Environmental Enrichment

NTP Board of Scientific Counselors Meeting

June 21, 2012

Presenter: Angela-King Herbert, NIEHS/DNTP, Cellular and Molecular Pathology Branch

Background

Environmental enrichment has been described as any measure that promotes expression of species-specific natural behaviors and inhibits abnormal behaviors (Brinkman, 1996). The National Research Council recently updated the *Guide for the Care and Use of Laboratory Animals* (*Guide*, NRC, 2011). The *Guide* addresses environmental enrichment:

> *All animals should be housed under conditions that provide sufficient space as well as supplementary structures and resources required to meet physical, physiologic, and behavioral needs. Environments that fail to meet the animals' needs may result in abnormal brain development, physiologic dysfunction, and behavioral disorders (Garner 2005; van Praag et al. 2000; Würbel 2001) that may compromise both animal well-being and scientific validity. The primary enclosure or space may need to be enriched to prevent such effect ….An appropriate housing space or enclosure should also account for the animals' social needs. Social animals should be housed in stable pairs or groups of compatible individuals unless they must be housed alone for experimental reasons or because of social incompatibility…The primary aim of environmental enrichment is to enhance animal well-being by providing animals with sensory and motor stimulation, through structures and resources that facilitate the expression of species-typical behaviors and promote psychological well-being through physical exercise, manipulative activities, and cognitive challenges according to species-specific characteristics…Well-conceived enrichment provides animals with choices and a degree of control over their environment, which allows them to better cope with environmental stressors (Newberry 1995).*

Sztainburg et al. (2010) showed that enrichment was beneficial for the psychological and physical well being of animals. Animals in an enriched environment show decreased levels of anxiety-like behaviors in classic anxiety tests such as the elevated plus maze and the light dark transfer test. Male mice housed in cages enriched with nesting material had lower urine corticosterone levels, increased thymus weights, and consumed less feed and water than mice in standard (non-enriched) cages (Van Loo et al., 2004). The authors concluded that providing nesting material for a long period of time reduced stress and enhanced animal welfare.

Adrenocorticotropic hormones and corticosterone, markers of chronic stress, were significantly lower in individually housed rats with enriched cages, compared to controls in non-enriched cages (Belz et al., 2003**)**. Additionally, the author noted enriched rats appeared easier to handle

during acclimation and experiments. Konkle et al (2010) showed that corticosterone levels in enriched Sprague Dawley and Long Evans rats returned to baseline faster than the control non-enriched rats after a brief stressor.

Types of environmental enrichment include social and physical enrichment. Social enrichment allows animals to display social behaviors such as grooming, vocalization and play. Rats are very social animals and group housing is an excellent method for promoting social interaction. Although mice are not as social as rats, group housing also works well for female mice; male mice tend to fight when housed in groups unless introduced at weaning. Physical enrichment devices should be biologically relevant items that have intrinsic value and allow the animal to display species-appropriate behavior. One must recognize normal rodent behavior and distinguish that from stereotypical behaviors. Enrichment devices can help to decrease or alleviate stereotypical behaviors in the animals that may be associated with stress.

Rodents are nocturnal, and foraging and burrowing are part of their normal behavior. Mice and rats are thigmotactic; they prefer to be in close proximity to walls or other structures and avoid open spaces. They usually favor shelters (nest or other types of shelters); mice are nest builders, while rats prefer gnawing but will build a loosely constructed nest with the "right" materials. It has been shown that rats have a preference for paper strips as nesting material (Manser et al., 1998).

Several factors must be considered when implementing an environmental enrichment program. The enrichment devices must be compatible with the aims of the study. This is especially important in studies that follow Good Laboratory Practice regulations. Enrichment devices must be analyzed for contaminants to prevent the introduction of confounding variables. Furthermore, enrichment devices must have minimal impact on husbandry practices and cleaning procedures. Devices that require excessive staff time and labor for incorporation into studies are not acceptable. The enrichment item must also have minimal impact on observation of animals. For example, the use of large amounts of nesting materials can result in mice building very intricate nests in which concealment of the animals becomes an issue. Care must be taken to ensure that the enrichment device does not impact research results.

Environmental Enrichment in NTP Studies

Modifications to the NTP animal care and use program to include environmental enrichment in NTP rodent studies is important. Including environmental enrichment should enhance animal well being by providing sensory and motor stimulation, improve the quality of experimental data, allow animals to have choices and control over their environment, and fulfill recommendations of the *Guide* and the Association for Assessment and Accreditation of Laboratory Animal Care International guidelines.

The identification of appropriate enrichment devices to include in NTP studies has required careful consideration of compatibility with the study type and the scientific question(s) being researched. The NTP will now include enrichment devices in dosed feed, dosed water, and gavage studies and continue to explore appropriate environmental enrichment for inhalation and dermal studies.

The NTP is in the process of drafting detailed guidelines for the use of enrichment devices in NTP studies. These guidelines state, (1) all enrichment devices must be screened for contaminants prior to use, (2) nesting material shall be autoclaved or irradiated to prevent the introduction of microbes to the cages, (3) other types of enrichment devices must be sanitized or discarded after use, (4) all animals on the study including sentinels shall receive the enrichment device, and (5) staff training on the use of the enrichment device and importance of the program are essential to ensure adherence. Testing laboratories must develop standard operating procedures (SOPs) to ensure that the devices are used consistently throughout the study. The use of enrichment devices will be phased in over a period of time starting with short-term range finding studies, then 90-day studies, and lastly 2-year studies.

References

Belz EE, Kennell JS, Czambel RK, Rubin RT, Rhodes ME Environmental enrichment lowers stress-responsive hormones in singly housed male and female rats. Pharmacol Biochem Behav. 2003 Dec;76(3-4):481-6.

Brinkman C. Toys for the Boys: Environmental Enrichment for Singly Housed Adult Male Macaques (*Macaca fascicularis*) Lab Prim News. 1996 April;35(2) http://www.brown.edu/Research/Primate/lpn35-2.html#toy

Konkle AT, Kentner AC, Baker SL, Stewart A, Bielajew C. Environmental-enrichment-related variations in behavioral, biochemical, and physiologic responses of Sprague-Dawley and Long Evans rats. J Am Assoc Lab Anim Sci. 2010 Jul;49(4):427-36.

Manser CE, Broom DM, Overend P, Morris TH. Investigations into the preferences of laboratory rats for nest-boxes and nesting materials. Lab Anim. 1998 Jan;32(1):23-35.

National Research Council. *Guide for the Care and Use of Laboratory Animals: Eighth Edition*. Washington, DC: The National Academies Press, 2011. http://www.nap.edu/catalog.php?record_id=12910

Sztainberg Y, Chen A. An environmental enrichment model for mice. Nat Protoc. 2010 Sep;5(9):1535-9. Epub 2010 Aug 12.

Van Loo PL, Van der Meer E, Kruitwagen CL, Koolhaas JM, Van Zutphen LF, Baumans V. Long-term effects of husbandry procedures on stress-related parameters in male mice of two strains. Lab Anim. 2004 Apr;38(2):169-77.