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REGULAR ARTICLE

Receive, Retain and Retrieve: Psychological and Neurobiological Perspectives on Memory Retrieval

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Abstract

Memory and learning are interdependent processes that involve encoding, storage, and retrieval. Especially memory retrieval is a fundamental cognitive ability to recall memory traces and update stored memory with new information. For effective memory retrieval and learning, the memory must be stabilized from short-term memory to long-term memory. Hence, it is necessary to understand the process of memory retention and retrieval that enhances the process of learning. Though previous cognitive neuroscience research has focused on memory acquisition and storage, the neurobiological mechanisms underlying memory retrieval and its role in learning are less understood. Therefore, this article offers the viewpoint that memory retrieval is essential for selecting, reactivating, stabilizing, and storing information in long-term memory. In arguing how memories are retrieved, consolidated, transmitted, and strengthened for the long term, the article will examine the psychological and neurobiological aspects of memory and learning with synaptic plasticity, long-term potentiation, genetic transcription, and theta oscillation in the brain.

Keywords Memory · Learning · Consolidation · Synaptic plasticity · Neurotransmitters · Long-term potentiation

Introduction

Memory refers to the storage of perceived information, the cognitive process essential for learning and developing other cognitive skills. The human brain perceives the stimuli through sensory memory, stores them in short-term or working memory, and passes the information to long-term memory (Baars & Gage, 2010). Though sensory memory and short-term memory process the perceived representations,

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long-term memory is necessary for the long-term storage, retrieval, and association of information (Brem et al., 2013). Long-term memory significantly contributes to the unlimited storage and stabilization of information for memory retrieval. Further, memory storage, reactivation, and retrieval also play a significant role in learning. The retrieval of memory facilitates learning by accessing the relevant information and connecting them with the current stimuli (Packard & Knowlton, 2002).

Studies on cognitive neuroscience demonstrate that the storage and maintenance of memory are influenced by the transmission of information from sensory memory to long-term memory through the synaptic plasticity between neurons. Also, it is known that billions of neurons present in the human brain act as information messengers by transmitting information, thus strengthening them for a longer time (Knierim, 2014). This rapid and consistent transmission and strengthening of information are required for memory and learning (Raman et al., 2019).

Despite decades of research exploring the relationship between memory and learning, the holistic understanding of the psychological and neurobiological process of memory retrieval from long-term memory and its role in learning is still lacking. Therefore, this article provides the psychological, neurobiological, and biochemical perspectives of memory retrieval by shedding light on how long-term memory plays an important role in learning. In an attempt to know the neurobiological processes of memory and learning, the article explains the process of synaptic plasticity between neurons for the transmission of information and long-term potentiation for the strengthening and retention of memory that is necessary for learning. In addition, the article discusses the neurotransmitters, genetic transcription factors, and theta waves that are activated to transmit and strengthen the information for memory retention and retrieval.

Memory Retrieval

Memory retrieval is remembering and reinstating stored information from long-term memory. The retrieval of memory updates the old memories with new stimuli and environmental cues (Lockhart, 2001). The process of memory retrieval is equally important for learning, similar to the process of encoding and storing memory. Whenever the memory is encoded, the information forms a memory trace or engram. During retrieval, the memory traces are changed and reactivated for effective learning (Katkov et al., 2017; Woodward et al., 1973). The engram cells in the brain undergo biochemical changes that help to store and retain memory. While learning, the engram cells are activated and modified depending on the external stimuli (Han et al., 2021). These learning-induced changes by engram cells induce persistent changes in the neurons. During the perception of stimuli, the neuronal excitability state of engram cells decides the retrieval of memory (Tonegawa et al., 2018). Following that, the reactivation of those engram cells increases the excitability state during the retrieval. The reactivation or awakening of the engram cell for the process of retrieval requires contextual cues from the environmental stimuli. This process of influencing the engram out of its latent state into manifested activity is called

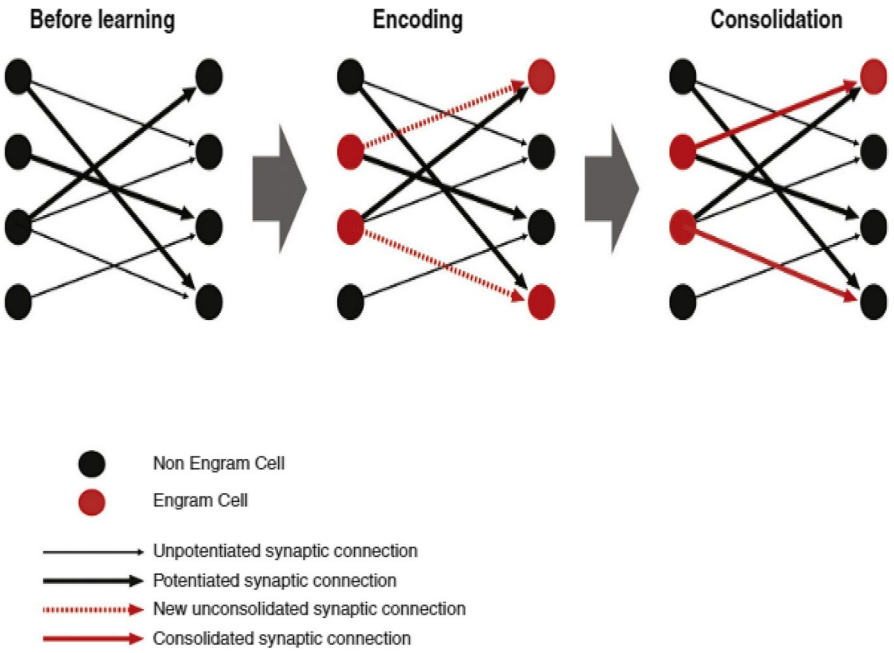

Fig. 1 Activation of engram cell. Modified and reused with permission from (Tonegawa et al., 2015)

ecphory (Steinvorth et al., 2006; Tulving et al., 1983). Figure 1 shows the activation of engram cells during encoding and the learning-induced changes during retrieval.

The effective retrieval of memory requires the rehearsal and reactivation of information. After the perception of memory, the spacing between the information encoded and the duration of information stored depends on the time window of memory (Kornmeier et al., 2014). The time window is a limited period within which additional information interferes with the primary memory, thus strengthening or weakening the memory (Bell et al., 2014). During this spacing, the information would be labile, and the process of memory consolidation stabilizes the information from short-term to long-term memory (Alberini & Ledoux, 2013). Further, the stabilized memory is reactivated by memory reconsolidation that modifies and strengthens the memory for permanent storage. The process of consolidation and reconsolidation strengthens and enhances the memory to be more accessible during

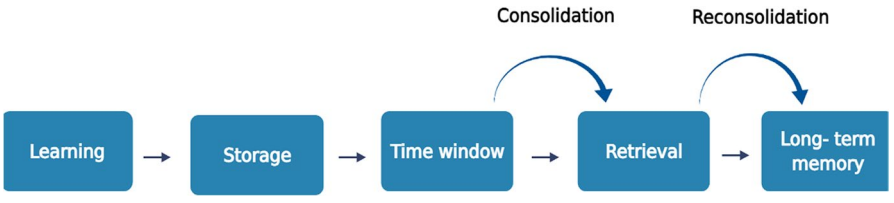

Fig. 2 Stabilization of memory

the retrieval (Alberini, 2011; Herszage & Censor, 2017). Figure 2 illustrates the process of consolidation and reconsolidation for the stabilization of memory.

Though the memories can be stabilized in the long-term memory, sometimes the stored memory may get interfered with or disrupted during retrieval, causing retrieval failure or forgetting of the memory (Anderson & Neely, 1996; Kerrén et al., 2021). The retrieval failure majorly occurs by memory decay and memory interference. Though long-term memory stores information for an extended period, some information fades or decays from long-term memory (Davis & Zhong, 2017). In an experimental study of memory decay, Ebbinghaus (1855) found the forgetting curve, which shows that memory decreases exponentially with time. The experiment proposes that any new information learned and processed in long-term memory decays if the information is not reactivated at regular intervals (Nelson, 1985). The time gap between first-time and second-time learning decides the saving measure of the primary input. This saving measure decides the retrieval of the information and also saves time when the information is learned for the second time (Miller, 2021). On relearning, the saving measure increases, and the information is relearned in a short interval of time. However, when a long time is taken to relearn the information, the measure of saving decreases leading to the decay of the memory (Murre & Dros, 2015). Retrieval failure also occurs when there is an interference of associated memories during retrieval. Proactive interference occurs when the previous knowledge interferes with the recently perceived information. Retroactive interference occurs when the newly learned information disrupts the already stored information in long-term memory (Chanales et al., 2019; Unsworth et al., 2013). Figure 3 explains the exponential nature of forgetting by plotting a forgetting curve with the time window between retention and memory decay that decides the storage period of the information.

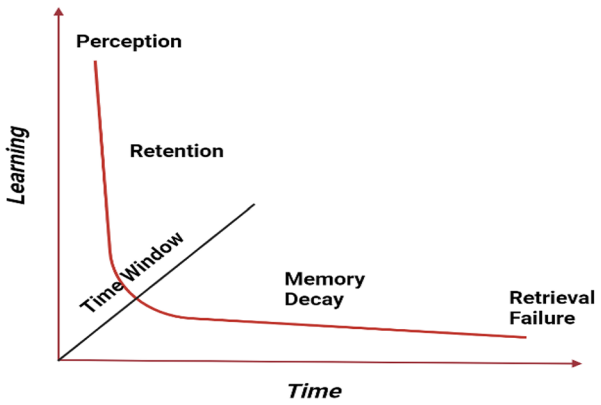

Fig. 3 Forgetting curve

Synaptic Plasticity

The retention of information in the memory traces and stabilization of information by memory consolidation requires the transmission of information from one neuron to another. The neurons are the fundamental units of the brain that transmit information perceived by the sensory region of the brain. Synaptic plasticity is the process of strengthening or weakening the synapses to effectively communicate with neurons. The synapse is the junction between the axon of one neuron and the dendrite of another neuron (Langille & Brown, 2018; Lee et al., 2021). Further, the neuron which initially passes the information is called a presynaptic neuron, and the neuron which receives the information is called a postsynaptic neuron (Abraham & Bear, 1996). According to Hebb's postulate, synaptic plasticity follows the principle, "the neurons that fire together, wire together" (Hebb, 1949). When neuron A is excited, it fires spikes or action potential that cause depolarization of neuron A which reaches a threshold to wire with neuron B (Choi and Kaang, 2022; Mittal et al., 2018). In addition, the synapses can be either excitatory or inhibitory; when neuron A is excited, and neuron B is also excited, there will be an increase in excitatory postsynaptic potential. When neuron A is excited, and neuron B is not excited, it inhibits the postsynaptic membrane potential (Adams et al., 2016; Druckmann et al., 2014). Also, the connection between the presynaptic and postsynaptic neurons is of two kinds, electrical synapse and chemical synapse. The electrical synapse uses the gap junction between neurons, and the chemical synapse uses the synaptic cleft, where the neurotransmitters transmit the information between the neurons (Goto, 2022).

The neurotransmitters are the chemical signals packed inside small sacs called vesicles in the presynaptic terminal. After the depolarization of the presynaptic neuron, the voltage-gated calcium ions present in the neuron move toward the neurotransmitters that activate its transmission. Further, the neurotransmitters pass through the synaptic cleft to reach the postsynaptic neuron (González-Espinosa & Guzmán-Mejía, 2013). Then the neurotransmitters are transmitted to the chemically gated channels on the recipient postsynaptic neuron (Südhof, 2012). When these chemically gated channels of the postsynaptic neuron open with sodium ions present on its surface, it causes excitation in the postsynaptic neuron, and when the channels open with potassium and chloride ions, it inhibits the postsynaptic membrane potential (Kneussel & Hausrat, 2016; Silva et al., 2021).

Therefore, the excitatory postsynaptic potential between the neurons decides the synaptic strength and effective synaptic plasticity (Fusi, 2008; Jackman & Regehr, 2017). Depending on the number of neurotransmitters released, the information gets transmitted and stored effectively in the memory. This synaptic plasticity plays a central role in storing memory traces or engram for further consolidation and reconsolidation of memory (Evans, 1990). The transmission of information from presynaptic neurons and postsynaptic neurons with synaptic plasticity increases the strength of the information for effective memory retrieval and learning. Thus, pairing the presynaptic and postsynaptic neurons by synaptic plasticity is essential for memory and learning (Abraham et al., 2019).

The neurotransmitters that are majorly involved in synaptic transmission are glutamate or glutamic acid (Glu). Glutamate is the excitatory neurotransmitter, where the excitatory neurotransmitters increase the efficacy of the presynaptic neuron with the action potential (Riedel et al., 2003). The neurotransmitter glutamate further activates the ionotropic glutamate receptor (iGluR) and metabotropic glutamate receptor (mGluR) (Gasbarri & Pompili, 2013). The iGluR are the ion channels that make the excitatory synaptic plasticity faster in the Central nervous system (CNS) in the hippocampus (Traynelis et al., 2010). The mGluR regulates neuronal excitability when the action potential is rapidly released in the hippocampal-dependent spatial learning and memory (Mukherjee & Manahan-Vaughan, 2013). But, the neurotransmitter gamma-aminobutyric acid (GABA), which is mostly present in Central Nervous System (CNS), inhibits the synaptic connectivity with the postsynaptic neuron (Barron, 2021; Zacharopoulos et al., 2021). Inhibiting the synapse from being connected with other synapses can stop the unwanted information from being processed and stored in long-term memory. This way, only the necessary information relevant to the previously held memory will be activated for synaptic plasticity (Schmitz et al., 2017). The inhibitory control of GABA also plays a significant role in associative learning, which forms semantic knowledge by connecting relevant information (Spurny et al., 2020).

The excitatory neurotransmitter glutamate increases synaptic plasticity, and the inhibitory neurotransmitter GABA decreases synaptic plasticity. Together, the role of glutamate and GABA in the right concentration levels will provide balance and cognitive control (Brown et al., 2021; Tian & Chen, 2021). Hence, neurotransmitters are the chemical messengers involved in memory and learning by transmitting relevant information and inhibiting irrelevant information (Yang et al., 2018).

Long-Term Potentiation

Long-term potentiation is a process that strengthens the synapses to retain memory for a longer time in the long-term memory. The synaptic connection between two neurons is activated by the presynaptic neuron, which depends on the experience of the external stimuli (Sumi & Harada, 2020). The synaptic efficacy increases when the presynaptic neuron stimulates the neurotransmitters repeatedly to be connected with the postsynaptic neuron (Stent, 1973). The repeated and persistent connection between the synapses with long-term potentiation increases the ability to store information permanently in long-term memory, which enhances memory retrieval and associative learning with new stimuli (Martinez & Derrick, 1996). The opposite process of long-term potentiation is long-term depression which reduces the strength between the neurons to be connected (Bliss & Cooke, 2011). Long-term depression is equally essential as long-term potentiation because it removes unnecessary information, allowing specific information for synaptic plasticity (Collingridge et al., 2010). The weakening of synaptic plasticity by long-term depression also enhances the process of memory retrieval and learning by inhibiting irrelevant memories. Thus, long-term depression develops the process of long-term potentiation and provides cognitive control.

The high-frequency stimulation of long-term potentiation occurs in the hippocampal region of the brain (Kemp & Manahan-Vaughan, 2004; Wang et al., 2021). The CA1 area of the hippocampus stores and retrieves long-term memory. The organization of the information in order in the CA1 neural area of the brain helps associate the information (Bartsch et al., 2011). Memory retention by the plasticity of synapses forming long-term potentiation of memory depends on the N-Methyl-D-aspartic acid or N-Methyl-D-aspartate (NMDA) receptor (Kumar, 2015). The long-term potentiation depending on the experience of the stimuli, can be divided into NMDA receptor-dependent and NMDA receptor-independent. NMDA receptor-dependent synapses connect better with the other neuron for long-term information storage than the NMDA-independent synapses (Sweatt, 2010). Together, the synaptic plasticity and the long-term potentiation with NMDA receptors and the genetic transcription of CREB and NF-kB in the region of CA1 in the hippocampus of the brain strengthen the information to be stored in long-term memory for effective retrieval and learning (Benito & Barco, 2010; Bito & Takemoto-Kimura, 2003).

Genetic Transcription

The stronger firing of the neurons for synaptic plasticity and long-term potentiation also requires genetic transcription. Specifically, the genetic activation of the cAMP response element-binding protein (CREB) in the process of synaptic plasticity is necessary for learning and memory (Kida, 2012). CREB is a transcription factor that binds to a specific DNA sequence called cAMP-response-element (CRE). The perception of stimuli, the experience, and the effect of the stimuli while learning trigger the phosphorylation of CREB-dependent gene expression (Gandolfi et al., 2017). The phosphorylation of CREB activates the synaptic plasticity between the neurons, such that the information is strengthened for the long-term potentiation of the memory (Deisseroth & Bito, 1996). Further, CREB activation in the neurons is involved in synaptic plasticity and long-term potentiation that binds the neurons for synaptic efficacy (Kaldun & Sprecher, 2019; Ortega-Martínez, 2015). Also, the CREB plays a role in initiating the process of memory consolidation, which stabilizes the information from short-term memory to long-term memory (Lonze & Ginty, 2002; Suzuki et al., 2011). The activation of the CREB gene allows switching between the memory phases that increase context-specific learning. By regulating the neuronal activity of synaptic plasticity, CREB enhances the storage of memory traces that can be reactivated during retrieval for effective learning (Wang et al.,

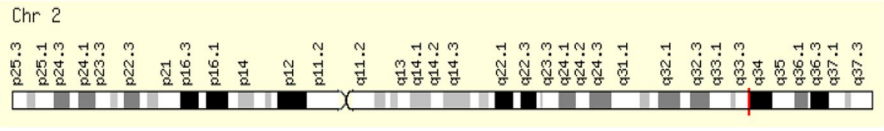

Fig. 4 Chromosomal location of the CREB gene (2q33.3)

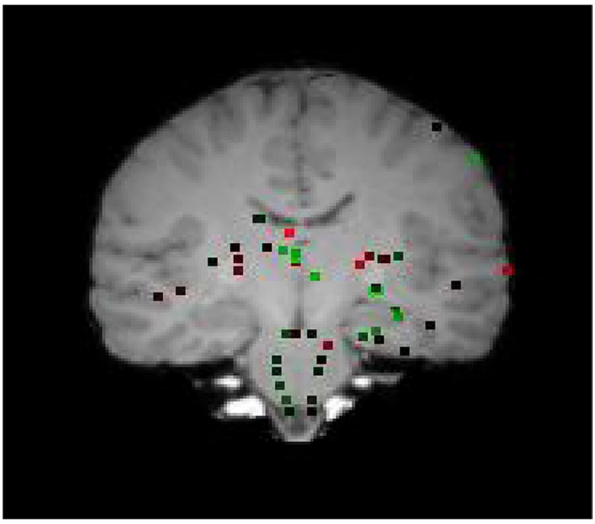

Fig. 5 CREB gene patterns from Allen Human Brain Atlas, human.brain-map.org

2018). Figure 4 represents the chromosomal location of the gene CREB, and Fig. 5 shows the genetic patterns of CREB.

Another transcription factor that regulates the functioning of neurotransmitters is the nuclear factor kappaB (NF-kB). NF-kB regulates neuronal transmission and synaptic plasticity by holding the memory trace or engram (Kaltschmidt & Kaltschmidt, 2015). With the activation of NF-kB, long-term potentiation is induced, forming memory traces. Following that, the new information forms the synaptic plasticity between the neurons. In this process, the older memory trace is reactivated, forming a connection between the prior knowledge and the external stimuli (Kaltschmidt et al., 2006). Also, the major activator for the synaptic activity of NF-kB is glutamate and Ca2+, which regulate the transmission of information (Kaltschmidt et al., 2005). This transmission of information through neurons by the activation of CREB and NF-kB positively increases memory retention and retrieval, which influences the learning experience. Figure 6 represents the chromosomal location of the gene NF-kB, and Fig. 7 shows the genetic patterns of NF-kB.

Theta Oscillations

Along with the neurotransmitters and the genetic transcription CREB, the hippocampal theta rhythm is activated to strengthen long-term potentiation. The theta oscillation in the brain is essential for encoding and retrieval of memory (ter Wal et al., 2021).

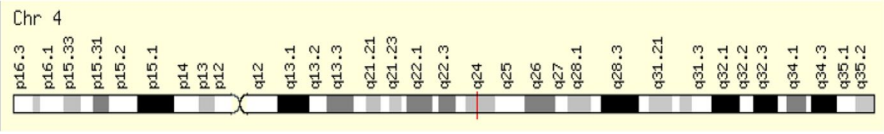

Fig. 6 Chromosomal location of the NF-kB gene (4q24)

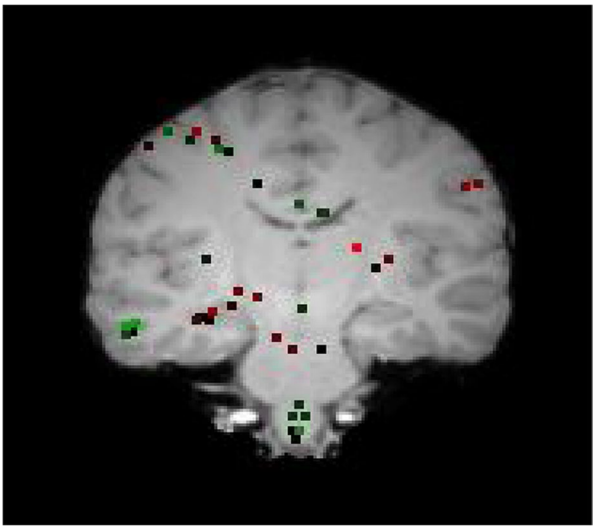

Fig. 7 NF-kB gene patterns from Allen Human Brain Atlas, human.brain-map.org

The theta waves measure between 4 to 8 HZ and the normal functioning of the theta rhythm within this frequency mediates memory and learning (Bastiaansen et al., 2005; Kikuchi et al., 2011). During memory retrieval, the theta waves get activated and update the memory for its retainment for a longer period. Depending on the higher or lower frequency of the theta waves, the stronger or weaker firing of synapses for long-term potentiation is determined (Jacobs et al., 2006). Besides that, the transmission of information for memory storage requires synaptic plasticity, and the strong firing of presynaptic and postsynaptic neurons results from the oscillations of the theta wave in the brain (Bland, 1986; Klimesch et al., 2001). The topographical map in Fig. 8 shows an increase in the theta wave during the retention and retrieval of memory.

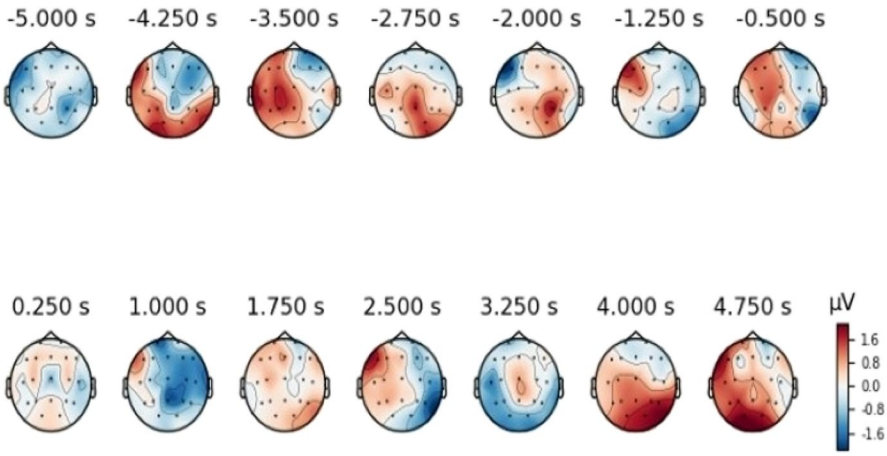

Fig. 8 Topographical map to show the activation of theta wave. The plot shows amplitude where the red color shows the positive amplitude of theta and blue shows the negative amplitude of theta. The darker red or blue indicates, the higher value of theta oscillation on an average time during the retrieval of information

Electroencephalography (EEG) and magnetoencephalography (MEG) studies have shown that theta oscillations in the brain are stimulated for hippocampal activation during working memory (Düzel et al., 2010; Gyorgy, 2002). Though the mechanism that facilitates theta brain oscillation in neural circuits is not clear, it is found that the theta burst stimulation (TBS), which is similar to the original theta activity in the brain, activates the memory consolidation and reconsolidation process, thus increasing the long-term potentiation of memory (Arai & Lynch, 1992; Larson & Munkácsy, 2015). Further, the theta burst by the human theta burst stimulation stimulates NMDA receptors that induce long-term potentiation for the storage, retainment, and retrieval of memory (Capocchi et al., 1992; McCalley et al., 2021).

EEG memory studies have involved theta burst stimulation in finding theta activity for memory storage and retrieval. The theta burst stimulation uses high-frequency stimulation bursts that resemble the original activation of theta in the hippocampal region using extracellular field potential recordings (Abrahamsson et al., 2016; Tse et al., 2018). Theta bursts are repeated to evoke synaptic plasticity, which induces long-term potentiation for memory and learning (Albouy et al., 2022; Wong et al., 1986). The theta rhythm coordinates the neural activity for synaptic plasticity and long-term potentiation that retains and retrieves memory for learning and creating a link with new knowledge. Table 1 gives an overview of the processes involved in the storage and retrieval of memory.

Conclusions

The consolidation of information from short-term memory to long-term memory stabilizes and retains the memory for retrieval and learning. The neurobiological mechanism underlying the consolidation and reconsolidation of memories occurs when neurons communicate and transmit information. As a matter of fact, memory and learning are interconnected neurobiological phenomena that depend on the firing of neurons during acquisition and the reactivation of neurons during retrieval.

The above discussion shows that the neural signals from synaptic plasticity are mediated by neurotransmitters, including glutamate and GABA. Further, the transmitted information is strengthened by long-term potentiation mediated by NMDA receptors. This transmission and strengthening of neurons for memory and learning are activated by CREB and NF-kB genetic transcription and oscillation of theta waves. Taken together, it is reasonable to conclude that the retainment and retrieval of memory through synaptic plasticity play an important role in learning. However, more neurobiological studies could be developed on the function of neurons in acquiring, transmitting, and retrieving memory.

Table 1 Summary of processes involved in memory and learning

Gene	Process	Neurotransmitter	Brain region	Function
CREB, NF-kB	Excitatory synaptic plasticity	Glu, iGluR, mGluR	CNS & Hippocampus	Spatial learning and memory
	Inhibitory synaptic plasticity	GABA	CNS	Associative learning
	Long-term Potentiation	NMDA	CA1 of Hippocampus	Organization of information
	Theta Oscillation	NMDA	Hippocampus	Memory retrieval

Abbreviations: *CREB* cAMP response element-binding protein, *NF- kB* Nuclear factor kappaB, *Glu* Glutamate, *iGluR* Ionotropic glutamate receptor, *mGluR* Metabotropic glutamate receptor, *GABA* Gamma-aminobutyric acid, *NMDA* N-Methyl-D-aspartate, *CNS* Central Nervous System

Data availability Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Conflict of Interest Both authors have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent This article has no study.

References

Abraham, W. C., & Bear, M. F. (1996). Metaplasticity: the plasticity of synaptic plasticity. *Trends in Neurosciences, 19*(4), 126–30. https://doi.org/10.1016/s0166-2236(96)80018-x

Abraham, W. C., Jones, O. D., & Glanzman, D. L. (2019). Is plasticity of synapses the mechanism of long-term memory storage? *NPJ Science of Learning, 4* (1), 9. https://doi.org/10.1038/s41539-019-0048-y

Abrahamsson, T., Lalanne, T., Watt, A. J., & Sjöström, P. J. (2016). Long-term potentiation by theta-Burst stimulation using extracellular field potential recordings in acute hippocampal slices. *Cold Spring Harbor Protocols, 2016*(6), 564–572. https://doi.org/10.1101/pdb.prot091298

Adams, P., Llano, D., Brunel, N., Hawkins, J., & Ahmad, S. (2016). Why Neurons Have Thousands of Synapses, a Theory of Sequence Memory in Neocortex. *Frontiers in Neural Circuits, 10*, 23. https://doi.org/10.3389/fncir.2016.00023

Alberini, C. M. (2011). The role of reconsolidation and the dynamic process of long-term memory formation and storage. *Frontiers in Behavioral Neuroscience, 5*(12). https://doi.org/10.3389/fnbeh.2011.00012

Alberini, C. M., & Ledoux, J. E. (2013). Memory reconsolidation. *Current Biology*, *23*(17), R746–R750. https://doi.org/10.1016/j.cub.2013.06.046

Albouy, P., Martinez-Moreno, Z. E., Hoyer, R. S., Zatorre, R. J., & Baillet, S. (2022). Supramodality of neural entrainment: Rhythmic visual stimulation causally enhances auditory working memory performance. *Science Advances, 8*(8), eabj9782. https://doi.org/10.1126/sciadv.abj9782

Anderson, M. C., & Neely, J. H. (1996). Interference and inhibition in memory retrieval. *Memory*, 3(8), 237–313. https://doi.org/10.1016/b978-012102570-0/50010-0

Arai, A., & Lynch, G. (1992). Factors regulating the magnitude of long-term potentiation induced by theta pattern stimulation. *Brain Research, 598*(1–2), 173–184. https://doi.org/10.1016/0006-8993(92)90181-8

Baars, B. J., & Gage, N. M. (2010). Learning and memory. *Cognition, Brain, and Consciousness,* 9, 304–343. https://doi.org/10.1016/B978-0-12-375070-9.00009-7

Barron, H. C. (2021). Neural inhibition for continual learning and memory. *Current Opinion in Neurobiology, 67*, 85–94. Elsevier Ltd. https://doi.org/10.1016/j.conb.2020.09.007

Bartsch, T., Döhring, J., Rohr, A., Jansen, O., & Deuschl, G. (2011). CA1 neurons in the human hippocampus are critical for autobiographical memory, mental time travel, and autonoetic consciousness. *Proceedings of the National Academy of Sciences of the United States of America, 108*(42), 17562–17567. https://doi.org/10.1073/pnas.1110266108

Bastiaansen, M. C., van der Linden, M., ter Keurs, M., Dijkstra, T., & Hagoort, P. (2005). Theta Responses Are Involved in Lexical-Semantic Retrieval during Language Processing. *Journal of Cognitive Neuroscience, 17*(3), 530–541. https://doi.org/10.1162/0898929053279469

Bell, M. C., Kawadri, N., Simone, P. M., & Wiseheart, M. (2014). Long-term memory, sleep, and the spacing effect. *Memory, 22*(3), 276–283. https://doi.org/10.1080/09658211.2013.778294

Benito, E., & Barco, A. (2010). CREB's control of intrinsic and synaptic plasticity: implications for CREB-dependent memory models. *Trends in Neurosciences, 33*(5), 230–240. https://doi.org/10.1016/j.tins.2010.02.001

Bito, H., & Takemoto-Kimura, S. (2003). Ca2+/CREB/CBP-dependent gene regulation: A shared mechanism critical in long-term synaptic plasticity and neuronal survival. *Cell Calcium, 34*(4–5), 425–430. https://doi.org/10.1016/S0143-4160(03)00140-4

Bland, B. H. (1986). The Physiology and Pharmacology of Hippocampal Formation Theta Rhythms*. *In Progress in Neurobiology, 26*(1), 1–54. https://doi.org/10.1016/0301-0082(86)90019-5

Bliss, T. V. P., & Cooke, S. F. (2011). Long-term potentiation and long-term depression: a clinical perspective. *Clinics, 66*(S1), 3–17. https://doi.org/10.1590/s1807-59322011001300002

Brem, A. Katharine., Ran, K., & Pascual-leone, A. (2013). Learning and memory. *Handbook of Clinical Neurology, 116*, 693–737. https://doi.org/10.1016/B978-0-444-53497-2.00055-3. Elsevier B.V.

Brown, R. E., Bligh, T. W. B., & Garden, J. F. (2021). The Hebb synapse before Hebb: Theories of synaptic function in learning and memory before Hebb (1949), with a discussion of the long-lost synaptic theory of William McDougall. *Frontiers in Behavioral Neuroscience, 15*, 732195. https://doi.org/10.3389/fnbeh.2021.732195

Capocchi, G., Zampolini, M., & Larson, J. (1992). Theta burst stimulation is optimal for induction of LTP at both apical and basal dendritic synapses on hippocampal CA1 neurons. *Brain Research, 591*(2), 332–6. https://doi.org/10.1016/0006-8993(92)91715-q

Chanales, A. J. H., Dudukovic, N. M., Richter, F. R., & Kuhl, B. A. (2019). Interference between overlapping memories is predicted by neural states during learning. *Nature Communications, 10*(1), 5363. https://doi.org/10.1038/s41467-019-13377-x

Choi, D. il, & Kaang, B.-K. (2022). Interrogating structural plasticity among synaptic engrams. *Current Opinion in Neurobiology, 75*, 102552. https://doi.org/10.1016/j.conb.2022.102552

Collingridge, G. L., Peineau, S., Howland, J. G., & Wang, Y. T. (2010). Long-term depression in the CNS. *Nature Reviews Neuroscience, 11*(7), 459–473. https://doi.org/10.1038/nrn2867

Davis, R. L., & Zhong, Y. (2017). The Biology of Forgetting—A Perspective. *Neuron, 95*(3), 490–503. Cell Press. https://doi.org/10.1016/j.neuron.2017.05.039

Deisseroth, K., & Bito, H. (1996). Signaling from Synapse to Nucleus: Postsynaptic CREB Phosphorylation during Multiple Forms of Hippocampal Synaptic Plasticity. *Neuron, 16*, 89–101. https://doi.org/10.1016/s0896-6273(00)80026-4

Druckmann, S., Feng, L., Lee, B., Yook, C., Zhao, T., Magee, J. C., & Kim, J. (2014). Structured Synaptic Connectivity between Hippocampal Regions. *Neuron, 81*(3), 629–640. https://doi.org/10.1016/j.neuron.2013.11.026

Düzel, E., Penny, W. D., & Burgess, N. (2010). Brain oscillations and memory. *Current Opinion in Neurobiology, 20*(2), 143–149. Elsevier Ltd. https://doi.org/10.1016/j.conb.2010.01.004

Ebbinghaus, H. (1855). *Memory: A Contribution to Experimental Psychology* (1913th ed.). Columbia University.

Evans, R. B. (1990). William James, "The Principles of Psychology," and experimental psychology. *Source: The American Journal of Psychology 103*(4). Winter. https://www.jstor.org/stable/1423317?seq=1&cid=pdf. Accessed 16 Sep 2021

Fusi, S. (2008). Neuroscience: A quiescent working memory. *Science, 319*(5869), 1495–1496. https://doi.org/10.1126/science.1155914

Gandolfi, D., Cerri, S., Mapelli, J., Polimeni, M., Tritto, S., Fuzzati-Armentero, M. T., Bigiani, A., Blandini, F., Mapelli, L., & D'Angelo, E. (2017). Activation of the CREB/c-Fos pathway during long-term synaptic plasticity in the cerebellum granular layer. *Frontiers in Cellular Neuroscience, 11*, 184. https://doi.org/10.3389/fncel.2017.00184

Gasbarri, A., & Pompili, A. (2013). Involvement of glutamate in learning and memory. *Identification of Neural Markers Accompanying Memory,* 4*,* 63–77. https://doi.org/10.1016/B978-0-12-408139-0.00004-3

González-Espinosa, C., & Guzmán-Mejía, F. (2013). Basic elements of signal transduction pathways involved in chemical neurotransmission. In *Identification of Neural Markers Accompanying Memory, 8*, 121–133. https://doi.org/10.1016/B978-0-12-408139-0.00008-0

Goto, A. (2022). Synaptic plasticity during systems memory consolidation. *Neuroscience Research, 183*, 1–6. https://doi.org/10.1016/j.neures.2022.05.008

Gyorgy, B. (2002). Theta Oscillations in the Hippocampus. *Neuron, 33*(3), 325–340. https://doi.org/10.1016/s0896-6293(02)00586-x

Han, D. H., Park, P., Choi, D. il, Bliss, T. V. P., & Kaang, B. K. (2021). The essence of the engram: Cellular or synaptic? *Seminars in Cell and Developmental Biology., 125*, 122–135. https://doi.org/10.1016/j.semcdb.2021.05.033

Hebb, D. (1949). *The Organization of Behavior* (1st ed.). Psychology Press.

Herszage, J., & Censor, N. (2017). Memory Reactivation Enables Long-Term Prevention of Interference. *Current Biology, 27*(10), 1529-1534.e2. https://doi.org/10.1016/j.cub.2017.04.025

Jackman, S. L., & Regehr, W. G. (2017). The mechanisms and functions of synaptic facilitation. *Neuron, 94*(3), 447–464. Cell Press. https://doi.org/10.1016/j.neuron.2017.02.047

Jacobs, J., Hwang, G., Curran, T., & Kahana, M. J. (2006). EEG oscillations and recognition memory: Theta correlates of memory retrieval and decision making. *NeuroImage, 32*(2), 978–987. https://doi.org/10.1016/j.neuroimage.2006.02.018

Kaldun, J. C., & Sprecher, S. G. (2019). Initiated by CREB: Resolving gene regulatory programs in learning and memory: Switch in cofactors and transcription regulators between memory consolidation and maintenance Network. *BioEssays*, *41*(8), 1900045. https://doi.org/10.1002/bies.201900045

Kaltschmidt, B., & Kaltschmidt, C. (2015). NF-KappaB in long-term memory and structural plasticity in the adult mammalian brain. *In Frontiers in Molecular Neuroscience, 8*(November), 1–11. https://doi.org/10.3389/fnmol.2015.00069

Kaltschmidt, B., Ndiaye, D., Korte, M., Pothion, S., Arbibe, L., Prüllage, M., Pfeiffer, J., Lindecke, A., Staiger, V., Israël, A., Kaltschmidt, C., & Mémet, S. (2006). NF-κB Regulates Spatial Memory Formation and Synaptic Plasticity through Protein Kinase A/CREB Signaling. *Molecular and Cellular Biology, 26*(8), 2936–2946. https://doi.org/10.1128/mcb.26.8.2936-2946.2006

Kaltschmidt, B., Widera, D., & Kaltschmidt, C. (2005). Signaling via NF-κB in the nervous system. *Biochimica Et Biophysica Acta - Molecular Cell Research, 1745*(3), 287–299. https://doi.org/10.1016/j.bbamcr.2005.05.009

Katkov, M., Romani, S., & Tsodyks, M. (2017). Memory Retrieval from First Principles. *Neuron, 94*(5), 1027–1032. https://doi.org/10.1016/j.neuron.2017.03.048

Kemp, A., & Manahan-Vaughan, D. (2004). Hippocampal long-term depression and long-term potentiation encode different aspects of novelty acquisition. *Proceedings of the National Academy of Sciences, 101*(21), 8192–8197. https://doi.org/10.1073/pnas.0402650101.

Kerrén, C., Bramão, I., Hellerstedt, R., & Johansson, M. (2021). Strategic retrieval prevents memory interference: The temporal dynamics of retrieval orientation. *Neuropsychologia*, 154, 107776. https://doi.org/10.1016/j.neuropsychologia.2021.107776

Kida, S. (2012). A Functional Role for CREB as a Positive Regulator of Memory Formation and LTP. *Experimental Neurobiology, 21*(4), 136–140. https://doi.org/10.5607/en.2012.21.4.136

Kikuchi, M., Shitamichi, K., Yoshimura, Y., Ueno, S., Remijn, G. B., Hirosawa, T., Munesue, T., Tsubokawa, T., Haruta, Y., Oi, M., Higashida, H., & Minabe, Y. (2011). Lateralized theta wave connectivity and language performance in 2-to 5-year-old children. *Journal of Neuroscience, 31*(42), 14984–14988. https://doi.org/10.1523/JNEUROSCI.2785-11.2011

Klimesch, W., Doppelmayr, M., Yonelinas, A., Kroll, N. E. A., Lazzara, M., Rohm, D., & Gruber, W. (2001). Theta synchronization during episodic retrieval: neural correlates of conscious awareness. *Cognitive Brain Research, 12*(1), 33–8. https://doi.org/10.1016/s0926-6410(01)00024-6

Kneussel, M., & Hausrat, T. J. (2016). Postsynaptic Neurotransmitter Receptor Reserve Pools for Synaptic Potentiation. *Trends in Neurosciences, 39*(3), 170–182. https://doi.org/10.1016/j.tins.2016.01.002

Knierim, J. J. (2014). Information processing in neural networks. *From Molecules to Networks: An Introduction to Cellular and Molecular Neuroscience, 19*, 563–589. https://doi.org/10.1016/B978-0-12-397179-1.00019-1

Kornmeier, J., Spitzer, M., & Sosic-Vasic, Z. (2014). Very similar spacing-effect patterns in very different learning/practice domains. *PLoS ONE, 9*(3), e90656. https://doi.org/10.1371/journal.pone.0090656

Kumar, A. (2015). NMDA receptor function during senescence: Implication on cognitive performance. *Frontiers in Neuroscience, 9*, 473. https://doi.org/10.3389/fnins.2015.00473

Langille, J. J., & Brown, R. E. (2018). The synaptic theory of memory: A historical survey and reconciliation of recent opposition. *Frontiers in Systems Neuroscience*, *12*, 52. https://doi.org/10.3389/fnsys.2018.00052

Larson, J., & Munkácsy, E. (2015). Theta-burst LTP. In. *Brain Research, 1621*, 38–50. https://doi.org/10.1016/j.brainres.2014.10.034

Lee, E., Lee, S., Shin, J. J., Choi, W., Chung, C., Lee, S., Kim, J., Ha, S., Kim, R., Yoo, T., Yoo, Y. E., Kim, J., Noh, Y. W., Rhim, I., Lee, S. Y., Kim, W., Lee, T., Shin, H., Cho, I. J., … Kim, E. (2021). Excitatory synapses and gap junctions cooperate to improve Pv neuronal burst firing and cortical

social cognition in Shank2-mutant mice. *Nature Communications*, *12*(1). https://doi.org/10.1038/s41467-021-25356-2

Lockhart, R. S. (2001). Memory retrieval. *International Encyclopedia of the Social and Behavioral Sciences*, *68*(27), 9613–9618. https://doi.org/10.1016/b0-08-043076-7/01523-0

Lonze, B. E., & Ginty, D. D. (2002). Function and regulation of CREB family transcription factors in the nervous system. *In Neuron, 35*(4), 605–623. https://doi.org/10.1016/s0896-6273(02)00828-0

Martinez, J. L., & Derrick, B. E. (1996). Long-Term Potentiation And Learning. *Annual Review of Psychology, 47*, 173–203. https://doi.org/10.1146/annurev.psych.47.1.173

McCalley, D. M., Lench, D. H., Doolittle, J. D., Imperatore, J. P., Hoffman, M., & Hanlon, C. A. (2021). Determining the optimal pulse number for theta burst induced change in cortical excitability. *Scientific Reports*, *11*(1), 8726. https://doi.org/10.1038/s41598-021-87916-2

Miller, R. R. (2021). Failures of memory and the fate of forgotten memories. *Neurobiology of Learning and Memory*, 181, 107426. https://doi.org/10.1016/j.nlm.2021.107426

Mittal, A. M., Singh, S. S., & Gupta, N. (2018). Sensory Coding: Neurons That Wire Together Fire Longer. *Current Biology, 28*(10), R608–R610. https://doi.org/10.1016/j.cub.2018.04.003

Mukherjee, S., & Manahan-Vaughan, D. (2013). Role of metabotropic glutamate receptors in persistent forms of hippocampal plasticity and learning. *Neuropharmacology, 66*, 65–81. https://doi.org/10.1016/j.neuropharm.2012.06.005

Murre, J. M. J., & Dros, J. (2015). Replication and analysis of Ebbinghaus' forgetting curve. *PLoS ONE*, 10(7), e0120644. https://doi.org/10.1371/journal.pone.0120644

Nelson, T. O. (1985). Ebbinghaus's contribution to the measurement of retention: Savings during relearning. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *11*(3), 472–9. https://doi.org/10.1037//0278-7393.11.3.472

Ortega-Martínez, S. (2015). A new perspective on the role of the CREB family of transcription factors in memory consolidation via adult hippocampal neurogenesis. *Frontiers in Molecular Neuroscience, 8*, 46. https://doi.org/10.3389/fnmol.2015.00046

Packard, M. G., & Knowlton, B. J. (2002). Learning and Memory Functions of the Basal Ganglia. *Annual Review of Neuroscience, 25*(1), 563–593. https://doi.org/10.1146/annurev.neuro.25.112701.142937

Raman, D. V., Rotondo, A. P., & O'Leary, T. (2019). Fundamental bounds on learning performance in neural circuits. *Proceedings of the National Academy of Sciences of the United States of America, 116*(21), 10537–10546. https://doi.org/10.1073/pnas.1813416116

Riedel, G., Platt, B., & Micheau, J. (2003). Glutamate receptor function in learning and memory. *Behavioral Brain Research, 140*(1–2), 4714. https://doi.org/10.1016/s0166-4328(02)00272-3

Schmitz, T. W., Correia, M. M., Ferreira, C. S., Prescot, A. P., & Anderson, M. C. (2017). Hippocampal GABA enables inhibitory control over unwanted thoughts. *Nature Communications*, *8*(1), 1311. https://doi.org/10.1038/s41467-017-00956-z

Silva, M., Tran, V., & Marty, A. (2021). Calcium-dependent docking of synaptic vesicles. *Trends in Neurosciences, 44*(7), 579–592. https://doi.org/10.1016/j.tins.2021.04.003

Spurny, B., Seiger, R., Moser, P., Vanicek, T., Reed, M. B., Heckova, E., Michenthaler, P., Basaran, A., Gryglewski, G., Klöbl, M., Trattnig, S., Kasper, S., Bogner, W., & Lanzenberger, R. (2020). Hippocampal GABA levels correlate with retrieval performance in an associative learning paradigm. *NeuroImage*, *204*, 116244. https://doi.org/10.1016/j.neuroimage.2019.116244

Steinvorth, S., Corkin, S., & Halgren, E. (2006). Ecphory of autobiographical memories: An fMRI study of recent and remote memory retrieval. *NeuroImage, 30*(1), 285–298. https://doi.org/10.1016/j.neuroimage.2005.09.025

Stent, G. S. (1973). A Physiological Mechanism for Hebb's Postulate of Learning. *Proc Natl Acad Sci U S A, 70*(4), 997–1001. https://doi.org/10.1073/pnas.70.4.997

Südhof, T. C. (2012). Calcium control of neurotransmitter release. *Cold Spring Harbor Perspectives in Biology*, *4*(1), a011353. https://doi.org/10.1101/cshperspect.a011353

Sumi, T., & Harada, K. (2020). Mechanism underlying hippocampal long-term potentiation and depression based on competition between endocytosis and exocytosis of AMPA receptors. *Scientific Reports*, *10*(1), 14711. https://doi.org/10.1038/s41598-020-71528-3

Suzuki, A., Fukushima, H., Mukawa, T., Toyoda, H., Wu, L. J., Zhao, M. G., Xu, H., Shang, Y., Endoh, K., Iwamoto, T., Mamiya, N., Okano, E., Hasegawa, S., Mercaldo, V., Zhang, Y., Maeda, R., Ohta, M., Josselyn, S. A., Zhuo, M., & Kida, S. (2011). Upregulation of CREB-mediated transcription enhances both short- and long-term memory. *Journal of Neuroscience, 31*(24), 8786–8802. https://doi.org/10.1523/JNEUROSCI.3257-10.2011

Sweatt, J. D. (2010). Long-Term Potentiation—A candidate cellular mechanism for information storage in the central nervous system. In *Mechanisms of Memory, 7*, 150–189. https://doi.org/10.1016/b978-0-12-374951-2.00007-x

Ter Wal, M., Linde-Domingo, J., Lifanov, J., Roux, F., Kolibius, L. D., Gollwitzer, S., Lang, J., Hamer, H., Rollings, D., Sawlani, V., Chelvarajah, R., Staresina, B., Hanslmayr, S., & Wimber, M. (2021). Theta rhythmicity governs human behavior and hippocampal signals during memory-dependent tasks. *Nature Communications*, *12*(1), 7048. https://doi.org/10.1038/s41467-021-27323-3

Tian, W., & Chen, S. (2021). Neurotransmitters, cell types, and circuit mechanisms of motor skill learning and clinical applications. *Frontiers in Neurology 12*, 616820. https://doi.org/10.3389/fneur.2021.616820

Tonegawa, S., Morrissey, M. D., & Kitamura, T. (2018). The role of engram cells in the systems consolidation of memory. *Nature Reviews Neuroscience, 19*(8), 485–498. https://doi.org/10.1038/s41583-018-0031-2

Tonegawa, S., Pignatelli, M., Roy, D. S., & Ryan, T. J. (2015). Memory engram storage and retrieval. *Current Opinion in Neurobiology, 35*, 101–109. https://doi.org/10.1016/j.conb.2015.07.009

Traynelis, S. F., Wollmuth, L. P., McBain, C. J., Menniti, F. S., Vance, K. M., Ogden, K. K., Hansen, K. B., Yuan, H., Myers, S. J., & Dingledine, R. (2010). Glutamate receptor ion channels: Structure, regulation, and function. *Pharmacological Reviews, 62*(3), 405–496. https://doi.org/10.1124/pr.109.002451

Tse, N. Y., Goldsworthy, M. R., Ridding, M. C., Coxon, J. P., Fitzgerald, P. B., Fornito, A., & Rogasch, N. C. (2018). The effect of stimulation interval on plasticity following repeated blocks of intermittent theta burst stimulation. *Scientific Reports*, *8*(1), 8526. https://doi.org/10.1038/s41598-018-26791-w

Tulving, E., le Voi, M. E., Routh, D. A., & Loftus, E. (1983). Ecphoric Processes in Episodic Memory [and Discussion]. *Biological Sciences, 302*(1110), 361–371. http://www.jstor.org/stable/2395999

Unsworth, N., Brewer, G. A., & Spillers, G. J. (2013). Focusing the search: Proactive and retroactive interference and the dynamics of free recall. *Joumal of Experimental Psychology: Leaming. Memory, and Cognition*, *39*(6), 1742–1756. https://doi.org/10.1037/a0O33743

Wang, H., Xu, J., Lazarovici, P., Quirion, R., & Zheng, W. (2018). cAMP response element-binding protein (CREB): A possible signaling molecule link in the pathophysiology of schizophrenia. In *Frontiers in Molecular Neuroscience, 11*, 255. https://doi.org/10.3389/fnmol.2018.00255

Wang, J. H., Wu, C., Lian, Y. N., Liu, L., & Li, X. Y. (2021). *Targeting long-term depression of excitatory synaptic transmission for the treatment of neuropathic pain*. John Wiley and Sons Inc. https://doi.org/10.1111/febs.16200

Wong, J. L. D., Lynch, G., & Larson, J. (1986). Patterned stimulation at the theta frequency is optimal for the induction of hippocampal long-term potentiation. *Brain Research, 368*(2), 347–350. https://doi.org/10.1016/0006-8993(86)90579-2

Woodward, A. E., Bjork, R. A., & Jongeward, R. H. (1973). Recall and Recognition as a Function of Primary Rehearsal. *Journal of Verbal Learning and Verbal Behavior, 12*(6), 608–617. https://doi.org/10.1016/s0022-5371(73)80040-4

Yang, Y., Lu, J., & Zuo, Y. (2018). Changes of Synaptic Structures Associated with Learning, Memory and Diseases. *Brain Science Advances*, *4*(2), 99–117. https://doi.org/10.26599/bsa.2018.2018.9050012

Zacharopoulos, G., Sella, F., Kadosh, K. C., Hartwright, C., Emir, U., & Kadosh, R. C. (2021). Predicting learning and achievement using GABA and glutamate concentrations in human development. *PLoS Biology, 19*(7), e3001325. https://doi.org/10.1371/journal.pbio.3001325

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