Alzheimer's Impact on Neural Pathways and Brain Structures

Aaron Wang

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Background

Fascination with the brain has only intensified as scientists decode this complex organ. Although it makes up a tiny fraction of the body's weight, the brain consumes around 20% of the body's blood supply and surpasses supercomputers in processing power. One of its most special features is the ability to recall and reimagine the past, called memory. Though not fully understood, memory constantly shapes identity and is central to the human experience. Alzheimer's disease, marked by memory loss, is becoming increasingly common with age.

Many parts of the brain are involved in storing and remembering. Based on extensive research and observation, the hippocampus, amygdala, cerebellum, and prefrontal lobe are believed to be the main structures involved in memory encoding and storage (University of Hawaii, n.d.).

A Basic Breakdown of the Brain

The brain is actually made up of many parts, and the brain itself is part of a larger organ system: the Central Nervous System (CNS). The CNS comprises the spinal cord and the brain, with the brain as the primary focus of this article. Going down another level, the brain is actually composed of several sub-organs, with the main ones being the cerebellum, pons, medulla oblongata, thalamus, hypothalamus, hippocampus, amygdala, and cerebrum. Sub-organs that are less relevant to memory will be oversimplified to spend more time flushing out the relevant parts. The cerebellum, although it means "little brain," is one of the most important parts of the brain. Located toward the back of the skull, it controls hand-to-eye coordination and muscle movement. The pons, located in front of the cerebellum but behind the front of the brain (forebrain), as well as being above the spinal cord, is involved in making facial expressions. The

medulla oblongata, located at the top of the spinal cord, controls metabolic and homeostatic processes, such as heart rate and breathing. The thalamus, located above the medulla oblongata, controls and processes sensory signals and acts as a distribution center, directing signals from afferent neurons (neurons that bring signals to the brain) to the appropriate parts of the brain for processing. The hypothalamus, located right next to the thalamus, is instrumental in controlling metabolic functions, hormones, and body temperature. The hippocampus, located around the thalamus, is important to memory processes. The hippocampus sorts through memories and distributes them to relevant areas of the brain for storage. The amygdala, attached to the hippocampus, controls our emotions. Because of its close proximity to the hippocampus, it probably plays a role in the emotional experience associated with a memory. Finally, the cerebral cortex is one of the most prominent parts of the brain. This cortex can be further broken down by function into cortices, or lobes. The prefrontal lobe, located at the front and behind the eyes, controls rational thought and reasoning. The temporal lobes, located behind the prefrontal lobe, interpret sound and language. The occipital lobe, located at the back of the brain, interprets visual images and signals. Information from our eyes travels here and is interpreted into images. The parietal lobe, located slightly in front and above the occipital lobe, contains structures that interpret senses. It is able to process signals of touch and other stimulations.

The Brain and Memory

When someone experiences something, the experience is first encoded and then stored. There is a massive difference between these two concepts. Encoding is the process of converting information into something the brain can interpret. On the other hand, storage is the actual storing of the encoded memories that can be recalled later.

Storage

In an experiment performed by Karl Lashley, rats were made to run and remember mazes. Then, lesions were induced on their brain to see if their maze performances were affected. In the studies, lesions induced after the rats had already remembered the maze had no significant effect on their performance. Soon, Lashley proposed the equipotentiality theory, which held that the entire brain was involved in memory storage and that if one area was damaged, another could take over. This shows that memory storage is relatively resistant to damage.

Encoding

The encoding of memories becomes more complex (not saying that storage isn't complex; in fact, it is not understood how neurons actually store these memories), with specific structures of the brain being involved. Here is where the hippocampus, amygdala, and cerebral cortex become relevant.

From multiple experiments and observations, the hippocampus was isolated as an important player in memory creation. People who had removed or damaged their hippocampus retained past memories made before the damage but were unable to remember anything after (Corkin et al., 1997). This shows that the hippocampus facilitates proper encoding of new sensory inputs and information, as people without a hippocampus have lost that function.

The amygdala also plays an important role in memory creation. Being attached to the hippocampus, it is almost obviously involved in memory. The amygdala regulates emotions as well as how emotions are attached to memories. In an experiment, the amygdala of rats was neutralized. As a result, they were no longer able to associate fear, the conditioned response, to a

specific musical tone, which was the conditioned stimulus (Josselyn, 2010). This meant that the amygdala was no longer able to sustain that memory of fear with the tone.

If extrapolated, this could also explain why traumatic memories or memories with high emotions are able to be stored deeply and be recalled well.

Alzheimer's and Brain Structures

As people get older, their brain normally shrinks a little, but it is not as significant as the shrinkage experienced by people with Alzheimer's. This shrinkage is caused by the accelerated loss of neurons as well as the malfunctioning of helper cells. When compared to a healthy brain, the brain of an Alzheimer's patient looks more shriveled, with more enlarged ventricles and cavities than the normal brain. This could explain issues with memory storage and recall, but from the equipotentiality theory, other brain parts can take over. However, brain damage still has an undeniable impact, and if other areas of the brain are damaged as well, the integrity of those memories that have been stored may decline in quality. Additionally, encoding is affected.

The Hippocampus

The first area affected by Alzheimer's is the hippocampus. In the early stages of the disease, the hippocampus experiences neuronal loss and plaque buildup. It was further observed that plaque buildup reduces the efficiency of the hippocampus and disrupts input processing. Furthermore, specialized cells in the area lose functionality, and the area shrinks (Rao et al., 2022). Encoding issues can be rationalized by this phenomenon. Memories formed after damage to the hippocampus may still be stored, but because they were encoded improperly, issues occur with recall. This fits into the overall narrative of Alzheimer's, as patients can recall events from

early in their lives in detail but cannot recall short-term events or memories made after damage to the hippocampus. As a result, Alzheimer's makes it extremely hard or even impossible to create and retain new memories.

The Amygdala

With the early onset of Alzheimer's disease, the amygdala is also observed to undergo atrophy. Deteriorating in tandem with the hippocampus, the shrinking of the amygdala was found to be associated with the onset of aberrant motor behavior, which is described as repetitive and meaningless actions (Poulin et al., 2011). Other than that, the role of the amygdala in Alzheimer's disease is still poorly understood and requires more research.

The Cellular Level

Many people think of the brain as being made of neurons, but there are actually many different cellular components, including neurons, that help the brain function.

Neurons

Let's start with the neuron. The neuron is one of the main components of the brain, responsible for communicating and transporting information throughout the brain and body. Neurons are recognizable for their numerous branchlike extensions, connections, and their slender cell body. The structure of this cell is very unique.

The cell body of a neuron usually operates in a similar way to other cell bodies, meaning that it contains a nucleus, membrane-bound organelles, synthesized proteins, and other things.

For the purposes of this article, there is nothing too special about the cell body of the neuron other than the lessons about the parts of a cell in school.

However, the neuron is unique in the way that it communicates, characterized by its branches. These branches are called dendrites. It receives and sends signals via synapses, which are contact points for neurons to communicate with other neurons. With these synapses, chemicals called neurotransmitters are released and received. Neurotransmitters tell the next cell what to do, meaning that they either inhibit or excite an electrical charge within the next neuron. When the signals from neurotransmitters are strong enough, they trigger an electric impulse, which is called an action potential. Through this process, information is exchanged in the form of electrical impulses and chemical signaling.

The axons also assist in transporting signals. The axon is a fiber that transmits electrical impulses to and from neurons. When the action potential is initiated, a signal travels along the axon terminal and is converted into other neurotransmitters to be passed along.

In addition, axons have helper cells. Axons can be covered by a myelin sheath, which is a protective fatty layer that helps expedite electrical signals. This fatty layer is produced by Schwann cells and oligodendrocytes, a type of helper cell that is another important player in the brain. These helper cells are typically referred to as glial cells.

Glial Cells

Glial cells are one of the most commonly found cells in the brain, even surpassing the neuron itself. Glial cells are basically cells that assist the neuron, whether it be by structurally supporting neurons, protecting neurons, or facilitating proper interactions between neurons.

There are several types of glial cells. The first is astrocytes. Making up the majority of cells in the brain, astrocytes have many functions. Astrocytes structurally support neurons and also regulate the extracellular surroundings. It also provides homeostatic functions as well as promotes synapse formation (Wei, 2023). These cells, being bigger than neurons, look like stars and look similar to neurons in the sense that they also have numerous extensions projecting from their cell bodies. Being so important to the brain, these cells also play a role in the onset of Alzheimer's disease.

Another type of glial cell is the oligodendrocyte. These cells have only one main function, which is to produce the myelin sheath to protect the axon. An oligodendrocyte can actually support and produce myelin sheaths for multiple cells at a time, meaning that it can grow to be quite spread out. Also assisting in myelin sheath production, Schwann cells line some axons. Not as relevant to the brain, as it is not found in the central nervous system, it also supports the integrity and efficiency of axons.

Another extremely important glial cell is called the microglia. These cells function and complement the immune system in the brain. It responds to unwanted intrusions such as pathogens, as well as clearing up debris. It also maintains the integrity of the brain in general by minimizing inflammation. As Alzheimer's is usually characterized by the buildup of debris and inflammation in some cases, microglia may also be an important player in the disease.

Impact of Alzheimer's on the Cellular Level

Let's analyze the effects of Alzheimer's disease on a microscopic level. With the onset of the disease, cell death is observed to occur, as well as the deterioration of synapses. This leads to the breaking of many connections and, therefore, inhibits communication. In a study, it was

observed that plaques and tangles found in the brain actually seemed to directly cause cells to initiate cell death. With the cells coming into contact with the debris, an RNA gene called MEG3 was observed to spike and directly cause the cell to initiate self-destruction. (Balusu et al., 2023).

Another phenomenon that was observed with the start of Alzheimer's was myelin breakdown. As plaques begin to show, the effects are felt by oligodendrocytes first, as they are particularly vulnerable (Maitre et al., 2023). As a result, oligodendrocytes start shrinking or dying out, therefore leaving existing myelin sheaths vulnerable to debris, inflammation, and plaques. With the breakdown of myelin sheaths, the efficiency of neural impulses decreases significantly, with electrical impulses being leaked out into the cell's surroundings and creating weak impulses. Therefore, connections between cells deteriorate significantly and may even die out without use.

What about the debris and plaques? Microglia are sometimes observed suffering from dysfunctions where they actually start to damage cells. It is not really understood about the cause of the malfunction, but with the increase of toxic amyloid plaques, microglia started to damage synapses and release secretions that damage cells (Hansen et al., 2018). These malfunctioning cells induce more inflammation and can speed up the process of Alzheimer's. Microglial interactions with Alzheimer's may act as a mixed blessing, and more research is required to understand the nature and causes of these malfunctions.

Astrocytes are a key player in homeostasis, as mentioned above. However, when Alzheimer's occurs, a calcium (Ca^{2+}) imbalance is observed. The regulation of Ca^{2+} is important because proper levels support cellular function, as it can act as a messenger and release neurotransmitters. However, with the imbalance in Ca^{2+}, inflammation in the brain and

neurodegeneration can occur (Benedetto et al., 2022). As astrocytes are an essential player in regulating Ca2+ levels by being a buffer, as well as coordinating Ca2+ levels. However, with the imbalance, it's implied that something is wrong with the function of astrocytes. Despite the malfunction not being well understood and requiring more research, a correlation has been established, and more research could be done on the topic.

Conclusion

Alzheimer's is a multifaceted problem, with many nuances and no clear-cut cause. This article aimed to provide an introductory dive into how Alzheimer's affects the brain from a broader sense as well as a more microscopic sense. Because Alzheimer's is so complicated, it's important to grasp a big picture of the disease and consider multiple perspectives, so it is encouraged that the reader should explore the broad impacts of Alzheimer's as well as impacts on the cellular level.

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