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The Hippocampus: A Review of the Development and Importance of the Hippocampus During a Person's Stage of Learning, Aging, and Injury

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Abstract. It has been recognized that the brain is one of the most important and complicated organs in the human body, and it is what sets humans apart from animals, but insight into how the brain controls behaviors, and through what processes people have become the way they are today lacks. Studying the distinct functions of organisms inside of the human brain, it is acknowledged that the hippocampus plays an important role in determining our personalities, learning abilities, and orienting skills. This review introduces the role of the hippocampus in different stages of a person's life (toddler, adolescence, and during and after adulthood), dominant functions of small parts of the hippocampus, and brain diseases that are caused by damage to the hippocampus such as Alzheimer's (AD) and Parkinson's (PD). Many common behaviors that are performed every day could be explained by brain mechanisms, and the brain diseases that we hear of constantly but feel distant about actually have many characteristics shared in common. The information is provided with the purpose of arousing readers' awareness of brain health by introducing hippocampal functions, brain chemicals, and pathologies of brain diseases. The most practical ways of preventing and detecting brain diseases along with the mechanisms behind those methods are summarized. Since AD and PD are two high-risk brain diseases, tips for interacting with patients who have AD and PD are also provided so that people will have an idea of how to treat their loved ones if they are affected by those diseases.

Keywords: cognitive science, hippocampus, Alzheimer's and Parkinson's, learning ability, brain disease prevention

1. Introduction

In the impressive study of neuroscience, not only the brilliance of the metabolism and self-regulation of the brain should be recognized, but also the significance of one particular organism within the brain that plays an important role in humans' learning, memory forming, and mapping—the hippocampus. Today, neuroscience has become one of the most valued and popular subjects in science and, in the past 20 years, many groundbreaking results have yielded and benefited human society. Scientists have connected social stress with brain responses using external devices, such as electroencephalograms, in their studies [1]. Having an insight into how everyday behaviors are connected to the human brain, particularly, the hippocampus, leads to an appropriate assessment of the brain stages and strengths and abilities of a person from neurobiology. Moreover, most people have heard of diseases such as AD and PD but have few ideas about their causes and mechanisms. This paper explains those diseases understandably and brings up the most practical ways of preventing and treating those diseases so that people no longer feel distant and fear of those diseases.

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2. Anatomy of the brain and hippocampus

2.1. Regional division of the hippocampus and the function of its surrounding brain features

The hippocampus locates in the allocortex, which is hidden in the medial temporal lobe (MTL), and there is one hippocampus on each side of the brain. Thus, the hippocampus cannot be seen from the surface of the brain but only in dissections. The hippocampus belongs to the limbic system of the brain which also contains the prefrontal cortex, another essential component of the brain that controls the learning and assessment ability of a person. The hippocampus is within a larger formation called the "hippocampus formation" which includes instruments that serve the nerve pathways. Adjacent to the hippocampus in the formation are sections of gyrus: the tail of the hippocampus connects with the parahippocampal gyrus which contains smaller sections called the entorhinal cortex and subiculum which are important for the flow of information into the hippocampus; in between those cortex and the hippocampus is a small region of brain matter called the dentate gyrus which is responsible for modifying incoming information so that the hippocampus can be associated with new sensory memories with past experiences.

2.2. Cellular composition of the hippocampus

The hippocampus is mostly made up of pyramidal neurons whose dendrites, unlike other types of cells, extend out from the apex and base [2]. The basal dendrites extend towards the lateral ventricles where circulate nutrition and waste for the brain; the apical dendrites then extend towards the dentate gyrus, where information has been modified. The axons of the pyramidal cells then send projections from the hippocampus to other parts of the brain.

2.3. Anatomical features

The name "hippocampus" comes from the Greek word "seahorse" because, when the organism is being looked at individually, it resembles the shape of a seahorse. The hippocampus is made of multiple layers of tissues: most layers contain pyramidal cells, but some contain dendrites and basket cells, and some layers contain hippocampal afferent fibers extended from the entorhinal cortex. The hippocampus itself is separated into four sections: from CA1 to CA4, where CA1 is adjacent to the subiculum, and CA2 to CA4 adjacent to the dentate gyrus. All sections of the hippocampus co-work with each other and the brain parts adjacent to them to modify incoming information and output information to other parts of the brain.

3. The function of the hippocampus during learning stage

3.1. Development and role of the hippocampus during early stages of learning

As a toddler grows older, his or her brain cells started to become connected, and communications between neurons and synapses form in a way that helps the toddler adapt to his or her surrounding environment the best: this is when the personality of the child starts to form, and the brain, at this point, also filters what kind of cognitive abilities and potential skills the child would have in his or her life later [3]. The hippocampus has already started to store memories and create associations between experiences and locations at that stage. As a child approaches puberty, along with the second round of overproduction in other brain regions, the hippocampus' growth in volume also explains teenagers' strong memory and learning ability. Entering adulthood, even though the human brain stops transforming in the same way as in its earlier stages and has become most efficient, it is still essentially malleable. For example, experiment data has shown that a London cab driver, who memorizes the whole map of London, has a hippocampus that is larger in volume than average because he or she has to use the function of memory in their daily work. Thus, through specific activities, the hippocampus and other parts of the brain could be strengthened and volumetrically grow.

3.2. Forming many varieties of memories

Usually, humans' memories could be categorized into two types: explicit and implicit memory. Explicit memories are intentional recollections of episodes and facts that usually takes time to learn and remember, whereas implicit memories are usually instincts and skills.

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The hippocampus recalls a past episode after the person receives an exterior stimulus by connecting certain features in the new stimulus with features that have already been preserved. As each hippocampal cell is assigned to store different features of past experiences, when a certain feature of a new event is present, the corresponding hippocampal cells react to that stimulus. Thus we are not only able to recognize certain situations, but also able to compare and assess them [4].

In this case, the hippocampus is responsible for all types (stages) of memories: incoming sensory memories could either stay and disappear soon as short-term memories or be stored as long-term memories. On the other hand, the hippocampus' capture of working memories is similar to the process of attaining a skill. For example, a person's capability of solving a math problem would be working memory. Researchers have found a surprising correlation between short-term memories and working memories, "while researchers typically separate working and short-term memory into two different categories, research often finds a significant overlap between the two" [5].

3.3. Pattern separation

Pattern separation takes place in the hippocampus and dentate gyrus: neuron patterns and activities that represent different information and experiences are formed with the least overlap with each other to complete pattern separation. To be more specific, once a person receives information from his or her senses, the brain would convert the representative elements in the information into a "sparse code", which, containing only a few units at a time, does not overlap with units in existing sparse codes, allowing the person to recognize and distinguish similar experiences rapidly [6].

Experiments have provided evidence of such activities taking place dominantly in certain hippocampus regions. Scientists use a cue mismatch paradigm to measure the place cell firing pattern in CA1 and CA3 regions when rotating subjects to expose them to different angles of a room [7]. Another group of scientists then do a similar study but, instead of keeping the subject in one room, they showed the subjects individual environments [8]. The result shows that the CA1 region performs significant pattern separation when the subjects are exposed to distinct information (the second study) while it shows less activity when subjects are exposed to information that is associated (the first study). In addition, CA3 demonstrates the opposite patterns of activities: it is more active when subjects are exposed to associated information (the first study) and, instead of performing pattern separation, it performs pattern completion— the neuronal activity where neurons that represent information that is associated overlap completely to form the full picture of a memory (experiment results are shown in Figure 1)[6].

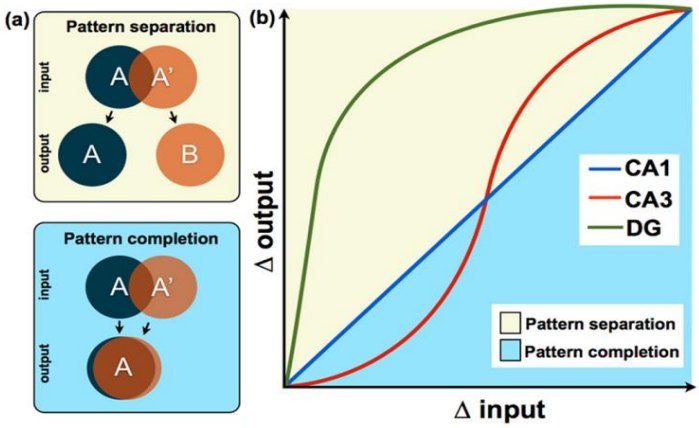

Figure 1. Different hippocampal regions and their role in pattern separation and pattern completion: CA1 vs CA3 [8].

3.4. Cognitive flexibility

Cognitive flexibility refers to a person's capacity to switch attention and operation between distinct situations and changing rules. It could also refer to one's capability to consider multiple factors when performing a task.

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Adapting to new situations—applying and modifying old information and strategies to new situations—is essentially the process of generating, updating, modifying, and integrating past and present information in response to the demands and constraints of new environments and experimental tasks [9]. Such a neuronal process takes place in the hippocampus and the prefrontal cortex. In other words, with the support of the hippocampus, people draw on their past experience when experimenting with new tasks: for example, people handle complex social moments at a dinner party based on their experience with the culture, language, and even the people around, which is stored in their hippocampus.

3.5. Navigation

Navigation cells either in, or outside of, the hippocampus form a network that stores spatial memories. Spatial memories include the locations of occurrences and objects, affecting one's ability to plan and remember a route to a location. The hippocampus offers one a spatial map of an environment using feature references and working memories.

Place neurons found in the hippocampus fire in a specific way when a person explores a new environment, forming the full map of the environment by representing locational features. Head direction cells then represent the neural substrate of the organism's perceived directional heading in the environment and enable accurate navigation [10]. Reliable evidence of the hippocampus' role in navigation is that people who suffer from amnesia, which is mostly caused by hippocampal deterioration, commonly experience disorientation as an effect [11].

4. The hippocampus in aging and disease states

4.1. Aging

A gradual decline in memory, especially working and short-term memories, signals normal aging. Even though experiments have not confirmed the chance of age-related deterioration or shrinkage of the hippocampus, a positive correlation between the size of the hippocampus and the strength of memory is proven [12]. Other than potential volumetric and structural change during the aging of the hippocampus, hippocampal activations and synaptic plasticity could be reduced in the elderly because of the inevitable increased oxidative stress and neuroinflammation that affect intracellular signaling and gene expression [13]. To be more specific, an aged brain's reducing basement membrane leads to vascular leakage, allowing the neurotoxic protein to approach the brain and causing oxidative stress and inflammation. Unfortunately, the hippocampus would be one of the first brain structures that suffer from this aging process [13].

4.2. Alzheimer's disease (AD)

The Alzheimer's Association defines Alzheimer's disease as an irreversible, progressive brain disease that slowly destroys memory and thinking skills, eventually even the ability to carry out the simplest task [14]. It is important to recognize the difference between AD and dementia: dementia is a broad term for any mental disorder caused by brain diseases. AD is the most common cause of dementia, making up 60% of dementia cases [15].

While brain cells' death and protein deposits are the main causes of common dementia [16], hippocampal dysfunction is the main cause of AD: the hippocampus' incapability to convert short-term memories into long-term memories explains why patients with AD cannot recall things that happened recently. In an AD patient's hippocampus, neurons, the subiculum, and many stratum structures are bilaterally lost. The loss of connection between the dentate gyrus and the CA sections of the hippocampus, which happens in the later stage of the disease, leads to cognitive disorders [17].

4.3. Parkinson's disease (PD)

Parkinson's disease is a degenerative neurological disorder that is characterized by the onset of tremors, muscle rigidity, slowness in movement, and stooped posture. Chronic disorders are caused by gradual loss and degenerations of neurons in the brain that are essential for motor functions [18]. Similar to that AD, the change in brain chemicals in PD patients harms their hippocampus. Studying the hippocampus, even though scientists have found no correlation between the size of the hippocampus of PD patients

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and memory, they have recognized the degeneration in hippocampal subfields (specifically subiculum, CA2, and CA3 fields) that has caused cognitive impairment and deficient in episodic recollection.

4.4. Mood Disorder

Oxidative damage and neuroinflammation also affect the hippocampus' capability to prevent stress and depression. A reduction in gliogenesis and extracellular fluid, as well as cellular shrinkage and dendritic retraction, have also been implicated in stress-related hippocampal atrophy [19]. Since hippocampal stress is a cause of continuous depression, people who suffer from depression usually show poor memory and reduced learning ability because of the change of mechanism in the hippocampus. Thus, a vicious cycle of growing depression and hippocampal damage would form if depression is not treated in time and correctly.

4.5. Epilepsy

Epilepsy is a chronic neurological disorder characterized by sudden and recurrent seizures which are caused by an absence or excess of signaling of nerve cells in the brain. The seizures caused by epilepsy, which is the classic symptom of epilepsy, are excessive stimuli to the brain and could harm brain health [20]. Epilepsy that starts from the temporal lobe could easily affect the chemicals in the hippocampus since the hippocampus is very sensitive to changes in brain activities. Untreated seizures caused by epilepsy could cause the hippocampus to shrink in size and partially inactive, which further leads to memory storage barriers in the brain [21].

4.6. Common ways to detect and prevent brain diseases, and ways to treat patients

Even though it is always safe to seek a doctor's diagnosis of AD, some signs can be followed for detecting AD:

- Memory Difficulties:
    - Difficulties to remember significant past events and dates.
    - Difficulties to associate locations with events, or simply a sudden loss of memories of well-traveled routes.
- Task Performing Difficulties:
    - Having extra difficulties at problem-solving or failing to perform skills that are well-attained.
    - Difficulties to find the correct words
    - Poor judgments and clumsiness.
- Compare to AD, PD's early symptoms are more subtle and easily mistaken as signs of simply tiredness and aging. Thus, those professional examinations are helpful to determine whether the abnormal physical change of patients are signs of PD:
    - Rapid Eye movements and Sleep Behavior disorder
    - Loss of sense of smell
    - Postural hypotension
    - Constipation [22]
- Mood disorder is common in the early stages of both AD and PD:
    - Sudden extremely negative emotions
    - Loss of initiatives

Other than being fully aware of brain disease patients' medical condition and respecting the medical routine they are given, we should be cautious and prevent frustrations while interacting with them. For example, creating distractions and leaving sharp objects around them should be avoided [23].

Moreover, people should be aware of the high chance of getting AD and start doing activities on a daily base that could lower the chance of AD. Since AD could be caused by dysfunction in the hippocampus, exercise training increases the oxygen level and vascular health is recommended. Games and social activities are good ways to keep the hippocampus active and prevent premature aging of the brain [24].

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Actions taken against the chance of epilepsy involve direct protection against brain injuries and exterior sources of infection:

- Prevention against traumatic brain injuries that disrupt the structures of the brain.
- Getting vaccinated against infectious brain diseases.
- Living a healthy lifestyle that enhances cardiovascular health [25]

5. Conclusion

The hippocampus has been active since the toddler stage to help store memory and skills. A pathway is formed by hippocampal subfields to receive, modify, and store information. Each CA field of the hippocampus has its dominant function such as pattern separation, pattern completion, and receiving information from the dentate gyrus. Since the hippocampus is responsible for learning abilities and is strongly malleable even after one's adulthood, cognitive flexibility and even personality depend on hippocampal developments. However, the hippocampus does not remain as efficient throughout one's whole life: since the hippocampus is a sensitive brain structure, the hippocampus is so sensitive that it is one of the first brain parts that experience the effects of aging. For example, both Alzheimer's disease and Parkinson's disease and the patients' following cognitive impairments and loss of memory are usually caused not only by direct hippocampal injury and degeneration but also by pressure and inflammation that comes from the whole brain. AD usually happens in people group who are over 65 years old, and the disease is characterized by one's loss of well-fixed memories and reduced abilities to problems solving. On the other hand, not all PD patients experience memory loss, but degeneration in the subfields of the hippocampus is commonly stimulated by changes in brain chemicals. Among the studies of those diseases, even though it is controversial whether the shrinkage of the hippocampus is certain and age-related, it is common for one to suffer from memory loss and cognitive impairment once hippocampus activity is reduced or any parts of the hippocampus are gone missing or injured. Among many of the precursors of those hippocampus-related brain diseases, mood disorder is mostly shared because hippocampal stress could reduce the hippocampus' ability to restrain depression or unbalanced chemicals. In terms of prevention of those brain diseases, it is important for people to always keep the brain active, thus, learning activities and aerobic exercises are always good choices to start with. People should be responsible for their own brain health and recognize that it is never too late to start caring for our own and our loved one's brain health.

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