s to stop the epileptic seizures that were killing them. Today, drastic surgery methods are a last resort for intractable seizures, as drugs can often help. It took about a year for the "split-brain" patients to recover to a point of feeling back to their unified self. (Granted my injury was highly different, but it also took about a year for me to feel like I could get back to my life again after my accident.) There were some interesting differences however. For example, visual information, like words or pictures, could be presented very briefly (milliseconds) to just one hemisphere which would go unnoticed by the other hemisphere. The experiments done by Sperry et al. involving this interesting quirk showed that the two hemispheres were both very competent at most things, but that they provide us with two different understandings, or perspectives, of our world. (Sperry, 1968) An example of one of these experiments, is that the word 'Face' was shown to only one hemisphere at a time. Just like how your right hand is processed by your left hemisphere, so too is your right visual field of view processed by your left hemisphere. (Wolman, 2012) So when 'Face' was shown to the left hemisphere, the patients responded when asked what they saw, that they saw the word 'Face'. Since the left hemisphere is the dominant one for verbal processing, this makes sense. However, when 'Face' was shown to the right hemisphere, the patient did not have access to the language processing capabilities found in the left hemisphere. As a result, the patient responded that nothing was seen. But (!) when asked to draw a picture of what was observed, the patient drew a picture of a face—an example, perhaps, of thinking without the use of language.

That was your CNS in a nutshell, now onto the other part of our Nervous System, the Peripheral Nervous System. The PNS is anatomically separate from the CNS, but functionally intertwined. (Fig. 1-1) It is not covered by

bone and so is susceptible to injury. However it can regenerate more easily than the CNS in humans. There are 2 main divisions of the PNS: motor and sensory. The sensory division relays information to the CNS from the environment. This includes information about temperature, pain, touch, joint positions, and muscle states. Information can be conducted from your skin to your spinal cord at 120 m/sec, or 268 mph! Since the PNS and CNS are intimately connected, there are a few parts that don't follow the map precisely. Take visual information which is sent into the CNS from your eyeball by the optic nerve, a part of the PNS. Visual information is first collected though by a specialized organ of vision found in the back of your eyeball, the retina, which is a piece of the CNS even though it is physically separated from the brain and spinal cord.

The motor division of the PNS has somatic (voluntarily controlled) and autonomic (subconsciously controlled) branches which execute the motor commands coming from the CNS to the muscles and glands. Its somatic motor neurons contact muscles directly. Each of the contact points is a called a Neuromuscular junction. When the CNS sends a message to the motor neuron, the motor neuron causes the muscle cell, called a skeletal muscle fiber, to contract. The PNS Autonomic division helps in executing information coming from the hypothalamus primarily. It consists of neurons that control Sympathetic and Parasympathetic responses as well as neurons that innervate smooth muscles, like your gut, through the Enteric branch.

CHAPTER 2

THE NEURON

The functional unit of the Nervous System is its specialized cell, the neuron. (Fig. 2-1) Neurons are the information carrying cells of the Nervous System, and they are helped by another important cell type, the glial cells. The glia, also called neuroglial cells or nerve glue cells, are a supportive cell type for the neuron.

A neuron does not exist in isolation, it is part of a chain, and/or network, of many neurons. For example, neuron 1 senses a stimulus and then imparts this information to neuron 2 which sends the information to neuron 3 and so on until the information gets to where it needs to go in your Nervous System, like a specific region of the cerebral cortex. A neuron is also highly sensitive to oxygen and glucose (a type of sugar) deprivation. The brain alone consumes 20% of the circulating glucose, and oxygen deprivation can occur after only 30 seconds of not breathing resulting in brain damage, especially if oxygen deprivation lasts 4 minutes or longer. Broadly speaking, there are two main types of neurons: projection neurons and local interneurons. Projection neurons connect major regions of the Nervous system. They are said to be excitatory when they cause the next neuron in the chain to become more active as well. Whereas inhibitory neurons stop the progression of signals in the neural chain. Local interneurons, which make up about ¼ of all neurons, integrate information locally in the Nervous System and can also be excitatory or inhibitory. A newly discovered neuron type, the Rosehip neuron, (Boldog & al., 2018) appears to be specific to human cerebral cortices —so it has not been found in the mouse cerebral cortex so far. Rosehip neurons may even make up about 10% of the human cerebral cortex. These neurons are primarily inhibitory in nature (using a neurotransmitter called GABA), and the fact that they are specific to humans might give some insight into why many Alzheimer's disease drugs are having affects in mice but not humans.

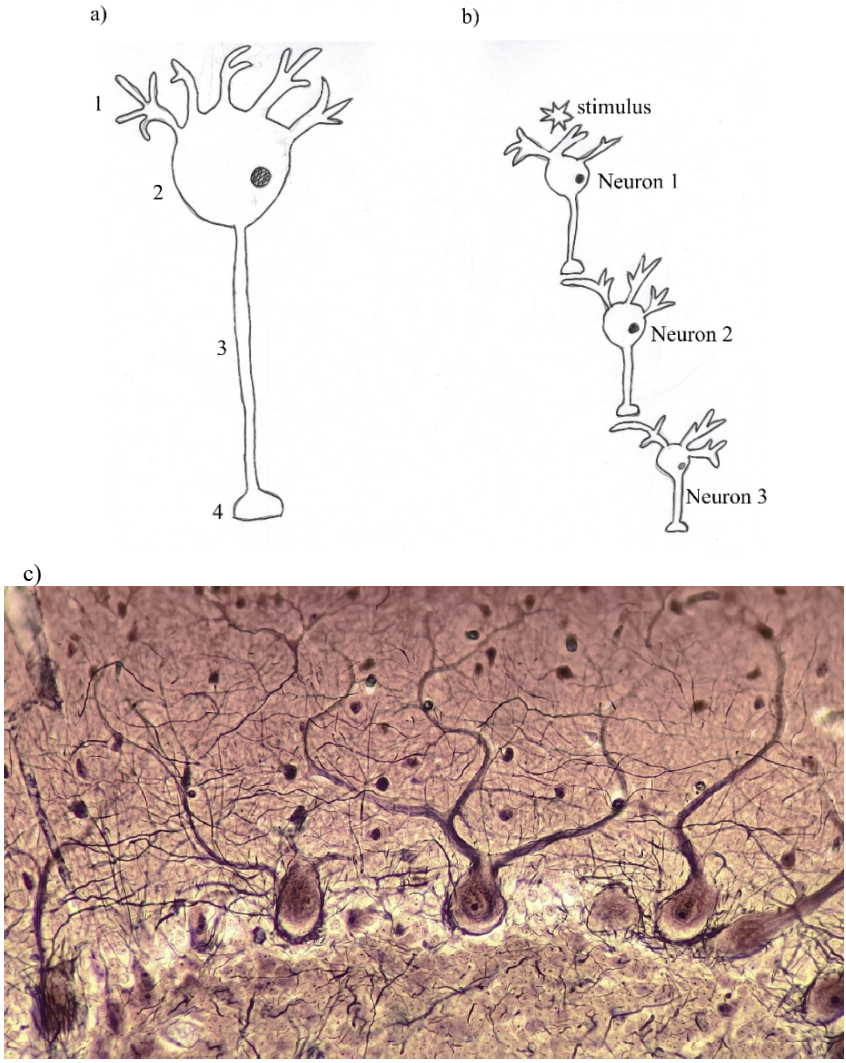

Fig. 2-1. a) A diagram of a neuron where: 1. dendrites 2. soma (nucleus a black circle) 3. axon 4. presynaptic terminal. The dendritic tree of a neuron (for example a retinal ganglion cell (Wong, Faulkner-Jones, Sanes, & Wong, 2000)) can be about 200 micrometers wide or the width of two human hairs side-by-side. b) A simple neural pathway or chain of neurons. c)Purkinje cells from a dog's cerebellum. The dendrites of these neurons are branching off of the round somas and up towards the top of this image. (Image by Lennart Rikk, Wikimedia Commons)

The neurons located in the cerebral cortex are organized into layers and columns. (Fig. 2-2) A good example of how neurons are organized into layers was drawn by the famous Spanish Neuroanatomist Santiago Ramon y Cajal who lived from 1852-1934. He defined the neuron doctrine which states that the Nervous System is made up of individual cells rather than one continuous web. The columns of the cerebral cortex are 300-600 micrometers wide. The diameter of a human hair is about 100 micrometers or 0. 1mm, so these columns are about the width of 3-6 hairs side by side. Each column contains 1000s of neurons and is thought to be the fundamental computational units of the cerebral cortex. Neurons within one column tend to have similar response properties. For example, all the neurons in one column might respond to information coming from your pinky finger, whereas the neurons in the neighboring column might process information coming from your ring finger.

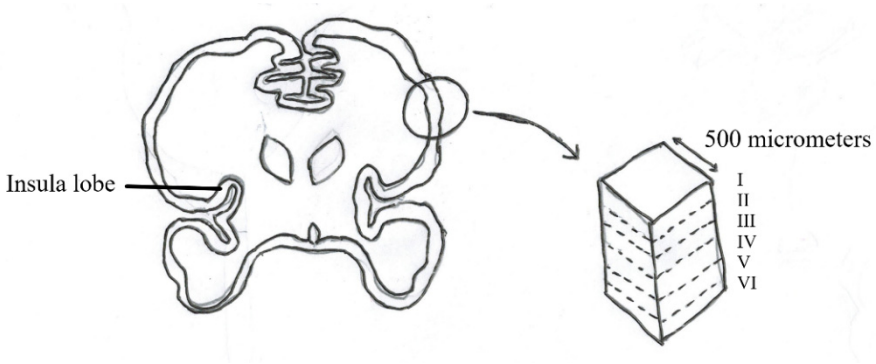

Fig. 2-2. A coronal slice of the cerebral hemispheres with a pop-out showing a column of the cerebral cortex and its 6 layers of neurons. Layer I is under the bones of the skull and layer 6 is just above the white matter of the cerebral hemispheres.

The layers of the cerebral cortex are usually divided into 6 main layers that organize inputs and outputs of the columns. Layer 1 is towards the skull, or pial, surface. Projection neurons are commonly found in layers 3, 5, and 6. Interneurons can be found in all the layers. Layer 4 is the input layer for sensory information coming into the sensory cortical areas, and can have sublayers (like a-c).

The human brain contains 86 billion neurons, whereas a mouse has 75 million neurons, a bee 1 million neurons, and the nematode worm, *C. elegans*, only needs 302. The neuron is a cell and so it shares many of the characteristics common to most cells. It is covered by a plasma membrane,

like a skin as one of my students aptly pointed out, which can have proteins stuck into it. The neuron has a nucleus to control cellular activities via the DNA it contains through a basic principle of Molecular & Cell Biology: a gene on DNA is transcribed by a polymerase into mRNA which is translated by a ribosome into a protein

Gene on DNA(transcribed by a polymerase) mRNA (translated by a ribosome)Protein

(where mRNA is short for messenger RNA). Lastly, the neuron is filled with cytoplasm and several organelles. The organelles each perform specific functions. For example, the endoplasmic reticulum, where many of the ribosomes are located, helps in processing proteins that are just made. The Golgi bodies help to package and direct those proteins to their proper places. The mitochondria are tiny energy processing factories that store energy, derived from food, in the molecule ATP (adenosine triphosphate). ATP can then be used as needed in cells to power their activities. Lysosomes breakdown waste material, and the intracellular matrix acts like a cellular skeleton, as well as being a molecular highway, within the cell.

A neuron differs from a generic cell in that its' main job is to intercommunicate with other neurons and cells. This greatly affects a neuron's structure, or shape. A quick overview of this intercommunication process: the neuron communicates, usually, with other cells via a specialized contact between the two cells called a synapse. A neuron first usually encodes information into the form of electrochemical signals, known as action potentials or nerve impulses, that travel along the long processes of neurons. These action potentials are translated into chemical messengers/molecules, called neurotransmitters, which carry the information from one neuron to the next cell across the tiny gap between the cells, known as the synaptic cleft of the synapse. Many drugs either mimic or interfere with neurotransmitters or the proteins they bind to (known as receptor proteins).

In order to do this communication, neurons have a specialized shape made up of 4 anatomically distinguishable regions: the dendrites, the soma, the axon, and the presynaptic terminal. The dendrites are the main part of the neuron that receives inputs, or information. To be more successful at this task, dendrites often have a repeated branching structure, like a tree, to increase the surface area available for collecting information. This surface area is further increased by the presence of spines along the dendrites. There are often 2 inputs/spine where one is excitatory and the other inhibitory. Most synaptic connections received by a neuron occur on its' dendrites. There are many different types of dendritic fields, depending on a neuron's

role. Also, some neurons, often the specialized sensory cells like photoreceptors in vision, don't have dendrites, but instead specialized structures for collecting environmental information. In the photoreceptor case, this environmental information would be photons of light. Photoreceptor cells might be more correctly called neurosensory cells since they don't fire action potentials.

The next anatomically distinguishable region of a neuron is its soma. The soma is the main cell body of the neuron where the nucleus is located. It leads into a specialized section called the axon hillock region where information is encoded into action potentials. Since the neuron releases neurotransmitter molecules to move information from itself to another cell, it is really a type of secretory cell. This requires a large nucleus and many ribosomes in order to manufacture proteins needed to make certain neurotransmitters, as well as many mitochondria to supply the energy for the whole intercommunication process.

The axon hillock merges into the main axon, whose role is to transport the information via action potentials along its length to other neurons, muscle cells, or glands—either near or far. The axon connecting your spinal cord to your toe is ~1 meter or 3.28 feet long, while one motor neuron in a whale was found to be ~10 meters long. Since some of this information must be transported across biologically vast distances, the information must be sent in such a way that is reliable and doesn't dissipate: hence the action potential. Figure 2-3 shows an action potential from a retinal ganglion cell located in the back of an eyeball of *Ambystoma tigrinum*. Although one action potential may carry motor information and another visual information, the waveform is the same. The neuron encodes information into action potentials not by changing the action potential shape, but rather by changing the quantity of action potentials made, or their frequency. It is a standard that all neurons can use and relate to. At this point in the nervous system, information is encoded into a 'digital' representation as the action potential is either fired or not, there is no halfway sending of one. These electrochemical signals are also rapid—they can move at 120 m/sec or 268 mph! They are brief, being only about 1 millisecond long, and their amplitude does not dissipate as it travels down the axon. The axon extends from the axon hillock region of the soma. The axon hillock region contains many specialized proteins in its plasma membrane, called voltage gated ion channel proteins, which are needed to create the action potential. Information coming from other regions of the neuron, especially the dendrites, is integrated, or summed, at the axon hillock and if this integration exceeds a certain electrical threshold, then an action potential is fired and

sent down the axon. Bundles of axons in the CNS are called tracts whereas bundles of axons in the PNS are called nerves (sometimes long axons that reach out to the edges of our body are often referred to as nerve fibers).

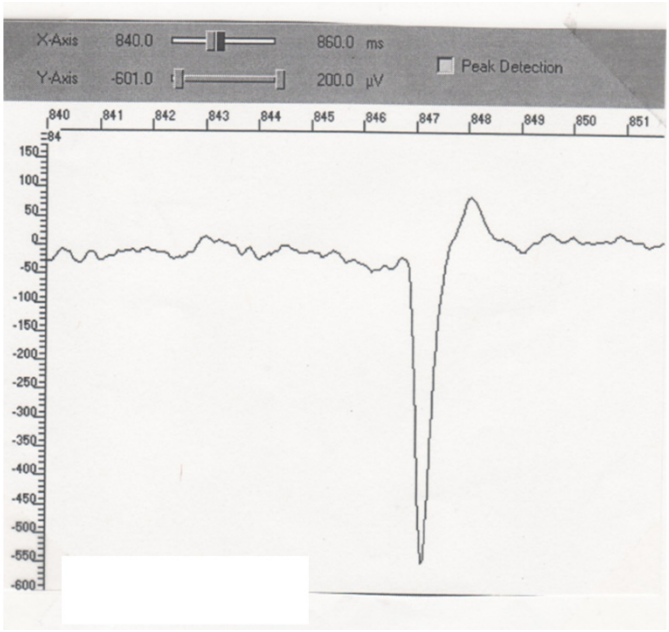

Fig. 2-3. An action potential recorded extra-cellularly (and so appears "upside down") from a neuron in the back of an eye of a salamander. (Recorded by Krishnaswamy, J. T. 2000)

The last anatomically distinguishable region of a neuron is the presynaptic terminal, sometimes just called the terminal, a synaptic bouton, or a synaptic end bulb. The use of the term presynaptic terminal is far more precise than axon terminal, as the axon terminal can refer to the point of the axon where it branches into several presynaptic terminals (as occurs with motor neurons) whereas the presynaptic terminal is the final end point of the neuron. The presynaptic terminal transmits the information from the neuron to the next cell, and is part of the synapse connecting the two cells. It is a swelling or bulge at the end of the axon, and contains tiny sacs, or secretory vesicles, that are filled with a chemical specific to the type of synapse, called the neurotransmitter. There are approximately a couple 1000 neurotransmitters in each vesicle. Neurotransmitters carry the information from the first neuron to the second neuron, by crossing the tiny synaptic cleft between