

Appendix 1:

Environmental Enrichment of Rodents

Introduction

A major objective of the NIH Animal Care and Use Program is to promote the humane care and use of animals in biomedical research and this guidance serves as a set of best practices to help achieve that goal. *The Guide for the Care and Use of Laboratory Animals* (NRC, 2011), hereafter referred to as *The Guide*, is one of the primary references regarding the implementation and management of the NIH Animal Care and Use Program. The *Guide* promotes the humane care and use of laboratory animals and strives to enhance animal well-being, the quality of research, and the advancement of scientific knowledge that is relevant to both humans and animals.

Rodents continue to represent the majority of animals used in biomedical investigations both at the NIH and worldwide (Harkness et al, 2010). Rodent biomedical research accounts for approximately 85 percent of vertebrate research conducted at the NIH. As such, it is important to address questions relevant to the humane care, management, and well-being of these laboratory animals. A critical component of the humane care of rodents is their microenvironment, including the primary enclosure where the animals are housed (NRC, 2011). Over the past decade the provision of an enriched, more complex, microenvironment has been demonstrated to promote the well-being of a variety of species used in biomedical research, including rodents. Today, the provision of environmental enrichment to rodents has become an integral component of most comprehensive animal care programs within the United States and Europe. Therefore it is the intent of this document to establish best practices for enrichment programs for rodents on the NIH Campus.

Environmental Enrichment Strategies

It is difficult to discuss the humane care and use of animals without concurrently discussing and balancing animal well-being with the goals of the biomedical research. The term environmental enrichment is problematic when used in the context of laboratory animal use and experimentation.. The difficulty stems from the earlier use of enrichment to examine effects on behavior, physiology, and neurobiology (cf., Benefiel et al, 2005; Hebb, 1949), versus provision of enrichment within home cages to enhance animal well-being (Baumans, 2005; Hutchinson et al 2005). The concept of home cage supplementation or enhancement has been proposed to replace the use of the term environmental enrichment (Benefiel et al, 2005). For the purpose of this document, enrichment is defined as: ‘an increase in the complexity of the environment in which the animal lives, with the goal of enhancing the animal’s welfare.’ Home cage enrichment may include housing animals in social groups; housing animals with structural or activity based cage supplementations or both. The end goal of enrichment is to provide the animals with the option and ability to engage in species typical behaviors through the use of structural, social, or activity based opportunities. The *Guide* states that animal programs should address the behavioral, physiological, and physical needs of the species, stocks, or strains of animals held in the laboratory. The addition of nesting material to the cage microenvironment has been demonstrated in mice not only to facilitate a range of behaviors, but also to facilitate thermoregulation (Gaskill et al, 2012). A successful enrichment program takes into account all aspects of a species’ natural behavior, including social organization, foraging behavior, and daily

activity of the animal (Poole and Dawkins, 1999; Steward and Raje, 2001). The Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC) has stated that environmental enrichment is an important method of improving the well-being of many laboratory animal species and may be accomplished by the provision of stimuli, structures, and resources that facilitate the expression of species-appropriate behaviors. Environmental enrichment, should be provided in a consistent manner across the animal program. When discussing the humane care and use of animals, it is important to discuss a balance between animal well-being and the goals of the biomedical research at hand (Weed and Raber, 2005). According to *The Guide*, “enrichment programs should be reviewed by the IACUC, researchers, and veterinarian on a regular basis to ensure that they are beneficial to animal well-being and consistent with the goals of animal use.” (Guide, Page 53). Bayne (2005), Jennings et al., (1998) and Olsson and Dahlborn (2002), provide comprehensive overviews of the relative issues regarding the effectiveness and usefulness of providing environmental enrichment to rodents

The NIH Intramural Research Program was surveyed to determine the status of enrichment strategies for rodents used in biomedical research (Hutchinson et al, 2005; OACU, 2013). The results of these surveys indicated two primary types of rodent enrichment strategies are being used throughout the NIH campus: addition of nesting material (e.g. Nestlets[®]) for mice and tubes (i.e. virgin paper, plastic, etc.) or nesting material (e.g. Nestlets[®]) for rats. Principal Investigators may, with scientific justification and IACUC approval, opt out of home cage enrichment.

Concerns Surrounding Enrichment Supplementation

Concerns have been raised regarding the impact of non-systematic application of enrichments (supplements) on ongoing research programs (Hutchinson et al, 2005; Weed and Raber, 2005, Baumans, 2005). Currently there are two divergent opinions regarding the provision of supplements for in home cage use. The first is that enrichment supplementation enhances the welfare of laboratory housed animals and does not affect the standardization of laboratory environments nor significantly affect the research results obtained (Würbel and Garner, 2007; Würbel 2007; Wolfer et al, 2004). The second is that non-systematic application of home cage enhancements results in a lack of standardization and may affect the research data obtained in unknown and potentially detrimental ways (Benefiel et al. 2005, Tsai et al, 2003; von Praag et al 2000). The introduction of genetically modified animals and differential effects of enrichment has also been identified as a possible problematic area (Dennis, 2000; NRC 2011).

Summary

Environmental enrichment strategies for rodents have been widely adopted across the NIH Intramural Research Program, the United States, and Europe (EU Council Directive, 2010/63/EU) to address the welfare of rodents used in biomedical research. Standardized strategies have been applied to a wide range of research situations with varying research goals without adverse results. All NIH programs should have an environmental enrichment plan for rodents used within their program. Enrichment plans should delineate the approach to be used within the program. In order to minimize the impact of enrichment supplementation as a research variable between facilities and programs at the NIH, it is recommended that each program adopt the addition of nesting material (e.g. Nestlet[®]) to the microenvironment as the minimum requirement for both socially housed and individually housed mice and nesting

material or a tube for rats. Programs choosing to go above this minimum must consider the introduction of additional research variables between their animals and animals housed in different facilities and programs. In all situations, the decision regarding whether or not to enhance the microenvironment of rodents housed in the intramural program at NIH ultimately rests with the Principal Investigator and the protocol review process in each Institute/Center's IACUC. Scientifically valid reasons for either enhancing or limiting the microenvironment should be provided to the IACUC during initial protocol review.

References

Baumans V. 2005. Environmental Enrichment for Laboratory Rodents and Rabbits: Requirements of Rodents, Rabbits, and Research. *ILAR J* 46: 162-170.

Bayne K. 2005. Unintended consequences of environmental enrichment for laboratory animals and research results. *ILAR J* 46:129–39.

Benefiel AC, Dong, WK, Greenough, WT. 2005. Mandatory “enriched” housing of laboratory animals: the need for evidence-based evaluation. *ILAR* 46:95-105

Dennis MB. 2000. Humane endpoints for genetically engineered animal models. *ILAR J* 41: 94-98.

EU Council Directive on the protection of animals used for scientific purposes -2010/63/EU. <<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:276:0033:0079:EN:Pdf> > Accessed 04.23.13

Gaskill BN, Gordon CJ, Pajor EA, Lucas JR, Davis JK and Garner JP. 2012 Heat or insulation: behavioral titration of mouse preference for warmth or access to a nest. *Plos One* 2012 7: 1-11

Hebb, DO. 1949. *The organization of behavior*. NY: Wiley

Harkness and Wagner's *Biology and Medicine of Rabbits and Rodents*, 5th edition

By John E. Harkness, Patricia V. Turner, Susan VandeWoude, Colette L. Wheler

Wiley-Blackwell and ACLAM, 472 p.

Hutchinson E, Avery A, Vandewoude S. 2005. Environmental enrichment for laboratory rodents. *ILAR J* 46:148–61.

National Research Council. 2011. *Guide for the care and use of laboratory animals*. Washington, DC: National Academy Press.

Olsson, IAS. & Dahlborn K. 2002. Improving housing conditions for laboratory mice: a review of ‘environmental enrichment’. *Laboratory Animals* 36: 243-270.

Poole T & Dawkins MS. 1999. Environmental enrichment for vertebrates. In: *The UFAW handbook on the care and management of laboratory animals*. 7th ed. (T. Poole, ed.). pp. 13-20. Blackwell Science, Oxford, United Kingdom.

Stewart KL & Raje SS. 2001. Environmental enrichment committee: its role in program development. *Lab Anim* 30:50-52.

Tsai PP, Stelzer HD, Hedrich HJ, Hackbarth H. 2003. Are the effects of different designs on the physiology and behaviour of DBA/2 mice consistent? *Lab Anim* 37:314-327.

van Praag H, Kempermann G, Gage FH. 2000. Neural consequences of environmental enrichment. *Nat Rev Neurosci* 1: 191-198.

Weed JL & Raber JM. 2005. Balancing animal research with animal well-being: establishment of goals and harmonization of approaches. *ILAR J.* 46:118-28

Wolfer DP, Litvin O, Morf S, Nitsch RM, Lip HP, Würbel H. 2004 Laboratory animal welfare: cage enrichment and mouse behavior. *Nature* 432:821–822.

Würbel H. Environmental enrichment does not disrupt standardization of animal experiments. 2007 *ALTEX* 24:70–73.

Würbel H & Garner JP. 2007. Refinement of rodent research through environmental enrichment and systematic randomization. *NC3Rs* # 9 pp 1-9. <http://www.nc3rs.org.uk>

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