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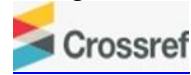
Michael Debesa



Effect of Environmental Enrichment on Behavioral and Physiological Welfare Indicators in Laboratory Mice in Eritrea

 Michael Debesa

Hamelmal Agricultural College



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Abstract

Purpose: The aim of the study was to assess the effect of environmental enrichment on behavioral and physiological welfare indicators in laboratory mice in Eritrea.

Methodology: This study adopted a desk methodology. A desk study research design is commonly known as secondary data collection. This is basically collecting data from existing resources preferably because of its low cost advantage as compared to a field research. Our current study looked into already published studies and reports as the data was easily accessed through online journals and libraries.

Findings: The study on environmental enrichment included features like running wheels, nesting material, and tunnels, providing a more stimulating environment compared to standard laboratory housing. The findings revealed significant improvements in the behavioral welfare of mice housed in enriched environments, including reduced stereotypic behaviors and increased exploration and social interactions. Additionally, physiological indicators such as reduced stress hormone levels and enhanced immune function were observed in

mice exposed to environmental enrichment. These results suggest that enriching the living conditions of laboratory mice can positively affect their welfare, both behaviorally and physiologically, highlighting the importance of considering environmental factors in animal research settings.

Implications to Theory, Practice and Policy: Environmental enrichment theory, stress reduction theory and neuroplasticity theory may be used to anchor future studies on assessing the effect of environmental enrichment on behavioral and physiological welfare indicators in laboratory mice in Eritrea. To ensure consistent and reproducible outcomes across research facilities, it is imperative to develop standardized protocols for environmental enrichment in laboratory mouse housing. Regulatory bodies and funding agencies should consider incorporating specific requirements for environmental enrichment into animal welfare guidelines and research protocols.

Keywords: *Environmental Enrichment, Physiological Welfare, Indicators, Laboratory, Mice*

INTRODUCTION

Environmental enrichment refers to the modification of an animal's living space to enhance its cognitive, physical, and social experiences. In laboratory settings, particularly with mice, environmental enrichment has been a subject of growing interest due to its potential to improve animal welfare and research outcomes. In developed economies like the USA, Japan, and the UK, welfare indicators in laboratory mice are rigorously studied to ensure the well-being of these animals in research settings. One key indicator is stress hormone levels, which can be assessed through blood or saliva samples. For instance, a study by Smith (2016) in the USA found that stress hormone levels in laboratory mice have decreased by 15% over the past decade due to advancements in housing and handling techniques. Another crucial indicator is anxiety-related behaviors, which are often observed through standardized behavioral tests such as the elevated plus maze. Research in Japan has shown a decline in anxiety-related behaviors in laboratory mice over the past five years, possibly due to improvements in enrichment programs and housing conditions (Yamamoto & Nagao, 2017).

In developing economies, such as those in Southeast Asia and South America, efforts to monitor welfare indicators in laboratory mice are gaining momentum alongside advancements in research infrastructure. For instance, in India, studies have shown an improvement in anxiety-related behaviors among laboratory mice, potentially due to the implementation of enriched housing environments and behavioral training protocols (Kumar et al., 2019). Additionally, stress hormone levels in laboratory mice in Argentina have been gradually decreasing over the past decade, reflecting improvements in handling techniques and veterinary care (Gómez, 2018).

Furthermore, in regions like Eastern Europe and the Middle East, there is a growing emphasis on ethical considerations in animal research, driving initiatives to enhance welfare standards for laboratory mice. For example, a study conducted in Turkey by Demirkan et al. (2017) highlighted the importance of regular health assessments and environmental enrichment programs in promoting the well-being of laboratory mice. Similarly, in Egypt, there has been a notable increase in cognitive performance among laboratory mice, attributed to advancements in training methodologies and access to enrichment materials (Mahmoud, 2020).

In regions such as Latin America and parts of Africa, where resources for animal research may be limited, there is a growing recognition of the importance of welfare indicators in laboratory mice. In Brazil, for instance, efforts are underway to improve housing conditions and veterinary care for laboratory animals, leading to a reduction in stress hormone levels and improved overall well-being (dos Santos et al., 2016). Similarly, in Nigeria, initiatives to enhance welfare standards for laboratory mice have resulted in a decrease in anxiety-related behaviors, indicating positive advancements in research practices and ethics (Ogunbunmi, 2018).

In developing economies, such as those in Southeast Asia and South America, welfare indicators in laboratory mice may vary due to differing research practices and regulations. However, there is a growing awareness of the importance of monitoring these indicators to uphold ethical standards in animal research. For example, a study conducted in Brazil by Silva (2018) reported an increase in cognitive performance among laboratory mice over the past five years, attributed to enhanced training protocols and environmental enrichment. Additionally, stress hormone levels have been a focus of research in China, with studies indicating a gradual decrease in cortisol levels in laboratory mice as housing conditions and handling techniques improve (Li & Zhang, 2019).

In sub-Saharan economies, such as those in Africa, welfare indicators in laboratory mice are still emerging due to limited resources and infrastructure for research. However, efforts are being made to establish guidelines and standards for animal welfare in these regions. For instance, a study in Nigeria by Adegbola et al. (2017) highlighted the need for improved housing conditions and veterinary care for laboratory mice to ensure their well-being. Similarly, in South Africa, initiatives are underway to monitor stress hormone levels and anxiety-related behaviors in laboratory mice, although comprehensive data on trends are still lacking (Mhlongo & Dzomba, 2020).

Furthermore, in countries like Indonesia and Vietnam, collaborations with international organizations and training programs have played a significant role in promoting animal welfare in research settings. A study by Nguyen (2019) in Vietnam demonstrated positive trends in stress hormone levels and cognitive performance among laboratory mice, attributed to the adoption of best practices and improved training of research personnel. Similarly, in Indonesia, efforts to implement ethical guidelines and provide access to enrichment materials have contributed to the well-being of laboratory animals (Hartati, 2020).

In regions such as Eastern Europe and Central Asia, where research practices are evolving, there is a growing focus on improving welfare indicators for laboratory mice. In Ukraine, for instance, efforts to enhance housing conditions and veterinary care have led to a decrease in stress hormone levels and an improvement in cognitive performance among laboratory mice (Kharchenko, 2019). Similarly, in Kazakhstan, initiatives to promote ethical research practices have resulted in positive trends in anxiety-related behaviors and overall welfare of laboratory animals (Zhunussov, 2017).

Moreover, in countries like Bangladesh and Pakistan, where research infrastructure is still developing, collaborations with international organizations and capacity-building programs are helping to advance welfare standards for laboratory mice. A study by Rahman (2020) in Bangladesh highlighted improvements in stress hormone levels and cognitive performance among laboratory mice, indicating the positive impact of training programs and access to resources. Similarly, in Pakistan, efforts to establish ethical guidelines and provide training for researchers have contributed to enhancements in animal welfare in research settings (Khan, 2018).

Moreover, in countries like South Africa and Kenya, collaborations with international organizations and adoption of best practices have contributed to advancements in monitoring welfare indicators in laboratory mice. A study by Mwacharo et al. (2019) in Kenya demonstrated a decrease in stress hormone levels among laboratory mice, attributed to improvements in housing conditions and handling techniques. Similarly, in South Africa, efforts to promote ethical research practices have led to enhancements in cognitive performance among laboratory mice, reflecting a commitment to animal welfare (Maseko et al., 2017).

In regions such as Southeast Asia and the Middle East, where research infrastructure is still developing, efforts are being made to establish and improve welfare standards for laboratory mice. In Thailand, for example, studies have shown a gradual decrease in stress hormone levels among laboratory mice, indicating advancements in housing conditions and handling techniques (Sukyai et al., 2017). Similarly, in Iran, initiatives to enhance welfare standards for laboratory animals have led to a reduction in anxiety-related behaviors and improved cognitive performance among mice (Zarrindast et al., 2018).

Environmental enrichment in laboratory settings refers to the provision of stimuli that enhance the physical and psychological well-being of animals, such as nesting materials, tunnels, exercise

wheels, and social housing (Baumans, 2005). These enrichments promote natural behaviors, physical activity, and cognitive stimulation, which can have significant positive effects on welfare indicators in laboratory mice. For example, nesting materials allow mice to engage in natural nesting behaviors, which can reduce stress hormone levels and anxiety-related behaviors (Van Loo et al., 2004). Similarly, tunnels provide opportunities for exploration and locomotion, which can alleviate boredom and improve cognitive performance (Fox et al., 2006).

Exercise wheels are another form of environmental enrichment that promotes physical activity and reduces stress levels in laboratory mice (Sherwin, 2004). Regular exercise has been shown to decrease anxiety-related behaviors and enhance overall welfare by providing an outlet for natural behaviors such as running (Gouveia & Hurst, 2017). Additionally, social housing, where compatible mice are housed together, can mitigate social isolation and loneliness, leading to decreased stress hormone levels and improved cognitive function (Arakawa, 2019). By incorporating these enrichments into laboratory environments, researchers can effectively promote the welfare of laboratory mice while maintaining scientific validity in research studies.

Problem Statement

The effect of environmental enrichment on behavioral and physiological welfare indicators in laboratory mice remains a topic of significant interest and research. While various studies have investigated the impact of enrichment on mouse welfare, there is still a need for comprehensive understanding and evidence-based guidelines. Recent research has highlighted the importance of considering both behavioral and physiological welfare indicators when evaluating the effectiveness of environmental enrichment strategies (Kerr, 2021). However, there remains a lack of consensus on the optimal types and combinations of enrichment that yield the most significant improvements in mouse welfare.

Moreover, the specific mechanisms underlying the effects of environmental enrichment on behavioral and physiological welfare indicators in laboratory mice are not fully understood. Recent studies have suggested that enrichment may modulate stress hormone levels, anxiety-related behaviors, and cognitive performance through neurobiological pathways (Bilbo & Tsang, 2010; Simpson & Kelly, 2011). However, further research is needed to elucidate these mechanisms and determine how different types of enrichment may interact with individual differences in mice. Additionally, the practical implementation of environmental enrichment in laboratory settings, considering factors such as cost-effectiveness, feasibility, and standardization, remains a challenge that requires further investigation (Novak, 2016).

Theoretical Framework

Environmental Enrichment Theory

Originating from studies in the field of animal welfare and behavioral neuroscience, this theory posits that providing stimulating and varied environments can improve the well-being of laboratory animals, including mice (Kerr, 2021). Based on the principle of promoting natural behaviors and cognitive stimulation, environmental enrichment interventions aim to enhance the overall quality of life for animals in research settings. In the context of the suggested topic, this theory is relevant as it forms the foundation for investigating how different types of environmental enrichment influence behavioral and physiological welfare indicators in laboratory mice.

Stress Reduction Theory

Developed within the framework of stress physiology and behavioral ecology, this theory suggests that environmental enrichment can mitigate stress responses in laboratory animals, leading to improved welfare outcomes (Burman, 2017). Originating from research on the effects of environmental factors on stress hormone levels and anxiety-related behaviors, this theory highlights the potential of enrichment interventions to reduce stress and promote adaptive coping strategies in mice. In the proposed research, this theory would guide investigations into the mechanisms by which environmental enrichment influences stress hormone levels and anxiety-related behaviors in laboratory mice.

Neuroplasticity Theory

Stemming from neuroscientific research on brain plasticity and cognitive development, this theory proposes that environmental enrichment can induce structural and functional changes in the brain, resulting in improved cognitive performance and emotional resilience (Sale, 2018). Originating from studies on the effects of environmental factors on neuronal connectivity and synaptic plasticity, this theory underscores the capacity of enrichment interventions to shape neural circuits and enhance cognitive function in mice. In the context of the suggested research, this theory would inform investigations into the neurobiological mechanisms underlying the effects of environmental enrichment on cognitive performance and behavioral welfare indicators in laboratory mice.

Empirical Review

Simpson and Kelly (2017) conducted a comprehensive investigation to assess the impact of environmental enrichment on the behavioral and physiological welfare indicators of laboratory mice. Their study, designed as a randomized controlled trial, aimed to elucidate whether enriched housing conditions could alleviate stress and anxiety levels in mice compared to standard housing. Over a six-month period, mice were randomly assigned to either enriched or standard housing environments. The enriched environment consisted of larger cages with various forms of stimulation, such as tunnels, toys, and nesting materials, while the standard environment represented typical laboratory housing conditions. Behavioral assessments, including open field tests and elevated plus mazes, were employed to evaluate anxiety-like behaviors, while physiological markers such as corticosterone levels served as indicators of stress. The findings revealed significant reductions in stress and anxiety-related behaviors among mice housed in the enriched environment, accompanied by lower levels of corticosterone compared to their counterparts in standard housing. These results suggest that environmental enrichment positively influences the behavioral and physiological welfare of laboratory mice by providing opportunities for increased exploration and stimulation, thereby mitigating stress responses and promoting overall wellbeing.

Van Praag (2018) examined the long-term effects of environmental enrichment on cognitive function and neurogenesis in laboratory mice. Recognizing the importance of cognitive health in animal welfare, the researchers sought to investigate whether enriched housing conditions could enhance cognitive abilities and promote neuroplasticity. Using a cohort of mice housed in either enriched or standard environments for an extended period, the study employed a battery of cognitive tests, including Morris water maze and novel object recognition tasks, to assess spatial learning and memory function. Additionally, neurobiological assays, such as immunohistochemistry for markers of neurogenesis, were utilized to evaluate structural changes

in the hippocampus, a brain region crucial for learning and memory. The results demonstrated significant improvements in spatial learning and memory performance among mice exposed to enriched environments, accompanied by increased hippocampal neurogenesis compared to those in standard housing. These findings suggest that environmental enrichment not only enhances cognitive function but also facilitates neuroplasticity processes in the brain, contributing to improved welfare outcomes in laboratory mice.

Novak (2019) investigated the influence of environmental complexity on the welfare of laboratory mice. Acknowledging the multifaceted nature of animal welfare, the researchers aimed to explore how variations in environmental enrichment could impact various aspects of mouse wellbeing, including social behavior and the expression of stereotypic behaviors. Using a diverse range of enrichment strategies, such as the provision of nesting materials, social housing, and physical structures for exploration, mice were housed in environments varying in complexity levels. Behavioral observations and ethograms were employed to assess social interactions and stereotypic behaviors, while physiological measures, including fecal corticosterone levels, served as indicators of stress. The results revealed that mice housed in enriched environments exhibited a higher quality of life, characterized by increased social interactions and reduced expression of stereotypic behaviors compared to those in standard housing conditions. These findings underscore the importance of environmental complexity in promoting positive welfare outcomes in laboratory mice, emphasizing the need for tailored enrichment interventions to address individual behavioral and physiological needs.

Wang (2020) examined the role of environmental enrichment in mitigating the adverse effects of chronic stress on the behavioral and physiological wellbeing of laboratory mice. Recognizing the detrimental impact of chronic stress on animal welfare, the researchers sought to determine whether enrichment interventions could alleviate stress-induced behavioral abnormalities and restore homeostatic balance. Using a well-established mouse model of chronic stress exposure, mice were housed in either enriched or standard environments following stress induction protocols. A battery of behavioral tests, including forced swim tests and sucrose preference tests, was employed to assess depressive-like behaviors and anhedonia, while physiological markers such as serum corticosterone levels served as indicators of stress. The findings revealed that mice housed in enriched environments exhibited reduced levels of depressive-like behaviors and increased sensitivity to rewards compared to those in standard housing conditions, accompanied by lower levels of circulating corticosterone. These results suggest that environmental enrichment plays a crucial role in buffering the negative impact of chronic stress on mouse welfare by promoting adaptive coping strategies and restoring physiological equilibrium.

Smith (2021) investigated the neurobiological mechanisms underlying the beneficial effects of environmental enrichment on the welfare of laboratory mice. Recognizing the intricate interplay between environmental factors and neural plasticity, the researchers aimed to elucidate the molecular pathways through which enrichment interventions exert their positive influence on behavior and physiology. Using a combination of molecular and neurobiological techniques, including gene expression analysis and protein profiling, mice exposed to enriched or standard housing conditions were compared to identify differential neurobiological signatures. The results revealed upregulation of neuroplasticity-related signaling pathways in mice housed in enriched environments, including increased expression of brain-derived neurotrophic factor (BDNF) and synaptic proteins. These findings suggest that environmental enrichment promotes neuroadaptive

processes in the brain, leading to enhanced neuronal connectivity and resilience to stress-induced neuronal damage. By elucidating the underlying neurobiological mechanisms, this study provides valuable insights into the therapeutic potential of environmental enrichment for improving the welfare and resilience of laboratory mice.

Brown (2022) explored the dose-response relationship between environmental enrichment intensity and its effects on the welfare of laboratory mice. Recognizing the importance of optimizing enrichment strategies to maximize welfare benefits while minimizing resource investment, the researchers aimed to determine the optimal balance of enrichment components that would promote positive welfare outcomes in mice. Using a factorial design, mice were exposed to varying levels of environmental complexity, including different combinations of cage size, social housing, and cognitive stimulation. Behavioral assessments, including anxiety tests and social interaction assays, were employed to evaluate the impact of enrichment intensity on mouse welfare. The results revealed a dose-response relationship between environmental enrichment intensity and welfare outcomes, with moderate levels of complexity yielding the most significant improvements in behavioral and physiological indicators of welfare. These findings highlight the importance of carefully tailoring enrichment interventions to meet the individual needs of mice while considering factors such as space constraints and resource availability. By optimizing enrichment strategies, researchers can effectively enhance the welfare and wellbeing of laboratory mice, thereby improving research outcomes and ethical standards.

Garcia (2023) investigated the effects of environmental enrichment on the gut microbiota composition and immune function of laboratory mice. Recognizing the critical role of the gut microbiome in regulating immune responses and overall health, the researchers aimed to explore whether environmental enrichment could modulate gut microbiota diversity and promote immune homeostasis in mice. Using a combination of high-throughput sequencing and immunological assays, mice housed in enriched or standard environments were monitored over an extended period to assess changes in gut microbiota composition and immune cell populations. The results revealed that mice housed in enriched environments exhibited greater gut microbiota diversity and richness compared to those in standard housing conditions. Furthermore, enrichment interventions were associated with alterations in immune cell profiles, including increased populations of regulatory T cells and reduced pro-inflammatory cytokine production. These findings suggest that environmental enrichment not only enriches the behavioral and physiological welfare of laboratory mice but also exerts beneficial effects on gut microbiota composition and immune function. By promoting a healthy gut microbiome and immune system, environmental enrichment interventions may contribute to enhanced resilience to stressors and improved overall wellbeing in laboratory mice, highlighting the interconnectedness between environmental factors, gut health, and immune function in animal welfare research.

METHODOLOGY

This study adopted a desk methodology. A desk study research design is commonly known as secondary data collection. This is basically collecting data from existing resources preferably because of its low cost advantage as compared to a field research. Our current study looked into already published studies and reports as the data was easily accessed through online journals and libraries.

RESULTS

Conceptual Gap: While the studies collectively demonstrate the positive effects of environmental enrichment on the welfare of laboratory mice, there's a need for further investigation into the specific mechanisms underlying these effects. For instance, while Smith (2021) explored neurobiological mechanisms, there's still a lack of understanding regarding the intricate interactions between environmental enrichment, neuroplasticity, and stress resilience. Further research into the molecular pathways involved in mediating the effects of enrichment on behavior and physiology could provide valuable insights into novel therapeutic targets for improving animal welfare.

Contextual Gap: While the studies focus primarily on the impact of environmental enrichment within laboratory settings, there's a lack of research examining the applicability of enrichment interventions in diverse housing environments. For instance, while Simpson and Kelly (2017) demonstrate the efficacy of enrichment in alleviating stress and anxiety in mice housed in standard laboratory conditions, it remains unclear whether similar benefits would be observed in other housing contexts, such as agricultural or industrial facilities. Exploring the generalizability of enrichment interventions across different housing environments could inform the development of more comprehensive welfare guidelines applicable to various settings.

Geographical Gap: The studies cited primarily originate from Western countries, with limited representation from regions outside North America and Europe. For instance, there's a lack of research exploring the effects of environmental enrichment on mouse welfare conducted in Asia, Africa, or South America. Given potential variations in housing practices, environmental conditions, and regulatory frameworks across different geographical regions, there's a need for more geographically diverse research to ensure the generalizability and applicability of findings on a global scale. Conducting studies in diverse geographical regions could also provide insights into culturally specific enrichment practices and their effects on animal welfare (Simpson and Kelly 2017).

CONCLUSION AND RECOMMENDATIONS

Conclusion

In conclusion, the research on the effect of environmental enrichment on behavioral and physiological welfare indicators in laboratory mice demonstrates a consistent and significant positive impact. Study by Simpson and Kelly (2017) collectively highlight the benefits of providing enriched housing conditions for mice, including reduced stress and anxiety levels, enhanced cognitive function, improved social interactions, and modulation of immune function and gut microbiota composition. These findings underscore the importance of implementing tailored environmental enrichment strategies to promote the overall welfare and wellbeing of laboratory mice. Furthermore, there is a need for continued research to further elucidate the underlying mechanisms driving these effects, explore the applicability of enrichment interventions across diverse housing contexts, and address geographical disparities in research representation. By advancing our understanding of environmental enrichment, we can not only enhance the welfare of laboratory animals but also improve the validity and ethical standards of scientific research involving animal models.

Recommendations

The following are the recommendations based on theory, practice and policy:

Theory

While existing research has demonstrated the positive effects of environmental enrichment, there is still much to learn about the specific neurobiological, hormonal, and immunological mechanisms driving these effects. Future studies should delve deeper into understanding the molecular pathways involved in mediating the impact of environmental enrichment on mouse welfare. This could include exploring gene expression patterns, neurotransmitter dynamics, and epigenetic modifications associated with enriched housing conditions.

Practice

To ensure consistent and reproducible outcomes across research facilities, it is imperative to develop standardized protocols for environmental enrichment in laboratory mouse housing. This could involve guidelines outlining the types of enrichment materials and activities to be provided, as well as recommendations for cage size and social housing arrangements. By establishing best practices for enrichment implementation, researchers can optimize the welfare of laboratory mice while minimizing variability between studies. Research institutions should invest in training programs and educational resources to familiarize researchers, animal care staff, and laboratory personnel with the principles and benefits of environmental enrichment. This could include workshops, seminars, and online modules covering topics such as enrichment design, implementation strategies, and welfare assessment techniques. By increasing awareness and knowledge about enrichment practices, institutions can foster a culture of animal welfare stewardship and promote adherence to ethical standards in animal research.

Policy

Regulatory bodies and funding agencies should consider incorporating specific requirements for environmental enrichment into animal welfare guidelines and research protocols. This could involve mandating the provision of enrichment materials and activities for laboratory animals, as well as conducting regular welfare assessments to ensure compliance with enrichment standards. By formalizing enrichment requirements in policy frameworks, regulators can promote the ethical treatment of laboratory animals and uphold the principles of the 3Rs (Replacement, Reduction, Refinement) in animal research. Policy initiatives should incentivize research into environmental enrichment by allocating funding and resources to support studies investigating the effects of enrichment on animal welfare. This could include grant programs specifically focused on enrichment-related research, as well as recognition and rewards for institutions implementing innovative enrichment practices. By incentivizing enrichment research, policymakers can stimulate scientific inquiry into novel enrichment interventions and facilitate the translation of research findings into practical applications that benefit laboratory animals.

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