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Information impact on synaptic arousal and formation of permanent memory trace

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Abstract: Memory trace is an effect of temporary arousal (perception, experience, action) that causes a specific change in the nervous system. Memory allows to record and recall various information, thus enabling to learn new things. It is an extremely active and dynamic process. The influence of emotions on memory is obvious, largely determined by the close cooperation of the amygdala (responsible for emotions) and the hippocampus (memory processes).

Keywords: memory, memory trace, consolidation, brain plasticity, engram, emotions.

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Memory can be defined as an ability to acquire, process, store and restore information. The essence of memory is the creation of permanent changes in the nervous system called memory trace. Memory formation consists of several phases: information preservation (memorization), information storage in the nerve cells responsible for it, information restoration (recall) and recognition of information type [1]. Due to duration of memory trace, three types of memory are classically distinguished: sensory, short-term memory (STM) and long-term memory (LTM). The mechanism of memory formation is complex, and virtually the entire central nervous system (CNS) is involved. Nerve impulses reaching the brain trigger many effector reactions in the nerve cells located in distant parts of the brain. The process involves the old and new

cortex, numerous brain centers and the hippocampus, which is the most important structure related to the anatomy of memory. Damage to the hippocampus usually causes the most severe memory impairment. The frontal lobe is the center of short-term memory while temporal lobe is the center of long-term one. New information is stored in the prefrontal cortex and following sent to the hippocampus — it is there where it undergoes processing and is preserved in the form of protein engrams in various centers of cerebral cortex [2].

When reviewing recent scientific research, a certain tendency and its direction can be noticed. Much of the research was devoted primarily to understanding biological mechanisms that make up memory and contribute to its storage. Studies on temporal lobe-dependent memory performed on vertebrates such as *Aplysia californica* and *Drosophila melanogaster* prove that molecular changes at all levels (post-translational, translational and transcriptional) have a significant impact on the formation of LTM [2–4]. In the near future, it seems necessary to take up steps in order to elucidate molecular mechanisms within RNA (e.g. RNA binding proteins, epigenetic regulation of RNA), which are responsible for the regulation of consolidation over individual systems and finally for the durability of LTM. The latest research techniques such as: iDISCO, CLARITY, in vivo optical protein control, epigenetic markers, gene editing and in vivo transcriptional imaging are supposed to help in understanding better the patterns of memory storage over time. That would allow to select effective methods of treating memory disorders (e.g. Alzheimer's disease, age-related memory loss, post-traumatic stress disorder) [5].

Creating memory trace

Memory is the result of chemical changes that take place in the nerve cells of the brain. Depending on severity and intensity of the stimulus, synaptic connections between neurons are stimulated. Continuous synaptic enhancements keep neural connections working together, making them much more efficient. This mechanism, which is the basis for the formation of memory trace, can be simply described as a new quality in the nervous system, created as a result of stimulation, lasting for a specified period of time. Research conducted in the USA has shown that noticeable parallel changes in the regions of postsynaptic and presynaptic membranes are the result of long term strengthening in the microstructures of synapses [6].

A memory trace is the product of various sensations induced by perception, experience, or action. It is created by an electric impulse (information) travelling from one synapse to the other. In this process, between the synapses, a memory trace (a place where information is exchanged) is formed, expressed as a chemical substance. The quality of the trace increases with multiple repetitions and especially when the process is accompanied by emotions. The formation traces is a continuous cycle.

While coding one, perception of the stimulus produces new, unstable engram. During consolidation, it is strengthened, given stability features and integrated with the existing layers of knowledge [7, 8].

Brain plasticity

The brain is one of those organs that works continuously. The slightest gesture, movement or thought activates millions of neurons. Each sensation initiates a new neural connection—if the brain considers it important, it will be remembered. At the level of nerve cells, formation and elimination of such connections is called synaptic plasticity [9].

The brain is most adaptable in its early stages of development. The functional changes are accompanied by those on the structural level. All those generated structural changes are the result of initial strengthening of the available neuronal networks. Numerous research in the area of cortical map reorganization suggests that there are no inactive sites in the brain. Regions not responding to external stimulation are rapidly being taken over by the surrounding neighborhoods. There is a view that this organ operates according to the “use it or lose it” principle [10]. For example, taxi drivers showed enlargement of the posterior parts of the hippocampus — that is regions of spatial memory allocation. It is believed that constant training of a given type of memory contributes to the above-average growth of the region directly responsible for it [11]. A similar relationship between the enlargement of the area responsible for the language (the posterior area located in the lower parietal cortex) was found in bilingual people [12]. The plasticity mechanism is best illustrated in an experiment in which small cats had one eyelid sewn together. It turned out that the eye that remained open stimulated more cells than usual in the brain, and after the previously covered eye was exposed, there was a permanent loss of spatial vision (amblyopia) [13].

Practical dimension of brain plasticity is especially important for one’s health and his development. It is important to strengthen the connections that support learning process and those responsible for desired reflexes or useful habits, as well as weaken the connections that will further result in addiction.

According to the Atkinson-Shiffrin’s model, sensory, short-term and long-term memory can be distinguished. In the process of remembering, first of all, all data goes to sensory memory, which has a large capacity but a relatively short storage time (several hundred milliseconds). Therefore, its content must be transferred to short-term memory, often called the working one [14].

The sensory phase described by Sperling is conditioned by the activity of the impulse that stimulates neurons towards action [15]. The author focused on the importance of the visual (iconic) form of sensory memory. Research in that field

was carried out by Vandembroucke *et al.*, emphasizing enormous possibilities of human visual perception. The input data captured by the retina of the eye is stored for a short time in order to allow attention processes to focus perception on a specific feature of the stimulus so that it can be seized and further remembered [16]. Haber proved in 1983 that the mechanism described above can occur, but only when the object is not in motion [17].

Short-term memory, on the other hand, has small capacity — information is stored for a maximum of one minute. It is easily disturbed, both as a result of various diseases and under the influence of strong stimuli. For about a minute, without preserving in the mind, we remember fleeting events or facts that caught our attention. Making use of such record is not complicated due to its limitation and constant availability of consciousness. Along with the development of neuroimaging, scientists were able to locate brain regions responsible for main STM components (Table 1) [18].

Table 1. Structures responsible for short-term memory [18].

VERBAL SIGNS	SPATIAL SIGNS	VISUAL SIGNS
<ul style="list-style-type: none"> — left inferior frontal cortex — left parietal cortex 	<ul style="list-style-type: none"> — right posterior dorsal frontal cortex — right parietal cortex 	<ul style="list-style-type: none"> — left inferior frontal cortex — left parietal cortex — left inferior temporal cortex

The actual memory segment with great data storage capacity is the long-term memory. The key role in this case is played by neurotransmitters and engraving proteins isolated from the hippocampal neurons of the Californian snail, which is an extremely convenient model to study due to its specific anatomical and cellular structure (20,000 large nerve cells). In mice, it was possible to recognize the type of protein (CREB) which is the carrier of LTM. Research proves its presence in all animal brains [2].

The sequence of events of the memory process is initiated by sensory memory, which in a few hundred milliseconds can record many details of an image. Seconds later, STM can perceive only a small number of them. Few days later, only the essence of what was observed before is remembered. LTM has a large capacity for images. Standing in his study showed the participants 10 000 images, each for a few seconds. Some of them were remembered with an accuracy of 83% [19].

Despite the fact that memory itself, considered to be permanent, has no time limit — all information can stay there as long as they are useful — such limitations occur at the stage of recording the memory trace [20]. To be effective, this process should take no more than a minute — after that time the record will be lost. In this case, memory cannot be improved by training, it can only be improved by stimulating the noradrenergic system [3]. Even if written in a permanent form, it is initially quite unstable and can be easily disturbed by pharmacological factors (long-term use of benzodia-

zepines, statins, opioids), molecular (within synapses or neurons) or behavioral (cognitive abilities, emotions, personality traits) [2–4].

For more efficient memory recall, all information is coded according to its characteristics. Every image captured by the senses is processed in such a way that it is possible to recreate its meaning. The process of strengthening and stabilizing memory is known as its consolidation. Recent research suggests that it is possible to lose the durability value again as a result of activating the content in the recall process. However, instability does not last long and memory may return to its initial state during the reconsolidation phase [21]. The process of consolidation and reconsolidation takes place in a rather uneven environment, therefore it is possible to strengthen and weaken the memory trace. Even though, latest research emphasizes the meaning of multiple consolidation through active restoration and recall of the saved data, which extends the duration time of their availability. The activated stimulus (scene or sound) can recall facts recorded many years before [22].

A disappearing memory trace can be refreshed by a repetition technique. Marchetti pointed to the importance of attention as a mechanism capable of dealing with limitations of human perception systems responsible for creating memory. Attention allows for a selective choice of quantitatively assimilable information. It selects and intensifies data that can be combined in different ways to build theoretically unlimited chains of constructs [23]. In some models, attention is assigned with the role of a separate element in the system with a supervisory status.

Despite the distinction between short- and long-term memory made by Donald O. Hebb in the 1940s, there are still many concepts that associate them into one process [24]. However, no reliable studies to unequivocally confirm this theory have been conducted [25].

It was possible, however, to identify an element considered to be a connection between STM and LTM in complex cognitive processes. According to some models, this function is performed by working memory (WM). WM can be described as an ability of temporary preservation and manipulation of information that is held activated for later usage in associated cognitive tasks. The three kinds of memory (STM, LTM and WM) are greatly interconnected to such an extent that they cannot work independently in any cognitive procedure. WM processes new information from STM as well as retrieves/puts in information from/to LTM contiguously. It suggests that WM connects STM and LTM and plays an important role in complex cognitive processes. For instance, during the task of calculation, STM is involved in storing the individual digits and their place within the number while WM retrieves arithmetic skills (addition or multiplication table) from LTM to manipulate the numbers in a proper order. Nie *et al.* [26], using functional magnetic resonance imaging (fMRI), located the areas of the brain responsible for these types of memory for numerical figures. The study was performed on a relatively small sample of respondents using three types of memory tasks for numbers. The results

showed variable patterns of activation in various cerebral areas responding to different types of memory tests. It was found that the most highly activated regions of STM for digits are localized in the visual cortex with mild right hemispheric predominance, and encoded by visual representation. On the other hand, LTM was encoded by semantics and activated left frontal cortex; the left hemispheric predominance was found. An important role of the subcortical structures (e.g. caudate nucleus and the marginal division of the striatum) in WM was also confirmed [26].

According to Alberini, STM is based on existing networks and post-translational modifications, while LTM is rather based on functional and structural changes in neural networks [27]. Any damage to certain brain structures provides more and more evidence supporting the thesis about the autonomy of both types of memory. People with parietal and temporal lobe abnormalities reveal short-term phonological predisposition deficit with no consequences for LTM. On the other hand, it is often found that in case of damage to the medial temporal lobe (MTL), LTM becomes disturbed while the functioning of STM is still preserved [28].

Emotions and memory

Memory largely depends on the load of positive or negative emotions evoked by a specific event. When the situation is exceptional, its potential for influencing the senses differ from usual state, an appropriate memory mechanism records the event with the image accuracy. Therefore, events with high emotional burden are remembered in detail after many years. Many of the described theories on emotional memory enhancement focus indeed on the level of stimulus arousal (words, images). A positive effect has been achieved in behavioral (the words “taboo” as a reinforcing element) [29], neuropsychological (evaluation of patients after temporal lobectomy) [30] and radiological (the influence of emotional stimuli in elderly people and people with dementia) aspect [31]. It should be noted, however, that the stimulation of emotional elevation through an event may affect the persistence of its memory. The evidence suggests that the details of negative events are better remembered than those with positive meaning or neutral ones. However, there are several studies which reveal that the mechanism of emotional reinforcement also applies to positive stimuli [32]. Positive impressions tend to be more distorted than negative ones. Presumably, emotional intensification of memory is the result of a more effective consolidation of memory traces as well as the modeling effect of the amygdala on the hippocampus. More efficient coding of this type of experience can directly strengthen the engram and later on its faster recognition. There is evidence that they automatically attract attention, but such interaction only occurs when the amygdala is properly structured and functioning [33].

For a person with their own internal sense of health assurance, a picture or description that somehow destroys it, will certainly not be pleasant. For example,

prohibition signs in various forms are constructed to evoke emotions that can be firmly encoded deep in the mind. In repeated, even superficial, contact with the warning product, substance or place in order to emphasize the effect of reception this coded data will be revived and recalled. Within time even emotional facts become distorted. Consistency in the portrayal of events is an individual trait. Not all those who have seen a warning that generated negative emotions will be able to identify when they saw it for the first time and where they came into contact with it [34]. A person who has seen, for example, a sign prohibiting the consumption of alcohol in pregnancy on television, may claim after a few months that the sign was shown by their father who commented on its meaning. Various signs and symbols are used to enforce or change our behavior patterns. It seems important to understand the psychological mechanisms that make it possible.

E. Scott Geller [35] formulated the following thesis:

- any alerts are more effective when they are in close proximity to the point where expected behavior change is desired
- they clearly state the intentions of the regulator or at least suggest an alternative solution
- the expected response is acceptable to the recipient
- information is presented in simple, clear language.

There is no consensus on the universality of this principle. General guidelines for the development of warnings have been provided, but they do not specify their effectiveness once being followed. Understanding and decision making are the two psychological key processes that characterize effective labeling. With regard to commonly known signs, even the obviousness of the purpose for their introduction does not affect effectiveness [36].

There is a view that emotional memory is characterized by a subjective freshness of remembering, not the details of it. The release of stress hormones contributes to the categorization of the received stimuli. It has been proved that stress changes morphology of neurons, suppresses their proliferation and reduces the volume of the hippocampus [37]. Injection of high doses of corticosteroids to rodents in a stressful environment caused disturbances in spatial memory, which is directly monitored by the hippocampus. It is assumed that this situation is caused by the mechanism of DNA methylation and histone modification in the hypothalamic-pituitary-adrenal axis [38]. In addition, memory activation occurs when corticosteroids and norepinephrine are released, initiating interactions in the proper structure of amygdala with other areas important for sensory and mnemonic processing. Anderson *et al.* believe that even briefly coexisting emotional and neutral events are coded more persistently [39]. At neuronal level, during the neuroimaging examination, one can observe a correlation between the level of the activity of amygdala and hippocampus in the processing of the emotional signal, as well as when recalling this modulated information in fronto-

orbital cortex [40]. The hippocampus, as a core element in building memory, is systemically connected to other collaborating centers. Every damage to the hippocampus directly converts into disorders within the centers. It is known that glial cells are involved in the processing and memory storage, still the underlying mechanism has not been fully understood. Their number was found to be above average in the brain of famous people (e.g. Einstein) [2]. Astrocytes contribute to the release of the so-called gliotransmitters (substances with a chemical structure similar to neurotransmitters). The studies found that astrocyte-defective mice could not distinguish between new things in their environment [41]. On the other hand, another experiment proved the impact of astrocytes disturbance on consolidation of memories and LTM. For this purpose, the rodent was deprived of the inositol 1,4,5-trisphosphate receptor type 2 (IP3R2) located in astrocytes, which acts as a link to other cells via calcium channels. At first, no cognitive difference was observed compared to the control group. However, after 2–4 weeks, individuals without the IP3R2 receptor made twice as many errors as those in the control group [42].

It should be noted that each situation is accompanied by a store of emotions, usually dependent on details, in normal circumstances even impossible to trace. The way some information is perceived differently, as mentioned above, is related to the course of its processing during the encoding. Over time, even emotional facts become distorted, but the consistency of the portrayal of events is an individual trait.

Summary

Memory creation is a dynamic process comprising several steps (encoding, consolidation, recovery, storage). The past two decades have enabled scientists to understand significantly the molecular and cellular mechanisms that occur in the brain during various phases of memory formation. This knowledge greatly enables the search for new methods of combating pathologies such as post-traumatic stress disorder (PTSD), anxiety, phobias and addictions. Nevertheless, the biology of memory formation, especially occurred in early stages of the development of the above-mentioned diseases, has not been fully understood.

Memory has a unique ability to store and recall information at a later time. It is an indispensable element of cognition and understanding the rules of the surrounding reality. Memories play an important role in the life of every individual, they control emotions, stimulate thinking, and influence decision making. Each day an individual receives a lot of information, mostly in the form of images or sounds. Some of it is important, worth coding in the mind, while others become negligible and lead to creating unnecessary burden. Even those data stored in memory resources are recalled selectively. Some of them are found and used in various processes while others are simply ignored.

Conflict of interest

None declared.

Abbreviations

LTM — long-term memory
STM — short-term memory
WM — working memory

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