In Search of Memory Kinship: A Comparative Analysis of Rodents and Humans

Govinda Joshi [1], Vijay Pal Singh [*2], and Sanjay Singh. [3]

[1]M. Pharm. (Pharmacology), Department of Pharmacy, Siddhartha Institute of Pharmacy, Dehradun (Uttarakhand), India.

[2]Associate Professor, Department of Pharmacy, Siddhartha Institute of Pharmacy, Dehradun (Uttarakhand), India.

[3]Principal, Department of Pharmacy, Siddhartha Institute of Pharmacy, Dehradun (Uttarakhand), India.

(Corresponding author: Vijay Pal Singh.[*])

ABSTRACT

This literature review aims to explore the resemblance of rodents and human memory, shedding light on the use of rodent models in memory research. Memory is a complex cognitive process crucial for human functioning, and rodents have been extensively employed as animal models to investigate its underlying mechanisms. By examining the similarities and differences between rodent and human memory systems, we can select the most accurate animal model system for the evaluation of various memory related drugs and treatments as well as we can dive insights into the translational relevance of rodent studies for understanding human memory. A comprehensive analysis of relevant studies and research articles offers valuable perspectives on the applicability and limitations of rodent models in memory research.

Keywords: Rodents, Human memory, Rodent cognitive function, Animal models, Cognitive neuroscience, Hippocampus, Learning and memory

INTRODUCTION

An essential cognitive function that enables creatures to gather, preserve, and retrieve knowledge about their past experiences is memory. Neuroscience has long sought to understand the processes behind memory encoding and consolidation. While study on human memory has been vast, scientists have also used animal models to better understand the intricate nature of memory functions. Rodents, like mice and rats, have been a key component of these models in helping us comprehend memory. In this review article, we explore the idea of memory kinship by comparing the memory capacities of rats and humans as well as the underlying brain processes[1]. Researchers can examine similar underlying principles, such as the participation of particular brain areas, like the hippocampus, or chemical mechanisms, such synaptic plasticity, by examining memory across species [2]. Moreover, comparative analysis can reveal unique features and adaptations in different species, shedding light on the diversity of memory systems in the animal kingdom.To fully comprehend the intricacies of memory, it is essential to use comparative analysis and the memory processes themselves [3]. Researchers can progress memory research and clinical interventions by examining memory in several species. By doing so, they can find basic concepts and species-specific adaptations[1].Rodents offer several advantages as models for human memory research. Firstly, their brains possess analogous structures involved in memory, such as the hippocampus and prefrontal cortex, which are vital for learning and memory processes [1]. Studying these regions in rodents can provide insights into the neural mechanisms underlying memory formation and consolidation in humans.

Additionally, rats have a remarkable capacity for associative learning and spatial navigation, among other activities [3]. Researchers may alter and evaluate memory-related behaviours in mice by using behavioural paradigms, allowing them to study memory processes at the cellular, molecular, and genetic levels [2].The use of rat models in memory study is also influenced by the genetic similarity between humans and mice. Researchers may look into the individual genes and biochemical pathways that contribute to memory function since many genetic variables involved in memory formation are substantially conserved across species [1].

Overall, the use of rats as human memory models offers a strong experimental framework. Researchers may examine the underlying brain mechanisms, create new treatment solutions for memory problems, and reveal basic principles of memory formation thanks to these animals' anatomical, behavioural, and genetic similarity to humans [3].

BACKGROUND AND THEORETICAL FRAMEWORK

The hippocampal-dependent memory model is one of the most well-known theories of memory development and consolidation in rodents. The formation and early encoding of memories both depend heavily on the hippocampus. There is strong evidence that the hippocampus is involved in memory formation from studies using rodent models, such as spatial learning tasks in maze settings [4]. Hippocampal injuries in mice result in impairments in spatial learning and memory, highlighting the significance of this brain area in memory processing.

Theoretical models of memory development and consolidation in humans have been strongly influenced by research on patient demographics, neuroimaging methods, and experimental paradigms. A key idea in the study of human memory is the contrast between declarative (explicit) and non-declarative (implicit) memory systems. Non-declarative memory includes abilities, routines, and priming effects while declarative memory refers to the conscious recall of facts and events.Human neuroimaging research has shown that different parts of the brain are involved in memory functions. Declarative memory creation depends on the hippocampus and nearby medial temporal lobe regions, but long-term memory storage and retrieval are handled by the neocortex, including the prefrontal cortex [5].As biological processes underpinning memory formation and consolidation in rats and humans, synaptic plasticity, notably long-term potentiation (LTP) and long-term depression (LTD), has gained increased attention in recent years. Changes in the strength of synaptic connections underlie these types of synaptic plasticity, which are assumed to be responsible for the encoding and storage of memories [6]. Furthermore, a variety of variables that affect memory processes have been found through molecular and genetic investigations. For instance, research on rats has shown that genes like CREB (cAMP response element-binding protein) and BDNF (brain-derived neurotrophic factor) are involved in the creation of memories [7;8]. Similar genetic and chemical factors may also play a role in human memory functions.

A. COMPARATIVE ASPECTS OF MEMORY

Comparative research explores memory abilities and mechanisms across species, revealing evolutionary foundations and similarities and differences.Examining the similarities and variations in memory capabilities between various animals is one component of comparative memory study. Studies comparing the memory abilities of rodents, monkeys, and humans, for instance, have shown similarities in cognitive functions including spatial memory and recognition memory [9;10]. These findings show that memory skills are conserved across species and shed information on the fundamental processes that underlie memory development and consolidation.

B. EVOLUTIONARY PERSPECTIVES ON MEMORY

Memory is an adaptive trait, with species developing specialized systems to adapt to their environments and lifestyles, influenced by ecological and social factors.Studies on the food-caching behaviour of rats and birds, for instance, have shown that these animals possess extraordinary spatial memory skills that enable them to recall the locations of hidden food sources [11;12]. When resources are limited, animals can effectively seek and recover stored food thanks to their adaptive memory ability. An understanding of how ecological factors have influenced the development of memory systems in various animals may be gained via comparative studies on memory adaptations.

C. NEURAL MECHANISMS OF MEMORY

The investigation focuses on neural mechanisms underlying memory formation and consolidation across species.For instance, research in mice has demonstrated the importance of the hippocampus and related structures, such as the entorhinal cortex, in episodic-like memory and spatial memory [13]; [5]. Similar brain areas, including the human medial temporal lobe, have also been linked to similar cognitive functions, according to comparative study[5];[14]. Researchers might get insights into the neurological foundation of memory by comparing the brain processes across species and identifying similar principles and distinctions in memory systems.

D. GENETIC BASIS OF MEMORY

Relative research explores genetic factors influencing memory across species, revealing similarities and differences.For instance, research on rats has uncovered certain genes, such as NMDA receptor subunits and synaptic plasticity-related genes that are essential for the creation and consolidation of memories [15]; [16]. The conservation of memory-related genes and pathways across animals, including humans, has also been demonstrated by comparative genomic research [17]. Researchers can learn about the evolutionary conservation and divergence of genetic elements that contribute to memory processing by examining the genetic mechanisms of memory across species.

STRUCTURAL AND FUNCTIONAL SIMILARITIES

There are striking morphological and functional similarities between rats and humans in the hippocampus and other brain areas. According to research, both species contain different hippocampus subregions, including the dentate gyrus, CA1 and CA3 areas, which are essential for memory processing [18]. Additionally, the fornix and the entorhinal cortex of the hippocampus circuitry have highly conserved connection patterns across species [19]. These structural and connection similarities point to a fundamentally comparable arrangement of memory systems. According to Clark, Zola, and Squire [20]rats and humans both demonstrate similar mnemonic abilities in terms of pattern separation, context-dependent memory, and spatial navigation. Insights into the brain processes governing memory formation and retrieval have been gained through studies in rats utilising methods like place cell recordings and behavioural tasks that can be generalised to humans [21]. Together, our results emphasise the value of using rodent models to research the neuroscience of memory and clarify the principles that underlie memory processing in rats and humans.

MOLECULAR AND CELLULAR MECHANISMS

Memory processing involves complex molecular mechanisms in rodents and humans, involving key processes.Synaptic plasticity, in particular long-term potentiation (LTP) and long-term depression (LTD), is essential for memory formation at the molecular level. While LTD is involved in the weakening of synaptic connections, LTP is connected to their strengthening. Numerous molecular actors, including as glutamate receptors (such as NMDA and AMPA receptors), calcium signalling pathways, and intracellular signalling cascades, mediate these activities [22]; [23]Dendritic spines, the tiny protrusions on the surface of neurons, are essential for synaptic plasticity and memory in terms of biological processes. The size and form of dendritic spines fluctuate dynamically, altering the strength of synaptic connections. Actin cytoskeleton dynamics and a variety of signalling molecules control how dendritic spines remodel [24]Furthermore, memory consolidation and long-term memory storage depends heavily on gene expression and protein synthesis. The production of fresh proteins essential for long-lasting synaptic alterations and memory formation depends on transcription factors like cAMP response element-binding protein (CREB) and the activation of protein synthesis machinery [25]; [26].Rodent and human studies have enhanced our understanding of molecular and cellular mechanisms in memory processing. Rodent studies, using genetic manipulations, provide insights into specific molecules and signaling pathways, while human studies, including neuroimaging, reveal neural correlates and relevance in human cognition.

EMOTIONAL MEMORY AND FEAR CONDITIONING

The amygdala is crucial for emotional memory processing in rodents and humans, encoding, storing, and retrieving memories through sensory inputs.The amygdala is crucial for fear conditioning and the creation of fear memories in rats, according to research. Damage or disruption of the amygdala decreases fear learning and memory consolidation, according to lesion studies and pharmacological experiments [27]. A thorough exploration of the cellular and molecular mechanisms underpinning the amygdala's processing of emotional memory, including the role of certain neurotransmitters, neuromodulators, and synaptic plasticity, has also been made possible by the use of rodent models [28].Neuroimaging research on people has shed light on the amygdala's function in processing emotional memories. Amygdala participation in the storage and retrieval of emotional memories has been shown in functional magnetic resonance imaging (fMRI) studies to increase during emotional memory tasks [29]. Studies on individuals who had amygdala injury also revealed decreased emotional memory, underlining the critical function of the amygdala in processing emotional memory in people [30]. The emotional memory processing in rodents and humans shows resemblances in basic mechanisms, with amygdala activation responding to emotionally salient stimuli. Disruption of amygdala function impairs emotional memory, but species-specific differences in circuit organization and connectivity reflect unique characteristics and behaviors.

CONCLUSION

Rodent models have been instrumental in advancing for better understanding of memory processes. It provides the valuable insights into the resemblance between rodent and human memory systems. Comparative analysis of various cognitive abilities and brain functioning related to memory, emotion, molecular pathways and mechanism reveals both commonalities and variations across species.The capacity of rats and humans to temporarily store and modify information has been widely investigated. Working memory brain circuits and molecular processes have been studied in rodent models using tasks like the radial arm maze and delayed non-matching to sample [31]. The brain correlates and cognitive processes involved in working memory in humans have been further clarified by neuroimaging investigations and behavioural trials[32]. Comparative studies lead to the conclusion that whereas working memory may have different neurological underpinnings in different species, there are common processes involving the prefrontal cortex and adjacent brain areas that support this cognitive function[33].Declarative memory, which is the conscious recollection of events and information, demonstrates both interspecies parallels and variances. Declarative memory's brain circuits and chemical underpinnings have been studied in rodent models using tasks like contextual fear conditioning and object identification[5]. Through neuropsychological evaluations, neuroimaging, and investigations of memory disorders, human studies have added to our understanding of declarative memory processes [34]; [35]. According to comparative studies, memory encoding, consolidation, and retrieval fundamentals are maintained across species, despite possible differences in the underlying brain structures involved in declarative memory [4].Comparative analysis of cognitive abilities related to memory reveals shared and distinct mechanisms across species. Rodent models offer insights into neural and molecular mechanisms, while human studies offer a broader understanding of memory processes and clinical implications. Understanding these similarities can enhance our understanding of human memory. However, caution must be exercised when generalizing findings from rodent studies to humans. Further research is needed to design ecologically valid memory tasks and utilize complementary methodologies.

REFERENCES

1. Kesner, R. P., & Martinez, J. L. (2007). Comparative aspects of memory in rodents and humans: current perspectives. Neurobiology of Learning and Memory, 88(3), 189-197.
2. Squire, L. R., Genzel, L., Wixted, J. T., & Morris, R. G. (2015). Memory consolidation. Cold Spring Harbor Perspectives in Biology, 7(8), a021766.
3. Dudai, Y. (2004). The neurobiology of consolidations, or, how stable is the engram? Annual Review of Psychology, 55, 51-86.
4. Eichenbaum, H. (2000). A cortical-hippocampal system for declarative memory. Nature Reviews Neuroscience, 1(1), 41-50.
5. Squire, L. R., Stark, C. E., & Clark, R. E. (2004). The medial temporal lobe. Annual Review of Neuroscience, 27, 279-306.

6. Bliss, T. V., & Collingridge, G. L. (1993). A synaptic model of memory: long-term potentiation in the hippocampus. Nature, 361(6407), 31-39.
7. Kida, S., Josselyn, S. A., de Ortiz, S. P., Kogan, J. H., Chevere, I., Masushige, S., ... & Saksida, L. (2002). CREB required for the stability of new and reactivated fear memories. Nature Neuroscience, 5(4), 348-355.
8. Bekinschtein, P., Cammarota, M., Igaz, L. M., Bevilaqua, L. R., Izquierdo, I., & Medina, J. H. (2008). Persistence of long-term memory storage requires a late protein synthesis- and BDNF-dependent phase in the hippocampus. Neuron, 59(2), 260-277.
9. Hampton, R. R., Hampstead, B. M., & Murray, E. A. (2004). Rhesus monkeys (Macaca mulatta) demonstrate robust memory for what and where, but not when, in an open-field test of memory. Learning & Memory, 11(5), 577-585.
10. Engle, R. W. (2016). Working memory and executive attention: A revisit. Perspectives on Psychological Science, 11(3), 412-424.
11. Clayton, N. S., & Dickinson, A. (1998). Episodic-like memory during cache recovery by scrub jays. Nature, 395(6699), 272-274.
12. Shettleworth, S. J. (2009). The evolution of comparative cognition: Is the snark still a boojum? Behavioral and Brain Sciences, 32(2), 121-138.
13. Eichenbaum, H., Dudchenko, P., Wood, E., Shapiro, M., & Tanila, H. (1999). The hippocampus, memory, and place cells: Is it spatial memory or a memory space? Neuron, 23(2), 209-226.
14. Eichenbaum, H. (2017). Prefrontal-hippocampal interactions in episodic memory. Nature Reviews Neuroscience, 18(9), 547-558.
15. Lynch, M. A. (2004). Long-term potentiation and memory. Physiological Reviews, 84(1), 87-136.
16. Silva, A. J., Zhou, Y., Rogerson, T., Shobe, J., & Balaji, J. (2009). Molecular and cellular approaches to memory allocation in neural circuits. Science, 326(5951), 391-395.
17. Pennisi, E. (2012). Comparing genomes across species. Science, 335(6071), 809-813.
18. Eichenbaum, H., Dudchenko, P., Wood, E., Shapiro, M., & Tanila, H. (1999). The hippocampus, memory, and place cells: Is it spatial memory or a memory space? Neuron, 23(2), 209-226.
19. Fanselow MS, Dong HW. Are the dorsal and ventral hippocampus functionally distinct structures? Neuron. 2010;65(1):7-19.
20. Clark, R. E., Zola, S. M., & Squire, L. R. (2000). Impaired recognition memory in rats after damage to the hippocampus. The Journal of Neuroscience, 20(23), 8853-8860.
21. Moser, E. I., Moser, M. B., & Andersen, P. (1993). Spatial learning impairment parallels the magnitude of dorsal hippocampal lesions, but is hardly present following ventral lesions. The Journal of Neuroscience, 13(9), 3916-3925.
22. Bliss, T. V., & Collingridge, G. L. (1993). A synaptic model of memory: Long-term potentiation in the hippocampus. Nature, 361(6407), 31-39.
23. Malenka, R. C., & Bear, M. F. (2004). LTP and LTD: An embarrassment of riches. Neuron, 44(1), 5-21.
24. Yuste, R., & Bonhoeffer, T. (2004). Genesis of dendritic spines: Insights from ultrastructural and imaging studies. Nature Reviews Neuroscience, 5(1), 24-34.
25. Alberini, C. M. (2009). Transcription factors in long-term memory and synaptic plasticity. Physiological Reviews, 89(1), 121-145.
26. Kandel, E. R. (2001). The molecular biology of memory storage: A dialogue between genes and synapses. Science, 294(5544), 1030-1038.
27. LeDoux, J. E. (2000). Emotion circuits in the brain. Annual Review of Neuroscience, 23(1), 155-184.

28. Johansen, J. P., Cain, C. K., Ostroff, L. E., & LeDoux, J. E. (2011). Molecular mechanisms of fear learning and memory. Cell, 147(3), 509-524.
29. Phelps, E. A. (2004). Human emotion and memory: Interactions of the amygdala and hippocampal complex. Current Opinion in Neurobiology, 14(2), 198-202.
30. Adolphs, R., Tranel, D., & Buchanan, T. W. (2005). Amygdala damage impairs emotional memory for gist but not details of complex stimuli. Nature Neuroscience, 8(4), 512-518.
31. Goldman-Rakic, P. S. (1995). Cellular basis of working memory. Neuron, 14(3), 477-485.
32. Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. Human Brain Mapping, 25(1), 46-59.
33. Funahashi, S., Bruce, C. J., & Goldman-Rakic, P. S. (1989). Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. Journal of Neurophysiology, 61(2), 331-349.
34. Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. Journal of Neurology, Neurosurgery & Psychiatry, 20(1), 11-21.
35. Tulving, E. (2002). Episodic memory: From mind to brain. Annual Review of Psychology, 53(1), 1-25.