Investigation of Memory Storage Conversion Focusing Hippocampus

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ABSTRACT: The data showed that the concentration of 2-thioalkylpentandioic acid in the brain cells of the mice increased significantly. Glutamate is involved in most aspects of normal brain function, but synaptic plasticity plays a major role in memory formation. Encryption specificity is an advanced theory that explains memory recovery as a process of encrypting and retrieving memories in the context of a situation. According to this two-stage theory, the memory recall initially involves retrieving information from a storage location and later includes verifying the authenticity of the retrieved information. Many areas of the brain are involved in memory restoration, but LTP is the best studied form and the one most closely associated with memory storage in mammals. Synaptic plasticity therefore continues to play a central role in the study of neuronal memory mechanisms and is therefore at the centre of the current discussion.

1. Introduction

Hippocampus is an important structure in mammalian brains, and one of its widely recognized functions is that hippocampus facilitates the consolidation of long-term memory storage. In other words, it plays a vital role in supporting the learning and memory process of animals [1]. A man named Henry Molaison has been suffering from memory vanishing after hippocampus was removed from both sides of his brain during a epileptic seizures surgery. Besides, Gilbert and Kesner (2002) identified that hippocampus was related to the associations between a stimulus and a spatial location during an experiment on rats.

Within the hippocampus, there are different kinds of neurons which serve as the primary functional units of the nervous system. And synapses are mainly responsible for the communications among those neurons (Sweatt, 2003). New neurons are generated every day in the Dentate Gyrus, where synaptic connections are made and information is transmitted to CA3. Previous research discovered that new neurons are involved in the process of new memory formation by adopting an approach to prevent the evolution of new DG neurons. However, it still remains unclear whether the specific mechanism through which the new neurons are used to store memory [2].

We tried to explore how the hippocampus works by refining the way it stores memory to the neural level. And the paper will concentrate on how the pieces and the structure of hippocampus participate in the operation of memory storage conversion. Here, we propose three possibilities: 1) New neurons are consumed to form new memories. 2) New neurons form synapses to make circuit to store memory effectively. 3) New neurons will generate stronger synapses to store memories through potentiation. The experiments described below will address these questions. In particular, I will use fluorescent labeling methods that make the dentate gyrus (DG) neurons produced by adult neurogenesis in an adult mouse fluorescent. At the same time, I will add fluorescent labels to DG neurons that are involved in storing a fear conditioning memory. This will make it possible to resolve whether new neurons are preferentially incorporated into neural circuits that are storing new memories [3].

2. Methodology

adult neurogenesis with a fluorescent Green Fluorecent Protein (GFP) marker. The GFP gene is carried on a retrovirus, which is injected into the mouse brain in the area of the hippocampus. The virus inserts itself and the GFP gene into the DNA of cells that are replicating their DNA. Thus in

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the hippocampus, only neural stem cells in the DG are infected and have the GFP gene added to a chromosome. All adult born neurons subsequently produced by the stem cell call the GFP gene too. My plan is to switch the GFP gene in the virus to a Cyan Fluorescent Protein (CFP; a blue fluorescent protein) [4].

A more recent paper by Denny et al (2014) uses a method to identify neurons in the hippocampus that store a memory during fear conditioning. The method relies on the transcription of the Arc gene in neurons that are 'active', that is – having rapid action potentials. In these transgenic mice, the Arc gene is fused to a gene that encodes the recombinase protein called CRE. When the CRE protein is made, it causes DNA recombination that activates expression of a GFP gene. When the animals undergo fear conditioning and are storing this memory in the hippocampus, the transcription (formation of mRNA) of the Arc gene is turned on in the active neurons in the hippocampus, which results in forming the CRE protein and causing recombination to turn on the GFP gene. This is a permanent change, so that these neurons are forever after labeled by GFP. Later, when we ask the mouse to remember the fear conditioning by returning it to the same cage in which it received an electric shock, some of these hippocampal neurons become active again as the memory is recalled. If the animals are immediately dissected and the hippocampus is stained with an antibody that binds to the Arc protein, we can see these neurons. According to the results of Denny et al (2014), the hippocampus neurons that are active during fear conditioning (formation of a memory) and during recall of the memory are very likely to be part of the neural circuit in the hippocampus that had stored that memory.

To determine whether neurons produced by adult neurogenesis are preferentially used to store new memories, mice carrying the transgenic genes for Arc-CRE and the recombination-sensitive GFP reporter gene will first be infected with the retrovirus that carries the CFP gene. After waiting two weeks for adult neurogenesis to produce new DG neurons that have the CFP label, the animals will be subjected to fear conditioning. This will induce the GFP label in all DG neurons are are involved in storing a memory. After one week, these animals will be returned to the cage where fear conditioning occurred in order to trigger recall of the memory (which will make the neurons encoding the memory active and turn on the Arc gene) [3][4]. The animals will then be killed and their hippocampus will be examined by antibody to the Arc protein, which will be attached to a red fluorescent dye. The hippocampus of these animals will then be examined by microscopy to identify the CFP-positive (new neurons), GFP and red fluorescent neurons in the DG (memory storage) in order to determine the overlap between these neurons. I will calculate the fraction of all DG neurons that are involved in storage of the fear memory and the fraction that are adult-born neurons. The results will address whether adult born neurons have a greater chance of being involved in memory formation than other DG neurons. If the adult born neurons are more likely than other (older) neurons to be involved in memory formation, this would prove that new neurons are indeed more available to be used in the formation of new memories [2].

Fear conditioning makes some neruons in the Dentate Gyrus become 'active' and they form a 'circuit' that is the storage of the memory. In other words, memory storage occurs in the dentate circuit as new neurons and old neurons are connected with each other to form synapses so as to achieve memory storage. Old memories and cells will be activated in the process of memory expression, and the cells reactivated in this process are components of memory traces in the dentate circuit of the brain. Denny's situational fear experiment tried to suppress the expression of related memory in the light heritage study of DG and CA3 cells, and finally found that DG is normally activated again and CA3 is reactivated. The activation level is associated with the strength of memory and the cells in adult-born granule DG contribute to the formation of memory traces. However, Germann et al. reported that the adaptive memory of mice was different from that in the research carried out by Kemp et al. There were two standard cages, one had wheels and the other didn't. The mice that could reach the wheel took advantage of the opportunity and were found to have new nerve cells twice as many as the sedentary ones, a number comparable to mice placed in rich environments. In the experiment, a higher rate of stem cell division was involved in the final effect, but it had no impact on the benefits of affluent people. When the mice were taken away from

the wheel for a period of time and then put back there again, some mice found that they could not get close to the cage while the others would show the performance as described in the first experiment. Therefore, fear conditioning can promote the formation of synapses in dentate circuit and the generation of memory through the expression of related proteins. Stimulating specific population of DG cells to recombine in the process of memory coding is enough to cause the expression of some corresponding memories. At the same time, we show that CA3 is reactivated at DG but many initially activated cells do not reactivate when terrible memories are recalled, indicating that only a small portion of a given set of activated cells may be dedicated to specific memory tracking.

Label the new neurons produced by adult neurogenesis with a retrovirus carring Blue Fluorecent Protein. In Denny's experiment, we used eyep (fluorescent green protein), arc (red fluorescent protein), and Hoechst (blue fluorescent protein) to label protein transcription in neurons, so as to observe the results pertaining to new neurons after a series of virus and protein transcription. That said, whether it can prove the memory connection between old neurons and synapses, and fluorescence in the data of protein transcription. The fluorescent protein (EYFP) line allows direct comparison between recently activated Arc^{+} cells and the permanently labeled EYFP + cells which are activated during the encoding process. 99% of the most recently activated Arc + cells are immune to the nuclear Cre recombinase expressed by Arc, Tamoxifen (TAM) and CFC, indicating a high fidelity between the expression of endogenous Arc protein and creert2 gene. In addition, the activated cells in DG were inhibited by photogenesis in the process of encoding fear memories, and CA3 inhibited the expression of corresponding memory. According to these results, we believe that the expression of DG and CA3 in activated cells is a part of memory trace [2].

Determine whether new neurons are used to store the fear conditioning memory. In order to evaluate situational learning, the animals were put back into the training environment and scored for fear behavior after training. It usually takes a short period of time to reduce fear. Similar to suggestive fear conditioning, situational fear conditioning shows both short-term and long-term forms. There is sufficient evidence that contextual fear conditioning is hippocampal dependent, mainly based on injury studies, selective infusion of drugs into the hippocampus, and hippocampal defects in transgenic animals [4]. However, there are still controversies over the hippocampal dependent conditioning of situational fear. A certain degree of control may not come as a surprise. The definition of “fear conditioning” is unclear. Generally speaking, when proteins in new neurons are expressed through retrovirus or other media, due to the plasticity of synapses, for the process of excitation and inhibition balance of brain, new synapses will regulate gene expression when connecting with old synapses, which is regulated by neurons.

3. Results and Discussion

This long-term consolidation process can be observed in patients with hippocampal damage who have relatively normal memories of childhood, but are impaired when they recall experiences that occurred during their amnesia. This is probably a process that stabilizes the memory in the brain. As memories consolidate, their long-term storage is distributed to different parts of the neocortex. It is not just about remembering things that most people pick up on in their everyday lives, but also about things in the past, such as the names of people and places.

By contrast, brain systems that depend on certain types of learning, such as those described above, are involved in the hippocampus, a brain system responsible for storing and restoring memory, and it includes pathways that are used not only in memory, but also in learning and memory processing. While groundbreaking studies have identified important memory classifications and helped to solidify the notion of functional localization on a broader anatomical level, they have provided little information about the mechanisms that operate at the finer levels of individual neurons and synapses. The next step forward allows the hippocampi to play a similar role in the formation and storage of memories.

When an animal enters a certain area of a spatial environment, the location of the cells refers to changes in the spatial orientation of the neurons in that area as well as to the location of the

synapses. According to the National Institute of Mental Health, excitatory neurotransmitters are responsible for promoting signal flow between nerve cells, thereby supporting the proper functioning of the cells. There are a number of different types of neurotransmitters such as acetylcholine, serotonin, dopamine, glutamate and GABA, which are able to send signals to and from nerve cells and play an important role in learning and memory under normal conditions. A series of 2-thioalkylpentandioic acid was synthesized and investigated in the study for its possible role as a memory storage medium.

The data showed that the concentration of 2-thioalkylpentandioic acid in the brain cells of the mice increased significantly. Glutamate is involved in most aspects of normal brain function, but synaptic plasticity plays a major role in memory formation. Encryption specificity is an advanced theory that explains memory recovery as a process of encrypting and retrieving memories in the context of a situation. According to this two-stage theory, the memory recall initially involves retrieving information from a storage location and later includes verifying the authenticity of the retrieved information. Many areas of the brain are involved in memory restoration, but LTP is the best studied form and the one most closely associated with memory storage in mammals. Synaptic plasticity therefore continues to play a central role in the study of neuronal memory mechanisms and is therefore at the centre of the current discussion.

4. Conclusion

By using GFP to label and transform the DG and Arc-related neurons in the hippocampus of adult mice, we can observe the related reactions of the active neurons related to Arc gene, such as DNA recombination, GFP gene expression, and mRNA transcription. These reactions show obvious phenomenon through antibody staining combined with Arc protein Recall to observe and infer. In other words, under the condition of fear, the related neurons in adult body will be activated, forming a circuit in DG and CA3 to reflect the learning, training and change of environment and events to respond to the changes of external conditions, which is guided by the transcription of related proteins and the rapid change of neuron action potentials.

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