STM JOURNALS

Research & Reviews: Journal of
Veterinary Science and Technology

https://journals.stmjournals.com/rrjovst

ISSN: 2319-3441 (Online)
ISSN: 2349-3690 (Print)
Volume 13, Issue 3, 2024
September–December
DOI (Journal): 10.37591/RRJoVST

Review RRJoVST

MicroRNAs in Animal Behavior: Regulation of Memory and Decision-Making in Mammals

Shad Ahmad[1,*], Mohd. Danish[2]

Abstract

MicroRNAs are small, non-coding RNA molecules that play a crucial role in post-transcriptional regulation of gene expression. In recent years, their significance has extended beyond cellular development and disease regulation, as emerging evidence suggests they are critical mediators in complex behavioral processes, including learning, memory, and decision-making. This article explores the role of miRNAs in regulating neural plasticity and cognitive functions in mammals, emphasizing their involvement in memory formation and cognitive decision-making. The biogenesis of miRNAs and their mechanisms of action specifically, the regulation of synaptic plasticity and long-term potentiation are key to understanding their impact on behavioral outcomes. Several miRNAs, such as miR-132, miR-134, and miR-124, have been identified as essential modulators of memory processes, influencing synaptic strength and neural circuit reorganization. Through the regulation of key molecular pathways, including brain-derived neurotrophic factor and cAMP response element-binding protein, miRNAs shape the structural and functional plasticity necessary for memory storage and retrieval. miRNAs are implicated in cognitive flexibility and decision-making, particularly within the prefrontal cortex. This region, vital for executive functions, is regulated by miRNAs that influence risk assessment, reward processing, and choice behavior. The intricate feedback loops between miRNAs, transcription factors, and other molecular regulators highlight their broad influence on cognition and behavior. Given their central role in cognitive processes, miRNAs have also emerged as potential therapeutic targets for neurodegenerative diseases and cognitive disorders. Targeting specific miRNAs holds promise for restoring cognitive function in conditions, such as Alzheimer's and Parkinson's diseases. However, challenges remain in the development of miRNA-based therapies, particularly in ensuring precise delivery and minimizing off-target effects. This review underscores the importance of miRNAs in behavioral regulation and calls for further research into their therapeutic potential in mammals.

Keywords: MicroRNAs, epigenetic regulation, animal behavior, memory formation

INTRODUCTION

MicroRNAs (miRNAs) are short, non-coding RNA sequences that play a crucial role in regulating gene expression after transcription. Since their identification, miRNAs have been acknowledged for their capacity to influence various cellular functions by interacting with messenger RNA (mRNA), either suppressing its translation or facilitating its breakdown. In mammals, miRNAs are essential for developmental processes, tissue specialization, and the preservation of cellular balance. Recent studies have broadened their importance, highlighting their role in regulating complex behaviors, especially in cognitive activities like learning, memory formation, and decision-making [1–3].

***Author for Correspondence**
Shad Ahmad
E-mail: shadahmad410@gmail.com

[1,2]Student, Department: Warner College of Dairy Technology, Sam Higginbottom University of Agriculture, Technology and Sciences, Allahabad, Uttar Pradesh, India

Received Date: September 18, 2024
Accepted Date: October 17, 2024
Published Date: October 30, 2024

Citation: Shad Ahmad, Mohd. Danish. MicroRNAs in Animal Behavior: Regulation of Memory and Decision-Making in Mammals. Research & Reviews: Journal of Veterinary Science and Technology. 2024; 13(3): 21–25p.

Studying miRNAs in mammals is essential for understanding how gene regulation can influence behavior at the molecular level. MiRNAs are key players in modulating this plasticity by targeting specific genes involved in synaptic function and neural circuit formation. Decision-making, a higher-order cognitive function that involves evaluating choices and outcomes, also appears to be regulated by miRNAs through their effects on neural networks in regions, such as the prefrontal cortex. The purpose of this article is to explore the molecular pathways through which miRNAs regulate these behavioral processes in mammals. By focusing on specific miRNAs that influence neural plasticity, synaptic activity, and cognitive functions, this review aims to provide insight into the mechanisms through which miRNAs shape behaviors like learning, memory, and decision-making. Understanding these pathways is not only fundamental to neurobiology but also has potential applications in addressing cognitive disorders and developing miRNA-based therapeutic strategies [4].

miRNAs: Biological Function and Mechanism of Action

miRNAs are synthesized through a well-defined biogenesis process, beginning with the transcription of primary miRNAs (pri-miRNAs) in the nucleus. These pri-miRNAs are processed by the Drosha enzyme into precursor miRNAs (pre-miRNAs), which are then exported to the cytoplasm. In the cytoplasm, another enzyme called Dicer further processes the pre-miRNAs into mature miRNA duplexes. One strand of the duplex integrates into the RNA-induced silencing complex (RISC), directing it to the target mRNA through complementary base pairing. Once the mature miRNA is incorporated into the RISC, it attaches to the 3' untranslated region (3' UTR) of the target mRNAs, resulting in either translation inhibition or mRNA degradation [5]. The degree of complementarity between the miRNA and its target determines the outcome: near-perfect pairing usually results in mRNA degradation, while imperfect pairing leads to translational repression without degrading the mRNA. Through these mechanisms, miRNAs regulate gene expression post-transcriptionally, fine-tuning the levels of proteins produced in the cell. miRNAs exhibit tissue-specific expression, meaning that certain miRNAs are active only in particular tissues or cell types. This specificity allows miRNAs to play diverse functional roles across different biological systems in mammals. For example, some miRNAs are involved in neural development, while others regulate immune responses or metabolic processes. This functional diversity is essential for the precise control of gene expression required for the proper functioning of various organs and systems [6].

Role of miRNAs in Learning and Memory Formation

miRNAs play a critical role in the regulation of learning and memory formation by influencing neural plasticity and synaptic function. Several key miRNAs, such as miR-132, miR-134, and miR-124, have been identified as important regulators of these cognitive processes. miR-132, for example, is known to enhance synaptic plasticity by promoting dendritic growth and spine formation, which are essential for long-term potentiation (LTP), a cellular mechanism that underlies memory. miR-134, on the other hand, negatively regulates synaptic strength by modulating dendritic spine size, thus fine-tuning the strength of synaptic connections during learning. The molecular pathways through which miRNAs affect learning and memory primarily involve their regulation of genes that control synaptic plasticity, LTP, and dendritic spine morphology [7]. Similarly, miR-134 targets Limk1, a kinase that modulates actin cytoskeleton dynamics, thereby controlling the structural changes in dendrites necessary for memory consolidation. Experimental studies using animal models, particularly rodents, have provided strong evidence for the role of miRNAs in memory formation. In these studies, altering the expression of specific miRNAs, such as overexpression or inhibition of miR-132 or miR-134, has been shown to significantly impact cognitive functions like spatial learning and fear conditioning. These findings demonstrate the importance of miRNAs in regulating the molecular machinery required for memory storage and retrieval [8].

miRNAs and Decision-Making

miRNAs also play a significant role in decision-making by regulating cognitive functions that are largely centered in the prefrontal cortex, a region of the brain responsible for complex cognitive tasks, such as planning, risk assessment, and impulse control. The prefrontal cortex works in conjunction with other neural circuits, including those involved in reward processing and emotional regulation, to guide decision-making processes. Several miRNAs are involved in modulating cognitive flexibility, which is key to effective decision-making. For example, miR-128 has been shown to regulate cognitive processes related to the balance between action and inhibition, a critical factor in decision-making. miR-9 has been implicated in the modulation of neural plasticity within the prefrontal cortex, which allows for quick adjustments in behavior when circumstances change. These miRNAs help fine-tune the neuronal activity required for flexible cognitive responses to new information. Behavioral studies in animal models have demonstrated the influence of specific miRNAs on decision-making. For instance, altering the levels of miR-128 in mice has been linked to changes in risk assessment and reward evaluation, where the animals exhibited different choices based on perceived rewards or punishments. Another study on miR-9 showed that its disruption affected the animals' ability to shift strategies in response to new environmental cues, highlighting its role in cognitive adaptability [9].

Molecular Pathways Connecting miRNAs to Behavioral Outcomes

miRNAs influence behavioral outcomes by regulating molecular pathways that are crucial for neural plasticity, the brain's ability to adapt and reorganize itself. The brain-derived neurotrophic factor (BDNF) and cAMP response element-binding protein (CREB) signaling pathways are two major routes connecting miRNAs to neural plasticity. BDNF is essential for promoting synaptic growth and strength, while CREB is a transcription factor involved in long-term memory formation. miRNAs, such as miR-132 enhance synaptic plasticity by regulating BDNF expression, which in turn strengthens synaptic connections and promotes learning [9]. miR-124 and miR-134 modulate the activity of CREB, affecting processes like dendritic spine formation and LTP, both of which are critical for memory and learning. In addition to their direct role in neural signaling, miRNAs also influence behavior through epigenetic regulation. miRNAs can affect epigenetic changes by targeting enzymes like DNA methyltransferases (DNMTs) or histone deacetylases (HDACs), which modify chromatin structure and gene expression. For example, miR-137 is known to regulate histone modification enzymes, altering chromatin accessibility and thereby influencing the expression of genes involved in synaptic plasticity, miRNAs participate in complex feedback loops with other molecular players involved in behavioral regulation [10]. For instance, transcription factors like CREB not only regulate the expression of miRNAs but are also targets of miRNAs themselves, creating a feedback mechanism that fine-tunes the balance between gene activation and repression. Similarly, enzymes like kinases and phosphatases involved in synaptic signaling are regulated by miRNAs, ensuring precise control over the neural circuits that govern behavior. This intricate interplay between miRNAs, transcription factors, and enzymes ensures that behavioral outcomes, such as learning, memory, and decision-making, are tightly regulated and adaptable to environmental changes [11, 12].

miRNAs as Therapeutic Targets for Behavioral Disorders

miRNAs are emerging as promising therapeutic targets for various behavioral disorders, particularly neurodegenerative diseases, such as Alzheimer's and Parkinson's. These disorders are characterized by significant impairments in memory and cognitive function, often linked to dysregulation of miRNAs that control synaptic plasticity and neural communication. For instance, altered expression of miR-29 and miR-181 has been associated with cognitive decline in Alzheimer's disease, while miR-132 has been implicated in the pathogenesis of Parkinson's disease. The potential of miRNA-based therapies lies in their ability to restore normal behavior and cognitive function by modulating the expression of specific miRNAs involved in neural plasticity. For example, strategies that inhibit overexpressed miRNAs or replace lost miRNAs could help reinstate the balance necessary for synaptic health and cognitive processes. Early studies have shown promising results in animal models, where miRNA modulation led to improvements in memory and cognitive tasks, suggesting that targeting miRNAs could be an effective therapeutic approach. As research progresses, the prospects of miRNA-based therapies look promising. Innovations in delivery systems, like nanoparticles and viral vectors, are being investigated to enhance targeting precision and effectiveness. Moreover, a deeper understanding of the regulatory networks involving miRNAs could pave the way for more refined therapeutic strategies, potentially transforming the management of behavioral disorders and enhancing cognitive function in affected individuals [13, 14].

CONCLUSIONS

miRNAs play a pivotal role in shaping learning, memory, and decision-making processes through their regulatory influence on neural plasticity and cognitive functions. Key findings highlight that specific miRNA, such as miR-132, miR-134, and miR-124, are essential in modulating synaptic plasticity, LTP, and the structural dynamics of neural circuits. Their involvement extends beyond mere gene regulation; miRNAs also influence epigenetic mechanisms and participate in complex feedback loops with transcription factors and other signaling molecules. This intricate interplay underscores the significance of miRNAs in facilitating cognitive flexibility, memory consolidation, and decision-making strategies, thereby impacting overall behavioral outcomes in mammals. Looking ahead, future research directions should explore the broader implications of miRNAs in other cognitive processes, such as social behavior, emotional regulation, and adaptation to environmental changes. Investigating the role of miRNAs in these contexts could deepen our understanding of animal behavior and the underlying molecular mechanisms. Additionally, the potential for miRNA-based therapeutic interventions in treating cognitive disorders offers exciting possibilities for advancing neuroscience and behavioral medicine. Continued exploration of miRNA functions and their pathways will not only enhance our comprehension of brain function but may also lead to novel strategies for addressing neurodegenerative diseases and behavioral disorders, ultimately improving cognitive health and quality of life.

REFERENCES

1. Codocedo JF, Inestrosa NC. Environmental control of microRNAs in the nervous system: implications in plasticity and behavior. Neurosci Biobehav Rev. 2016;60:121–38.
2. Mallick A. MicroRNA. In: Encyclopedia of Animal Cognition and Behavior. Cham: Springer International Publishing; 2022. pp. 4293–6.
3. Cardoso SD, Teles MC, Oliveira RF. Neurogenomic mechanisms of social plasticity. J Experim Biol. 2015;218(1):140–9.
4. Bahlakeh G, Gorji A, Soltani H, Ghadiri T. MicroRNA alterations in neuropathologic cognitive disorders with an emphasis on dementia: lessons from animal models. J Cell Physiol. 2021;236(2):806–23.
5. Rajasethupathy P. Novel Small-RNA Mediated Gene-Regulatory Mechanisms for Long-term Memory. Columbia University; 2012.
6. Kołosowska KA, Schratt G, Winterer J. microRNA-dependent regulation of gene expression in GABAergic interneurons. Front Cell Neurosci. 2023;17:1188574.
7. Quinn RK, Brown AL, Goldie BJ, Levi EM, Dickson PW, Smith DW, et al. Distinct miRNA expression in dorsal striatal subregions is associated with risk for addiction in rats. Translat Psych. 2015;5(2):e503-.
8. Saab BJ, Mansuy IM. Neuroepigenetics of memory formation and impairment: the role of microRNAs. Neuropharmacology. 2014;80:61–9.
9. Wang W, Kwon EJ, Tsai LH. MicroRNAs in learning, memory, and neurological diseases. Learn Mem. 2012;19(9):359–68.
10. Bredy TW, Lin Q, Wei W, Baker-Andresen D, Mattick JS. MicroRNA regulation of neural plasticity and memory. Neurobiol Learn Mem. 2011;96(1):89–94.
11. Busto GU, Guven-Ozkan T, Davis RL. MicroRNA function in Drosophila memory formation. Curr Opin Neurobiol. 2017;43:15–24.
12. Bitetti A, Mallory AC, Golini E, Carrieri C, Carreño Gutiérrez H, Perlas E, et al. MicroRNA degradation by a conserved target RNA regulates animal behavior. Nat Struct Mol Biol. 2018;25(3):244–51.

13. Mansur F, Ivshina M, Gu W, Schaevitz L, Stackpole E, Gujja S, et al. Gld2-catalyzed 3′ monoadenylation of miRNAs in the hippocampus has no detectable effect on their stability or on animal behavior. RNA. 2016;22(10):1492–9.
14. Issler O, Chen A. Determining the role of microRNAs in psychiatric disorders. Nat Rev Neurosci. 2015;16(4):201–12.