Journal of
Pharmacology & Clinical Research
ISSN: 2473-5574

Juniper Publishers
key to the Researchers

Mini Review
Volume 11 Issue 2 - July 2025
DOI: 10.19080/JPCR.2025.11.555807

J of Pharmacol & Clin Res
Copyright © All rights are reserved by Reza Fartootzadeh

Hippocampus Physiology and Pharmacology in Normal State: An Overview

Reza Fartootzadeh*

Department of Physiology, Ramsar Campus, Mazandaran University of Medical Sciences, Ramsar, Iran

Submission: June 24, 2025; **Published:** July 10, 2025

***Corresponding author:** Reza Fartootzadeh, Department of Physiology, Ramsar Campus, Mazandaran University of Medical Sciences, Ramsar, Iran. E-mail Id: fartootzadeh@gmail.com

Abstract

The three-layered structure of the hippocampus distinguishes it from the cerebral cortex and makes it an interesting place for neural sciences studies, including in vivo and ex vivo LTP. The physiology of the hippocampus is fascinating, so that its unique regions undergo changes, such as neurogenesis and plasticity throughout life; new neurons form from stem cells in at least two areas in the brain: the hippocampus and the olfactory bulb. Therefore, neurogenesis occurs and contributes to learning and memory. Any reduction in the number of neurons in the hippocampus diminishes at least one type of hippocampal memory formation. These changes are important for learning and memory.

Along with learning and memory, the hippocampus also plays a key role in spatial navigation, emotions, and motor behaviours. Nearly all regions of the hippocampus are densely interconnected with various pathways originating from diverse areas of the brain. These include adenosine, dopaminergic, serotonergic, glutamatergic, GABAergic, noradrenergic, and cholinergic projections, each contributing unique functions to hippocampal processes. Among these, GABAA and glutamate are recognized as key players in long-term potentiation (LTP), as well as in learning and memory. This article provides an overview of hippocampal physiology and pharmacology under normal conditions.

Keywords: Hippocampus; Physiology and Pharmacology; Anatomy; LTP; Learning and Memory; Synaptic Plasticity

Abbreviations: LTD: Long-Term Depression; LTP: Long-Term Potentiation; AD: Alzheimer's Disease; DG: Dentate Gyrus; CA: Cornu Ammonis

Introduction

The hippocampus, an S-shaped structure in the medial portion of the temporal lobes of the brain [1, 2], is located in the posterior region of the limbic system [2]. Its resemblance to the seahorse encouraged its naming after this sea creature. Over the past century, the hippocampus has been identified as the main area for organizing emotional responses [3], recalling memories [4], and playing a crucial role in learning and memory [5]; however, it is also one of the most vulnerable parts of the brain in disorders like Alzheimer's disease (AD) [6].

Its relatively simple anatomy and synaptic connections make the hippocampus an ideal model at the forefront of research for neuroscientists, especially electrophysiologists, to study the mechanisms of long-term potentiation (LTP), long-term depression (LTD), and the bases of memory formation. LTP happens as a result of a surge in Ca^{2+} influx into the presynaptic neuron in reaction to tetanic stimulation. This Ca^{2+} influx triggers the Ca^{2+}/calmodulin-dependent adenylyl cyclase cascade, leading to an increase in cAMP levels [7]. Conversely, LTD represents a reduction in synaptic strength caused by weaker stimulation of presynaptic neurons, accompanied by a modest increase in intracellular Ca^{2+} concentrations [7]. The current study aims to provide a review of the anatomy, physiology, and pharmacology of the hippocampus under normal conditions.

Hippocampal Anatomy

Intrinsic Circuitry

The hippocampal curve and sulcus divide it into the dentate gyrus (DG), surrounded by the Cornu Ammonis (CA) fields, and the subiculum. The subiculum forms the dorsal section of the parahippocampal gyrus [8].

The CA fields, made up of pyramidal cells, are histologically divided into four regions (CA1–CA4), playing a crucial role in the matching and mismatching of obtained information [9, 10].

The DG, the deep area of the hippocampus, functions as a gateway and serves as an input area that receives signals from the entorhinal cortex. It plays a critical role in pattern separation, information processing, and associative memory [11-14]. The entorhinal cortex sends the main cortical inputs to the hippocampus through two pathways; one projects to the subiculum and CA1 (output layer) fields and the other one is the strongest projection to the DG. From the DG, projections extend to the CA3 field via mossy fibers. The CA3 field, in turn, establishes a feedback projection to the DG through excitatory mossy cells and also connects to the CA1 region through the Schaffer collateral pathway. Finally, CA1 sends major signals back to the entorhinal cortex via the subiculum, effectively completing this loop of neural communication [15-19].

The latest examinations have led to new investigations of the CA2 field, which has typically been viewed as a transitional area between the CA1 and CA3 fields. However, it is now evident that the CA2 region is a distinct unit with its specific functions [16, 20, 21].

Other cortical and subcortical connections

Besides the major projections from the entorhinal cortex, the hippocampus receives inputs from the perirhinal and postrhinal cortices, as well as subcortical inputs from structures like the amygdala, raphe nucleus, locus coeruleus, and medial septum. The CA1 and CA3 regions primarily send output signals to the lateral septum. Moreover, CA1 projects to other areas such as the prefrontal cortex, amygdala, and nucleus accumbens [22-25]. Notably, the nucleus accumbens plays a crucial role in nicotine dependency [26-28].

Hippocampal Physiology

The significance of the hippocampus in memory became evident with the discovery of LTP in the 1970s [29, 30]. This understanding was further supported by observations in patients with hippocampal damage, which led to anterograde and retrograde amnesia [31], as well as impairments in implicit memory [31, 32].

The physiology of the hippocampus is fascinating, featuring distinct regions that experience changes like neurogenesis and plasticity throughout a person's life. These changes play a crucial role in learning and memory [33]; Learning is the acquisition of a variety of information, while memory is the storage and retrieval of that information. Therefore, both processes should be considered as interconnected and complementary.

From a physiological perspective, memory can be divided into two main categories. The first is explicit memory, also known as declarative memory, which is linked to conscious thought and relies on the hippocampus. Explicit memory is divided into semantic memory for facts and episodic memory for events.

The second is implicit memory, or non-declarative memory, which operates outside of conscious awareness and typically does not depend on the hippocampus. Another distinct type of memory is working memory, which temporarily holds information while determining how to process or use it. A well-known example of this is remembering a phone number just long enough to dial it.

Working memory regions maintain connections with the hippocampus. Bilateral lesions in the ventral hippocampus, as well as conditions like Alzheimer's disease and similar disorders that damage CA1 neurons, result in significant impairments in short-term memory. Despite such damage, individuals generally retain working and implicit memory. While they lose the ability to form new long-term memories, they can still acquire new skills and preserve older memories. This underscores the critical role of the hippocampus in transforming short-term memories into long-term ones.

Research indicates that the experience-driven growth of new granule cells in the DG of the hippocampus may play a role in learning and memory [7]. However, there is still significant work required to fully elucidate the link between these newly formed cells and memory processing. The hippocampus, with its unique three-layered structure, stands apart from the cerebral cortex and remains a compelling subject of investigation in neural sciences. Techniques such as in vivo and ex vivo LTP studies [34] have proven invaluable in exploring the cellular mechanisms underlying memory formation—processes that ultimately drive learning and memory.

Furthermore, additional findings, such as head direction cells, place cells, and grid cells, demonstrate that the hippocampus plays a pivotal and essential role in memory formation. It offers a remarkable framework that integrates the various cognitive, sensory, and emotional aspects of information [2].

An essential component of hippocampal formation is Shaffer's Collaterals, which are axon branches originating from CA3 cells and projecting to the CA1 region. These connections are crucial for memory formation. Excitatory glutamatergic projections within these circuits play a key role in supporting neuronal plasticity [35-37].

The hippocampus is not only essential for learning and memory but also plays a crucial role in spatial navigation [38], emotions [3], and even motor behaviours [39]. For functions like spatial navigation and learning and memory, the hippocampus interacts with the neocortex, receiving information from the temporal, parietal, and occipital lobes [40]. When it comes to motor behavior, the hippocampus is part of the ventral striatal loop [41]. Regarding emotional behavior, it forms reciprocal connections with the amygdala and sends projections to the hypothalamus, which subsequently influences the release of adrenocorticotropic hormones [42].

Cellular arrangement and functional organization

A distinguishing feature of the hippocampus is its unidirectional tri-synaptic pathway, beginning in the entorhinal cortex

How to cite this article: Reza Fartootzadeh*. Hippocampus Physiology and Pharmacology in Normal State: An Overview. J of Pharmacol & Clin Res. 2025; 11(2): 555807. DOI: 10.19080/JPCR.2025.11.555807

and extending to the DG. From there, the mossy fibers of the DG connect with the pyramidal neurons in the CA3 region, whose axons form the Schaffer collateral fibers, which in turn synapse on the pyramidal neurons of the CA1 region [15-19, 35-37, 43]. Each region of this pathway exhibits a specific cellular arrangement and functional organization. For instance, the principal cells in the CA1 and CA3 regions are pyramidal cells, while in the DG, they are granule cells. These principal cells are excitatory glutamatergic neurons, supported by a significant number of interneurons [35-37, 43].

In addition to their structural and functional differences, these hippocampal areas exhibit varying levels of vulnerability to conditions such as AD, aging, and hypothyroidism [44-46]. They also display distinctive discharge patterns and respond differently to various influences like reward or stress [43, 47].

Notably, due to its capacity for neurogenesis, the DG is more heavily influenced by external factors, including activities like learning and exercise [48, 49].

Neurogenesis

The traditional view that neurons remain constant and do not grow in number after birth has been proven incorrect. Research shows that new neurons are generated throughout life from stem cells, primarily in the hippocampus and the olfactory bulb. This process, known as neurogenesis, is integral to learning and memory functions. A reduction in the number of neurons within the hippocampus can impair at least one category of memory production associated with this region.

Synaptic Plasticity

The history of synaptic discharge can lead to both short-term and long-term changes in synaptic function, allowing the synaptic transmission to be either strengthened or weakened based on past experiences. These alterations play a crucial role in the processes of learning and memory. Such changes can occur at either presynaptic or postsynaptic sites.

LTP refers to a rapid and enduring increase in postsynaptic potential, triggered by an elevation in intracellular Ca^{2+} following brief, repeated stimulation of the presynaptic neuron. This effect can persist for days and takes place in various regions of the central nervous system. However, it has been extensively studied in the hippocampus through two primary models: 1) LTP at Schaffer collaterals, which is postsynaptic and dependent on NMDA receptors, and 2) mossy fiber LTP, which is presynaptic and operates independently of NMDA receptors.

The phenomenon of synaptic plasticity and its response to various stimuli is a key feature of the hippocampus, differing significantly across its regions, particularly in the DG and CA1 areas [43]. The threshold for long-term potentiation (LTP) induction is notably higher in the DG compared to CA1, requiring stronger stimulation to induce LTP in the DG [50, 51]. For instance, in an avoidance learning model, heightened arousal enhances LTP in the DG but may inhibit LTP in the CA1 region [52]. Similarly, in an AD model, chronic stress suppresses both the early and late phases of LTP in the CA1 region, while leaving the late-phase LTP in the DG unaffected [53, 54].

Long-Term Memory

The encoding process for short-term explicit memory occurs in the hippocampus, while long-term memories are distributed across various regions of the neocortex. These fragments of information are interconnected through long-term changes in synaptic strength, enabling the retrieval of all related details through multiple pathways, cues, or links. Additionally, an emotional element influences whether these memories are perceived as pleasant or unpleasant.

Hippocampal Pharmacology

Nearly all regions of the hippocampus are extensively interconnected with a variety of pathways originating from diverse areas of the brain. These include adenosine, dopaminergic, serotoninergic, glutamatergic, GABAergic, noradrenergic, and cholinergic projections, each playing distinct roles within the hippocampus [55-58]. For example, GABAA subunits and N-Methyl-D-aspartate (NMDA) receptors are recognized as critical for LTP [59, 60] as well as learning and memory [61]. Notably, the hippocampus, particularly the CA1 layer, contains the highest concentration of NMDA receptors in the brain [61]. As a type of glutamate receptor, NMDA receptors play a key role in facilitating LTP [60].

The hippocampus, due to its unique physiology and high concentrations of NMDA receptors, exhibits significant plasticity essential for learning and memory. However, it is also highly vulnerable; damage to hippocampal projections or abnormalities in NMDA receptors can result in disorders such as schizophrenia and AD [62, 63]. These disruptions can impair the hippocampus's primary functions, including its critical roles in learning and memory [64, 65]. Neurodegenerative diseases often affect cognitive functions, particularly memory processes. In conditions such as AD, the capacity to remember can be significantly diminished due to disruptions in neuronal communication. Pathological changes occur in several neurotransmitter systems in AD, including glutamatergic, serotonergic, noradrenergic, and cholinergic systems [66]. This highlights the critical role that various neurotransmitters play in memory formation, with different transmitter systems contributing uniquely to mnemonic functions.

Neurotransmitter interaction with LTP

As discussed in previous sections, LTP, a key candidate for understanding learning and memory, appears to rely significantly on the role of glutamatergic receptors [59, 60]. Both NMDA and AMPA receptors are crucial to the LTP process: NMDA receptors contribute to the induction of LTP, while AMPA receptors are central to its expression. Additionally, GABA may play a role in LTP mechanisms, as blocking GABAergic receptors with antagonists tends to facilitate LTP induction. This indicates that LTP is in-

How to cite this article: Reza Fartootzadeh*. Hippocampus Physiology and Pharmacology in Normal State: An Overview. J of Pharmacol & Clin Res. 2025; 11(2): 555807. DOI: 10.19080/JPCR.2025.11.555807

fluenced by both the excitatory effects of glutamatergic systems and the inhibitory action of GABAergic systems. Consequently, these neurotransmitters are essential for learning and memory processes. Moreover, LTP may also be modulated by other neurotransmitter systems, including dopaminergic, cholinergic, serotonergic, and norepinephrinergic systems [66]. Dopaminergic projections appear to play a role in spatial learning [67] and motivational processes [68], while cholinergic projections are linked to attentional regulation and cognitive performance [69]. Meanwhile, serotonergic projections have a significant impact on emotional processes [70]. Although many neurotransmitter systems contribute to learning and memory, glutamate, GABA, acetylcholine, and dopamine exhibit stronger effects, with glutamate serving as the primary neurotransmitter driving learning and memory functions. [66].

Conclusion

The hippocampus's S-shaped structure makes it an excellent model in neuroscience research. Besides its unique anatomy, the hippocampus acts as a central hub with extensive connections to nearly every part of the brain. It is crucial for learning and memory and plays an important role in spatial navigation, emotional regulation, and even motor behaviors.

The various regions of the hippocampus are intricately interconnected through numerous pathways originating from diverse brain areas. These include adenosine, dopaminergic, serotonergic, glutamatergic, GABAergic, noradrenergic, and cholinergic systems, each contributing uniquely to hippocampal function.

Despite its essential role, the hippocampus is particularly vulnerable. Damage to its projections or abnormalities in NMDA receptors can lead to conditions like schizophrenia and AD. Such disruptions impair the hippocampus's core functions, greatly impacting learning, memory, and related processes.

This review offers a comprehensive overview of the key aspects of the physiology, pharmacology, anatomy, and pathophysiology of the hippocampus. Exploring these connections more deeply could lead to new therapeutic strategies for neurodegenerative diseases and help address impairments in learning and memory.

References

1. Gilbert PE, Brushfield AM (2009) The role of the CA3 hippocampal subregion in spatial memory: a process oriented behavioral assessment. Progress in Neuro-Psychopharmacology and Biological Psychiatry 33(5): 774-781.
2. Anand KS, Dhikav V (2012) Hippocampus in health and disease: An overview. Annals of Indian Academy of Neurology15(4): 239-246.
3. Zhu Y, Gao H, Tong L, Li Z, Wang L, et al.(2019) Emotion regulation of hippocampus using real-time fMRI neurofeedback in healthy human. Frontiers in human neuroscience 13: 1-14.
4. Rolls ET (2018) The storage and recall of memories in the hippocampo-cortical system. Cell and tissue research 373(3): 577-604.
5. McClelland J (2018) Role of the hippocampus in learning and memory: A computational analysis. Brain and Values: Psychology Press Pp: 535-547.
6. Fjell AM, McEvoy L, Holland D, Dale AM, Walhovd KB, et al. (2014) What is normal in normal aging? Effects of aging, amyloid and Alzheimer's disease on the cerebral cortex and the hippocampus. Progress in neurobiology 117: 20-40.
7. Barrett KE, Barman SM, Brooks HL, Yuan JXJ (2019) Ganong's Review of Medical Physiology, 26e. New York, NY: McGraw-Hill Education.
8. Aggleton JP, Christiansen K (2015) The subiculum: the heart of the extended hippocampal system. Progress in brain research 219: 65-82.
9. Cappaert NL, Van Strien NM, Witter MP (2015) Hippocampal formation. The rat nervous system. Elsevier Pp: 511-573.
10. Kumaran D, Maguire EA (2007) Match–mismatch processes underlie human hippocampal responses to associative novelty. Journal of Neuroscience 27(32): 8517-8524.
11. Hsu D (2007) The dentate gyrus as a filter or gate: a look back and a look ahead. Progress in brain research 163: 601-613.
12. Amaral DG, Scharfman HE, Lavenex P (2007) The dentate gyrus: fundamental neuroanatomical organization (dentate gyrus for dummies). Progress in brain research 163: 3-22.
13. Kesner RP (2007) A behavioral analysis of dentate gyrus function. Progress in brain research 163: 567-576.
14. Kesner RP (2018) An analysis of dentate gyrus function (an update). Behavioural brain research 354: 84-91.
15. Myers CE, Scharfman HE (2011) Pattern separation in the dentate gyrus: a role for the CA3 back projection. Hippocampus 21(11): 1190-1215.
16. Knierim JJ (2015) The hippocampus. Curr Biol 25(23): R1116-R1121.
17. Xu X, Sun Y, Holmes TC, López AJ (2016) Noncanonical connections between the subiculum and hippocampal CA1. Journal of Comparative Neurology 524(17): 3666-3673.
18. Witter MP (2007) The perforant path: projections from the entorhinal cortex to the dentate gyrus. Progress in brain research 163: 43-61.
19. Shinohara Y, Hosoya A, Yahagi K, Ferecskó AS, Yaguchi K, et al (2012) Hippocampal CA3 and CA2 have distinct bilateral innervation patterns to CA1 in rodents. European Journal of Neuroscience 35(5): 702-710.
20. Kerr KM, Agster KL, Furtak SC, Burwell RD (2007) Functional neuroanatomy of the parahippocampal region: the lateral and medial entorhinal areas. Hippocampus 17(9): 697-708.
21. Hitti FL, Siegelbaum SA (2014) The hippocampal CA2 region is essential for social memory. Nature 508(7494): 88-92.
22. Logothetis NK, Eschenko O, Murayama Y, Augath M, Steudel T, et al (2012) Hippocampal–cortical interaction during periods of subcortical silence. Nature 491(7425): 547-553.
23. Agster KL, Burwell RD (2013) Hippocampal and subicular efferents and afferents of the perirhinal, postrhinal, and entorhinal cortices of the rat. Behavioural brain research 254: 50-64.
24. Bubb EJ, Kinnavane L, Aggleton JP (2017) Hippocampal–diencephalic–cingulate networks for memory and emotion: An anatomical guide. Brain and neuroscience advances 1: 2398212817723443.
25. Kahn I, Andrews-Hanna JR, Vincent JL, Snyder AZ, Buckner RL (2008) Distinct cortical anatomy linked to subregions of the medial temporal lobe revealed by intrinsic functional connectivity. Journal of neurophysiology 100(1): 129-139.
26. Fartootzadeh R, Alaei H, Reisi P (2021) Mutual assistance of nucleus accumbens cannabinoid receptor-1 and orexin receptor-2 in response to nicotine: a single-unit study. Res Pharm Sci 16(2): 173-181.
27. Fartootzadeh R, Azizi F, Alaei H, Reisi P (2019) Functional crosstalk of nucleus accumbens CB1 and OX2 receptors in response to nicotine-in-

How to cite this article: Reza Fartootzadeh*. Hippocampus Physiology and Pharmacology in Normal State: An Overview. J of Pharmacol & Clin Res. 2025; 11(2): 555807. DOI: 10.19080/JPCR.2025.11.555807

duced place preference. Neuroscience letters 698: 160-164.

28. Fartootzadeh R, Azizi F, Alaei H, Reisi P (2019) Orexin type-2 receptor blockade prevents the nicotine-induced excitation of nucleus accumbens core neurons in rats: An electrophysiological perspective. Pharmacological Reports 71(2): 361-366.

29. Bliss TV, Lømo T (1973) Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. The Journal of physiology 232(2): 331-356.

30. Lømo T (2018) Discovering long-term potentiation (LTP)–recollections and reflections on what came after. Acta Physiologica 222(2): e12921.

31. Preilowski B (2009) Remembering an amnesic patient (and half a century of memory research). Fortschritte der Neurologie-psychiatrie 77(10): 568-576.

32. Markowitsch HJ, Pritzel M (1985) The neuropathology of amnesia. Progress in Neurobiology 25(3): 189-287.

33. Epp JR, Chow C, Galea LA (2013) Hippocampus-dependent learning influences hippocampal neurogenesis. Frontiers in neuroscience 7: 57.

34. Fartootzadeh R, Taheri RA, Nourani MR, Goudarzi K (2024) Orexin and cannabinoid systems modulate long-term potentiation of the hippocampus CA1 area in anesthetized rats. Iranian Journal of Basic Medical Sciences 27(4): 461-465.

35. Dumas TC, Uttaro MR, Barriga C, Brinkley T, Halavi M, Wright SN, et al (2018) Removal of area CA3 from hippocampal slices induces postsynaptic plasticity at Schaffer collateral synapses that normalizes CA1 pyramidal cell discharge. Neuroscience letters 678: 55-61.

36. Gipson KE, Yeckel MF (2007) Coincident glutamatergic and cholinergic inputs transiently depress glutamate release at rat schaffer collateral synapses. Journal of neurophysiology 97(6): 4108-4119.

37. de Sevilla DF, Buño W (2010) The muscarinic long-term enhancement of NMDA and AMPA receptor-mediated transmission at Schaffer collateral synapses develop through different intracellular mechanisms. Journal of Neuroscience 30(33): 11032-11042.

38. Chersi F, Burgess N (2015) The cognitive architecture of spatial navigation: hippocampal and striatal contributions. Neuron 88(1): 64-77.

39. Rolls ET (2023) Hippocampal spatial view cells for memory and navigation, and their underlying connectivity in humans. Hippocampus 33(5): 533-572.

40. Barnaveli I, Vigano S, Reznik D, Haggard P, Doeller CF (2024) Hippocampal-entorhinal cognitive maps and cortical motor system represent action plans and their outcomes. bioRxiv 2024.07. 04.602119.

41. Rolando F, Kononowicz TW, Duhamel J-R, Doyère V, Wirth S (2024) Distinct neural adaptations to time demand in the striatum and the hippocampus. Curr Biol 34(1): 156-170.

42. Šimić G, Tkalčić M, Vukić V, Mulc D, Španić E, , et al.(2021) Understanding emotions: origins and roles of the amygdala. Biomolecules 11(6): 823.

43. Alkadhi KA (2019) Cellular and molecular differences between area CA1 and the dentate gyrus of the hippocampus. Molecular neurobiology 56(9): 6566-6580.

44. Jackson TC, Rani A, Kumar A, Foster TC (2009) Regional hippocampal differences in AKT survival signaling across the lifespan: implications for CA1 vulnerability with aging. Cell Death & Differentiation 16(3): 439-448.

45. Gerges NZ, Alkadhi KA (2004) Hypothyroidism impairs late LTP in CA1 region but not in dentate gyrus of the intact rat hippocampus: MAPK involvement. Hippocampus 14(1): 40-45.

46. Dao AT, Zagaar MA, Levine AT, Alkadhi KA (2016) Comparison of the effect of exercise on late-phase LTP of the dentate gyrus and CA1 of Alzheimer's disease model. Molecular neurobiology 53(10): 6859-6868.

47. Gorter JA, van Vliet EA, Aronica E, Lopes da Silva FH (2002) Long-lasting increased excitability differs in dentate gyrus vs. CA1 in freely moving chronic epileptic rats after electrically induced status epilepticus. Hippocampus 12(3): 311-324.

48. Lee E-G, Son H (2009) Adult hippocampal neurogenesis and related neurotrophic factors. BMB reports 42(5): 239-244.

49. Yamashima T, Tonchev AB, Vachkov IH, Popivanova BK, Seki T, et al.(2004) Vascular adventitia generates neuronal progenitors in the monkey hippocampus after ischemia. Hippocampus 14(7): 861-875.

50. Trieu BH, Kramár EA, Cox CD, Jia Y, Wang W, et al.(2015) Pronounced differences in signal processing and synaptic plasticity between piriform-hippocampal network stages: a prominent role for adenosine. The Journal of physiology 593(13): 2889-2907.

51. Kramár EA, Babayan AH, Gavin CF, Cox CD, Jafari M, et al.(2012) Synaptic evidence for the efficacy of spaced learning. Proceedings of the National Academy of Sciences 109(13): 5121-5126.

52. Izaki Y, Arita J (1996) Long-term potentiation in the rat hippocampal CA1 region is inhibited selectively at the acquisition stage of discriminatory avoidance learning. Brain research 723(1-2): 162-168.

53. Tran TT, Srivareerat M, Alhaider IA, Alkadhi KA (2011) Chronic psychosocial stress enhances long-term depression in a subthreshold amyloid-beta rat model of Alzheimer's disease. Journal of neurochemistry 119(2): 408-416.

54. Alkadhi KA, Tran TT (2014) Chronic psychosocial stress impairs early LTP but not late LTP in the dentate gyrus of at-risk rat model of Alzheimer s disease. Brain research 1588:150-158.

55. Drake CT, Chavkin C, Milner TA (2007) Opioid systems in the dentate gyrus. Progress in brain research 163: 245-263, 813-814.

56. Sperlágh B, Sylvester Vizi E (2011) The role of extracellular adenosine in chemical neurotransmission in the hippocampus and Basal Ganglia: pharmacological and clinical aspects. Current topics in medicinal chemistry 11(8): 1034-1046.

57. Rose CR, Felix L, Zeug A, Dietrich D, Reiner A, Henneberger C (2018) Astroglial glutamate signaling and uptake in the hippocampus. Frontiers in Molecular Neuroscience10: 451.

58. Takács VT, Cserép C, Schlingloff D, Pósfai B, Szőnyi A, et al.(2018) Co-transmission of acetylcholine and GABA regulates hippocampal states. Nature communications 9(1): 2848.

59. Schummers J, Browning MD (2001) Evidence for a role for GABAA and NMDA receptors in ethanol inhibition of long-term potentiation. Molecular Brain Research 94(1-2): 9-14.

60. MacDonald JF, Jackson MF, Beazely MA (2006) Hippocampal long-term synaptic plasticity and signal amplification of NMDA receptors. Critical Reviews™ in Neurobiology 18(1-2): 71-84.

61. Bloodgood BL, Sabatini BL, Van Dongen A (2009) NMDA receptor-mediated calcium transients in dendritic spines. Biology of the NMDA Receptor Pp: 201-211.

62. Bartsch T, Wulff P (2015) The hippocampus in aging and disease: from plasticity to vulnerability. Elsevier 309: 1-16.

63. Santos VR, santana Melo I, Pacheco ALD, de Castro OW (2021) Life and death in the hippocampus: What's bad? Epilepsy & Behavior 121:106595.

64. Arias-Cavieres A, Fonteh A, Castro-Rivera CI, Garcia III AJ (2021) Intermittent Hypoxia causes targeted disruption to NMDA receptor dependent synaptic plasticity in area CA1 of the hippocampus. Experimental neurology 344: 113808.

How to cite this article: Reza Fartootzadeh*. Hippocampus Physiology and Pharmacology in Normal State: An Overview. J of Pharmacol & Clin Res. 2025; 11(2): 555807. DOI: 10.19080/JPCR.2025.11.555807

65. Konen LM, Wright AL, Royle GA, Morris GP, Lau BK, et al.(2020) A new mouse line with reduced GluA2 Q/R site RNA editing exhibits loss of dendritic spines, hippocampal CA1-neuron loss, learning and memory impairments and NMDA receptor-independent seizure vulnerability. Molecular brain 13(1): 27.

66. Myhrer T (2003) Neurotransmitter systems involved in learning and memory in the rat: a meta-analysis based on studies of four behavioral tasks. Brain Research Reviews 41(2-3): 268-287.

67. Kempadoo KA, Mosharov EV, Choi SJ, Sulzer D, Kandel ER (2016) Dopamine release from the locus coeruleus to the dorsal hippocampus promotes spatial learning and memory. Proceedings of the National Academy of Sciences 113(51): 14835-14840.

68. Kesner AJ, Calva CB,Ikemoto S (2022) Seeking motivation and reward: Roles of dopamine, hippocampus, and supramammillo-septal pathway. Progress in neurobiology 212: 102252.

69. Parikh V, Bangasser DA (2020) Cholinergic signaling dynamics and cognitive control of attention. Behavioral Pharmacology of the Cholinergic System 45: 71-87.

70. Vázquez-León P, Miranda-Páez A, Valencia-Flores K, Sánchez-Castillo H (2023) Defensive and emotional behavior modulation by serotonin in the periaqueductal gray. Cellular and Molecular Neurobiology 43(4): 1453-1468.

This work is licensed under Creative Commons Attribution 4.0 License
DOI: 10.19080/JPCR.2025.11.555807

Your next submission with Juniper Publishers will reach you the below assets

- Quality Editorial service
- Swift Peer Review
- Reprints availability
- E-prints Service
- Manuscript Podcast for convenient understanding
- Global attainment for your research
- Manuscript accessibility in different formats
  (Pdf, E-pub, Full Text, Audio)
- Unceasing customer service

Track the below URL for one-step submission
https://juniperpublishers.com/online-submission.php