Abstract

For a change to be considered enriching, the change must enhance animal welfare and improve biological functioning of the animals. A review of the literature shows that a consensus on the definition of changes constituting “environmental enrichment” has yet to be reached. For this reason, the results of studies on the effects of rodent enrichment are inconsistent. In many cases, changes have not been shown to be real improvements. However, enrichment is increasingly appreciated as a way to improve the well-being of rodents, providing them with opportunities for species-specific behaviors that might be available to them in the wild. Frequently defined as “change to the environment,” enrichment can be as complex as devices (frequently termed “toys”) or as simple as the provision of tissues from which mice readily construct nests. Nest making is a learned behavior in rats, and laboratory rats do show preferences for chewable objects in their environment. Rather than attempting a comprehensive review of the entire literature on environmental enrichment and its effects on rodent physiology and behavior, this paper focuses on husbandry and housing alterations that may improve the welfare of laboratory rodents. The effects of beneficial changes in housing and husbandry on rodent well-being and on experimental variability—and thus cost—are discussed. Areas that require more research are suggested. Also suggested are possible inexpensive and effective enrichment schemes for laboratory mice that might include reducing the cage floor space per mouse combined with providing nesting material.

Key Words: enrichment; housing; husbandry; mice; rats; rodents

Introduction

The literature on environmental enrichment for laboratory animals is expanding, with ever-increasing reports pertaining to laboratory mice and rats that emphasize the impact of enrichment on behavioral research, physiology, and overall well-being. This article deals exclusively with laboratory mice and rats, the great majority of animals used in biomedical research, and focuses on well-being. The reader is also referred to several reviews of rodent enrichment research (Chapillon et al. 2002; Jennings et al. 1998; Olsson and Dahlborn 2002). A comprehensive citation list that includes multiple rodent species may be found in van de Weerd and Baumans (1995). In addition, a few reports using deer mice in studies of environmental enrichment are available in the literature (Powell et al. 2000; Turner and Lewis 2003; Turner et al. 2002, 2003) but are not cited herein.

Methods of rodent “enrichment” described in the literature may be categorized as follows: devices (often referred to “toys”), social grouping, nesting materials (particularly with mice), and handling (particularly with rats). We focus on housing and husbandry changes that have been shown to affect (positively or negatively) the well-being of laboratory mice and rats, and emphasize cage complexity, stocking density, nest material, and husbandry methods.

Mice

Anxiety and Stress

Current consensus: Inbred strains of mice may vary in their anxiety response to a changed environment, and in some cases, the social dominance hierarchy of male mice may become unstable.

Van de Weerd and colleagues (1994) studied weanling male C57BL/6 (B6) and BALB/c (BALB)1 mice housed in enriched (nest boxes, opaque plastic tubes, Kleenex® tissues, and wood-wool with shavings as bedding) or standard (shavings only) environments for 2 mo. The B6 mice slept in the nest boxes and under the food hopper in the tissues and did not soil the enrichment objects. The BALB mice slept in the nest boxes and plastic tubes and soiled the enrichment objects. In the enriched cages, both strains slept in groups of two to three mice and maintained constant locations for urination, whereas both strains slept in large groups and urinated in random sites in the standard envi-

1 Abbreviations used in this article: B6, C57BL/6 mice; BALB, BALB/c mice; CoV, coefficients of variation; Guide, Guide for the Care and Use of Laboratory Animals; IVC, individually ventilated cage; NK, natural killer; PVC, polyvinyl chloride.
The B6 mice in the enriched cages consumed less food than those in standard cages, whereas there was no difference in food intake for the two groups of BALB mice. Neither strain displayed any differences in body weight based on cage configuration. Behavioral testing revealed that the B6 mice housed in the enriched condition were more reactive and alert compared with mice of the same strain housed in the standard condition. However, BALB mice housed in the enriched condition exhibited increased levels of anxiety.

In contrast to the results described above, Chapillon and colleagues (1999) found that anxiety behavior was reduced in BALB mice exposed to an environment that was enlarged and contained interconnected boxes and running wheels. They also reported that the enriched environment had no effect on spontaneous activity of B6 or BALB mice. The data reflected variable effects on body weight.

Aggression among male mice has been studied by Haemisch and Gartner (1994) as a model of stress and its consequences. Adult male DBA/2 and CBA mice were housed in enriched cages (polyvinyl chloride [PVC] platforms on vertical dividers that provided burrow-like passages) or standard cages, three per cage, for 6 wk. Intra-litter aggression from an intruder or between cage mates was monitored weekly and occurred in both mouse strains kept in enriched cages. The social dominance organization among the DBA/2 mice, which were more aggressive than the CBA mice, changed frequently as a consequence of the aggression, whereas no such shifts occurred among CBA mice housed in either condition. Plasma corticosterone levels were significantly elevated among DBA/2 mice housed in the enriched condition, and body weight gain was significantly delayed in both strains of mice housed in the enriched condition. The same group performed additional studies (Haemisch et al. 1994) with adult male DBA/2 siblings that, again, were housed three per cage for 6 wk under the same enriched or standard conditions. As before, DBA/2 mice housed in the enriched cages attacked intruders significantly more frequently than did mice in the standard cages. In addition, as found earlier, the position of the dominant male was less stable in the enriched cage groups than in the standard cage groups, and plasma corticosterone levels were significantly elevated in the enriched cage groups (Haemisch et al. 1994).

Barnard and coworkers (1996) studied the effects of enrichment of random-bred C57BL/6 male mice on aggressive behavior, immune function, and resistance to Babesia microti. Three, six, or 10 mice were housed at 70 days of age in plywood and glass cages (279 in²) that were unmodified or contained shelves and nest boxes. The authors reported no significant effects of group size on the measured parameters. For mice housed in modified cages, serum concentrations of testosterone decreased and corticosterone levels increased more slowly than among mice housed in unmodified cages. However, mice housed in the modified boxes exhibited increased aggression, which correlated with reduced resistance to B. microti and reduced serum immunoglobulin concentrations. The combined results of these studies suggest that changing a mouse’s environment does not necessarily have a positive impact on welfare and, therefore, cannot be technically considered as enrichment.

Benaroya-Milshtein and colleagues (2004) studied 1-mo-old male C3H/eB (sic: should be C3HeB/Fe) mice that were housed in standard plastic cages (105.7 in², 10 per cage) or in [enriched] wire mesh cages (218.5 in², 5 per cage) containing ladders, tunnels, and a running wheel. After 6 wk, the mice in the enriched environment exhibited less anxiety-like behavior and more activity compared with mice in the standard cages. In a stress paradigm that involved electric shocks, the enriched mice had shorter freezing times (times during which they were motionless). Serum corticosterone concentrations were significantly higher among mice housed in the enriched environment compared with controls. However, corticosterone levels increased significantly in control mice exposed to the stress paradigm but were unchanged in mice housed in the enriched environment and exposed to electric shocks. Natural killer (NK1) cell activity was enhanced among mice housed for 6 wk in enriched cages as well as among mice housed for 3 mo in enriched cages and exposed to electric shocks (compared with mice housed in standard cages and exposed to shocks). The differences in cage material, housing density, and group sizes might be considered confounding variables in this study.

Housing and Husbandry Conditions

Current consensus: The literature consistently supports the concept that laboratory mice can be housed with less floor space per mouse than the space recommended in the Guide for the Care and Use of Laboratory Animals (Guide) (NRC 1996). In addition, male mice and breeding and nonbreeding female mice use nestng material that can be as simple as paper tissues.

One could argue that the definition of enrichment should not be limited to changes in or additions to the physical environment. We tend to think of enrichment as the addition of nesting material or devices (which may, in fact, have no functional significance for the animal) to the cages. However, other, more subtle changes such as alterations to social groupings may be considered as enrichment. Such alterations can improve (or at least not compromise) the health and welfare of the animals substantially, and actually reduce the cost of producing and maintaining rodents.

The Report of the Rodent Refinement Working Party (Jennings et al. 1998) recommended considering the cage sizes stipulated at the time as minimal, but also noted that increasing the amount of empty cage space could increase aggression. Thus, cage size should not be increased without increasing cage complexity. However, the peer-reviewed publications on the floor space required to maximize well-being of laboratory mice collectively suggest that mice can...
be housed at densities higher than those recommended in the Guide (NRC 1996), even in the absence of devices or increased cage complexity, and that mice housed at higher densities are healthier and less aggressive than mice housed at lower densities (Fullwood et al. 1998; McGloine et al. 2001; Peters and Festing 1990; Smith et al. 2004a; Smith et al. manuscript in preparation; van Loo et al. 2001). Peters and Festing (1990) have reported that inbred BALB and outbred MF1 mice could be housed with as little as 27 cm² (4.2 in²) of floor space per mouse without affecting growth rate and adrenal weight. Cage accessories in the form of plastic tubes had no effect on growth rates of BALB mice but decreased growth rates of MF1 mice.

Fullwood and coworkers (1998) studied young adult male B6 mice that were housed with 5, 10, 15, or 20 in² of floor space per mouse for 5 wk. They found that decreased floor space resulted in no changes in body weight, enhanced lymphocyte responses to phytohemagglutinin, and increased adrenal weights and plasma glucocorticoid levels. These mice consumed or wasted more food and water than mice housed with more floor space. Mice housed with 10 in² of floor space had NK cell responses that were superior to the other groups. The same investigators (McGlone et al. 2001) then studied 3-wk-old BALB male and female mice that were housed with 5, 15, or 20 in² of floor space per mouse for 6 wk (males) or 7 wk (females). Among male mice housed with less floor space, they observed that the mice spent more time lying down, but there were no differences in the amount of time spent grooming or sitting. There were also no differences in growth rates among the groups, and mortality was decreased among mice housed with less floor space. Females housed at a higher density (less floor space per mouse) were heavier, had enhanced lymphocyte responses to phytohemagglutinin, and spent more time grooming and sitting. Van Loo and colleagues (2001) studied male BALB mice that were 7 wk old at study initiation and were held for 14 wk. The mice were housed in groups sizes of three, five, or eight, with 80 or 125 cm² (12.4 or 19.4 in², respectively) of floor space per mouse. They found that aggressive behavior was best prevented by housing mice in groups of three or five with the smaller amount of floor space.

One possible explanation for the results described above is that mice provided with less floor space have less defendable territory and are, therefore, less likely to behave aggressively with cage mates. We have performed experiments with young adult B6, NOD/LtJ, and BALB male and female mice and FVB/NJ female mice housed for 8 wk in three cage types with differing amounts of total floor space and floor space per mouse (ranging from ~5.6 to 12 in²). The results have led us to conclude that these animals can be housed with half the floor space recommended in the Guide (Smith et al. 2004a; Smith et al. manuscript in preparation), irrespective of total cage floor space. The following results were reported with the housing configuration that represents halving the floor space (~5.6 in² [36 cm²] per mouse): aggression was not noted; weight gain and food and water consumption were unaffected; and the cage microenvironment (in-cage ammonia and carbon dioxide concentrations, temperature, and humidity) was within accepted limits. In general, male and female urinary testosterone concentrations of mice housed with less floor space per animal were unchanged or lower than those for mice housed with more floor space. In contrast, early and excessive aggression, which necessitated euthanasia, was noted among FVB/NJ male mice housed in cages with 51.7 in² (333.5 cm²) or 112.9 in² (728.9 cm²) of floor space. This level of aggression applied to mice held at the housing density recommended in the Guide (approximately 12 in² per mouse) as well as higher densities. FVB male mice housed at any of four densities in “shoebox” cages with 67.6 in² (436 cm²) of floor space did not exhibit aggression until the fifth week of the 8-wk study. We conclude that FVB male mice, like SJL male mice which are known to be very aggressive (Jackson Laboratory 2004) should not be group housed for humane reasons.

Moons and colleagues (2004) tested the hypothesis that provision of shelter objects to laboratory mice would make them less habituated to humans and thus increase the time required for husbandry and experimental procedures. The investigators examined male FVB (inbred) and NMRI (outbred) mice housed in standard cages or cages provided with two PVC conduits. They recorded the following data weekly for 4 consecutive wk beginning when the mice were 10 wk old: food and water consumption, body weight, latency of catching, and behavior scores in response to sham manipulations. Food and water consumption and body weight were significantly affected by strain but not by the presence of enrichment. Cage enrichment decreased the time required to catch the outbred animals and did not increase the time required to catch the inbred mice. Although a subjective measure, resistance to being held for a sham injection was not different for enriched versus nonenriched groups. Thus, the presence of shelter, at least for one strain of outbred mice, may have a positive effect on acclimation of animals to husbandry and experimental procedures.

Nest building by and nest material preferences of laboratory mice have been the subjects of much research. When used by the animals, nesting material represents a relatively cost-effective enrichment measure. Female laboratory mice prepare nests even when not in a breeding condition (Sherwin 1997), and male mice also use nesting material (Watson 1993). Of the 39 mice provided with a commercial nesting product and/or paper towels (in addition to bedding), 36 mice constructed nests during the first dark cycle, and the remaining three animals constructed nests during the next 48 hr. The mice began manipulating the paper towels almost immediately after the material was placed in the cages. The mice frequently made nests ultimately from a mixture of the two products (although there was an indication that they preferred the paper towels), and the nests were normally constructed in an area of the cage that had been used for sleeping before provision of the nesting materials (Sherwin 1997).
In a study similar to the one described above, van de Weerd and colleagues (1997b) evaluated preferences of male and female B6 and BALB mice for six types of nesting material. Importantly, there were no differences noted between the strains. Tissues or paper towels were clearly preferred to paper strips or no nesting material, and paper was preferred over wood products. Van de Weerd and coworkers (1997a) reported subsequently that all B6 and BALB mice in their study used nesting material to build nests, and that these mice weighed more than mice not furnished with nesting materials; however, the mice that were not given nesting materials consumed more food. Watson (1993) observed that individually housed mice spent the majority of their time in nests when provided. The provision of nesting material resulted in increased body weight and/or decreased food consumption, and behavioral test responses were unaffected. In contrast, enhancing cage complexity (usually by the introduction of inserted devices for climbing or hiding) or providing more floor space did affect outcomes of behavioral testing.

Olsson and Dahlborn (2002) reviewed 40 studies performed between 1987 and 2000 and concluded that "mice will work for access to nesting material and make use of this material to make nests in which they rest" (p. 243). They also reported that nine studies documented increased male aggression among mice provided with increased cage complexity, four studies showed no effect, and one showed a decrease in posthusbandry aggression. These studies used multiple strains of inbred and random-bred mice. Similar to increasing cage floor space, increasing cage complexity may somehow increase territoriality among male mice. Provision of nesting material without changes to cage complexity did not have this effect.

Transfer of nesting material during cage cleaning has reportedly reduced aggression among male mice housed three per cage (van Loo et al. 2003), although we have been unsuccessful in reducing aggression among male SJL/J mice housed in breeding configurations using this approach (D.J.C., unpublished data). Van Loo and coworkers (2004) addressed the issue of social contact versus enrichment with male mice that were permitted to spend time (1) near a familiar cage mate or an empty cage, or (2) near a familiar cage mate or in direct contact with nesting material (tissue paper). The mice preferred to sleep in close proximity to a familiar cage mate, and the need to engage in social behavior increased with age. Tissue paper was used largely for sleeping. It was concluded that single housing has negative consequences but that the presence of nesting material may partially compensate for that deprivation.

Thus, for mice, the enrichment strategy that has the most consistently beneficial effect and is most cost-effective is the provision of nesting material. The material affords a hiding place for mice housed in transparent cages and also helps maintain a comfortable temperature for the animals. Certain types of bedding may contribute to the animals’ sense of well-being and temperature regulation. Among the many bedding materials available from commercial sources are hardwood chips, recycled paper, pine shavings, and corn cob bedding. These materials exhibit great variability in absorbency and capacity for control of in-cage ammonia levels (Smith et al. 2004b). Despite the lack of evidence that exposure of mice to very high ammonia concentrations is deleterious for the animals, animal facilities must comply with the same government standards that are in effect regarding exposure of humans in the workplace. Concentrations can be reduced by opening mouse cages within a laminar flow hood, a practice that also reduces caretaker exposure to Mus m 1, a potent allergen present in mouse urine (Schweitzer et al. 2003). Several nesting materials (e.g., Nestpaks®) are also available commercially (Smith et al. 2004b). Mice use these products, which resemble large tea bags, to prepare nests almost immediately after placement in the cage.

The optimal nesting material must be favored by the mice, be durable or disposable, and be free of toxins or other contaminants. The most simple approach to the provision of nesting material is to give the mice access to paper tissues. The tissues can be placed on top of the cage because the mice take great pleasure in pulling them into the cage. It is necessary to use care when providing nesting material to breeding mice because some types of materials will stick to the neonates, which leads to dehydration and/or death (Jennings et al. 1998). Cotton nesting material has also been associated with conjunctivitis in athymic nude mice (Bazille et al. 2001).

Rats

Anxiety and Stress

Current consensus: Enrichment by provision of devices has inconsistent effects on corticosterone levels.

Belz and colleagues (2003) examined the physiological effects of enrichment on 8-wk-old male and female Sprague-Dawley rats provided with Kong Toys® or Nestlets®. The rats were exposed to baseline levels or mild stress (injections of physiological saline). Animals of both sexes housed in the enriched cages had lower baseline corticosterone and adrenocorticotropic hormone levels than rats in standard cage environments. Adrenocorticotropic hormone responses to mild stress were significantly lower in female rats housed under the enriched condition.

In contrast, Moncek and colleagues (2004) report the following: Male Wistar rats kept for 40 days in an enriched condition (10 rats per large [775.2 in²] Plexiglas cage including devices [e.g., “toys, tunnels, swings and running wheels”], which were exchanged three times per week) had plasma and adrenal corticosterone concentrations that were higher and adrenals that were 15% larger than observed for control rats housed three to four per 161.2 in² wire mesh cage. The enriched rats were also occasionally given small amounts of bread, cheese, peanuts or apples, yet they gained
significantly less weight than the controls. Exposure to repeated handling resulted in a more rapid extinction of corticosterone responses to challenge with the antianxiety agent buspirone. The fact that enrichment resulted in larger adrenals and increased adrenocortical function was interpreted to reflect a state of chronic stress (Moncek et al. 2004). However, this study had multiple variables and is another example in which the housing density and cage materials could have been confounding variables.

**Housing and Husbandry Conditions**

Current consensus: Nest building is a learned behavior in rats, and these rodents show preference for objects that can be chewed. Normal husbandry activity can result in elevated heart rates and mean arterial blood pressures, and these effects are less pronounced among group-housed rats.

Van Loo and Baumans (2004) report that nest-building behavior is a learned activity in laboratory-reared Wistar rats that had access to nesting material from birth, from weaning, or from 8 wk of age. Rats exposed to nesting materials relatively late (after 8 wk of age) soiled and ate more of the provided material and made simple nests, whereas rats exposed early made elaborate nests. Thus, nesting material may be considered appropriate enrichment for rats when it is provided from the time of birth.

In an effort to identify the objects most preferred by rats, Chmiel and Noonan (1996) exposed animals to a free-choice paradigm that included 15 different objects. Surprisingly, the rats did not prefer cage partitions or hollow pipes in which they could hide, nor did they prefer most of the objects that could be manipulated within the cage. The clear preference was for chewable objects: A block of wood with predrilled holes was the most attractive and permitted the rats to exercise an important species-specific behavior.

Sharp and colleagues (2002) studied stress-like responses of male Sprague-Dawley rats that were housed individually or in groups of two or four per cage. They measured heart rate, mean arterial blood pressure, movement, and home cage behavior and after several procedures including cage changing. Resting heart rates and arterial blood pressures were consistently lower among rats housed per cage compared with the other two groups. Rats housed four per cage also maintained lower heart rates and arterial blood pressures during husbandry procedures than rats housed singly. Arousal behavior was observed in all groups after cage changing, but rats housed four per cage returned to sleeping behavior more quickly than rats in the other housing groups. The authors conclude that common procedures induce stress-like responses in male rats and that group housing can reduce the magnitude and duration of those responses.

**Effects of Environmental Changes on Experimental Variability**

An argument can be and has been made that permitting a laboratory animal to exhibit species-specific behavior will result in fewer behavioral abnormalities or other pathologies. A concern raised by the research community is whether enrichment increases the variability within groups in experiments. In a study with Wistar rats, high degrees of variability were found in adrenal weights, interscapular brown adipose fat, and epididymal adipose tissue from animals provided with aspen gnawing blocks, solid or wire bottom cages, and variable numbers of rats per cage. Body weight and growth were less variable (Mering et al. 2001). The authors concluded “some of the physiological parameters are susceptible to variability attributable to environmental modifications in general whereas some are not. . . . Variation of different parameters may vary from one experiment to another and between different environments thus hindering the estimations of appropriate number of animals” (p. 80).

Unfortunately, some of the studies that purport to show increased variability as a consequence of enrichment use very small numbers of animals or cages. For instance, BALB, B6, and A strain mice (two cages per strain per treatment) were used to evaluate the effects of enrichment on a variety of physiological parameters (Tsai et al. 2002). The enriched condition consisted of cages with nest boxes, climbing rods, and nesting material. The enriched groups had higher coefficients of variation (CoV1) for many of the parameters, and strain differences were not consistent. The authors caution that such variability could lead to an increase in the number of animals required for experiments.

In a recent study by Tsai and coworkers (2003a), 60 DBA/2 breeding pairs (20 pairs per group) were housed within a ventilated cabinet, on a “conventional” open rack or on an individually ventilated cage (IVC) rack, in enriched (nest boxes, climbing rods, and nesting material) or nonenriched cages (Tsai et al. 2003a). Reproductive performance was tracked from 10 to 40 wk of age. The breeding indices (defined by the authors as pups per dam per week) were found to be similar for all housing types for nonenriched groups; however, the CoV in the IVC rack were higher for most parameters. Enrichment led to a decrease in the number of pups born. These investigators conducted another study (Tsai et al. 2003b) with same-sex groups of 3-wk-old DBA/2 mice housed four per cage for 12 wk in standard cages, cages enriched with nest boxes, climbing bars, and nest material, or cages enriched with horizontal and vertical dividers. The mice (two cages per treatment group per sex) were then tested for several behavioral and physiological traits. Sex differences among the three groups were not consistent for several variables, including the following: growth rate; relative spleen, kidney, and heart weights; food drive; and elevated plus maze performance. The two enrichment groups frequently had higher CoV than the standard cage group.
Van de Weerd and colleagues (2002) examined the effects of environment on variability in mouse behavior and physiology during potency testing for tetanus vaccine and stress-induced hypothermia. Neither body weight nor food consumption varied for mice kept in enriched or standard conditions. The authors noted that enrichment did not influence variability, but they cautioned that such variation is parameter dependent.

The eventuality of increasing the number of animals required to reach clear-cut experimental conclusions could greatly increase the cost associated with biomedical research. Increasing the number of animals also is at odds with the goals espoused by Russell and Burch (1959). In devising enrichments that change the space and/or utilization of space in the cage, one must keep in mind that ideally, no changes should affect the dimensions of the caging systems currently in use. Rodent caging systems are very expensive, and replacing existing equipment would place an undue burden on institutions. This burden, in turn, places limitations on the enrichment methods that are reasonable to implement. Furthermore, enrichment studies have revealed sex- and strain-specific differences that depend on enrichment schemes, so it is premature to consider any sweeping changes.

Variability of Results Despite Environmental Constancy

Neurobehavioral genetics has become an important area of research with the development of readily available genetically modified and characterized mice. However, it is not unusual for different laboratories to record variable results, even when using “the same” mice tested in “the same way.” In an effort to understand this variability, three laboratories studied six mouse behaviors using exactly the same inbred strains and one null mutant strain (Crabbe et al. 1999). Test apparatus, protocols, and all features of animal husbandry (including, e.g., bedding, husbandry intervals and days, handling) were rigorously standardized. Mice received from external laboratories were shipped at the same time and habituated for the same period. Experiments were started on the same days at the same hours of the day. Certain variables (e.g., tap water, test and housing room configurations, air handling systems, and humidity) could not be controlled. One of the three sites required fitting cages with filter tops. Some of the test results were not site dependent, whereas some were strikingly different in the different laboratories. For instance, anxiety levels of all mouse strains were consis-tently lowest in one of the three laboratories. The mice with the null mutation gave different activity results in all three laboratories. These results are unsettling to investigators working in the field of neurobehavioral genetics and imply that some almost undetectable environmental differences may have had large behavioral consequences. Even more worrisome was the fact that none of the investigators was able to replicate earlier results from one of the laboratories with the null mutant—despite the fact that the earlier findings had been replicated four times. In an attempt to explain the discrepancies, the lead investigator suggested that subtleties such as experimenter appearance (one research assistant was highly allergic to mice and wore a respirator) or scent may have played a role (Enserink 1999).

The microbiological status of the mice is one variable that was not addressed in the report described above. The fact that two facilities housed the mice in open cages makes this a troubling issue. The animals were housed long enough in each facility to have sustained infection with any agents indigenous to the home colonies, and it is conceivable that acute infection with an agent that targets the nervous system or induces a febrile response could alter behavioral responses.

Additional Comments

It must be remembered that well-being can be improved only if the normal behavior and physiology of the animals are understood. As Jennings and coworkers (1998) noted, the domestication of mice was accompanied by selection for certain characteristics; however, laboratory mice also have maintained many of the attributes of their wild ancestors. For example, laboratory mice, like their forebears, like to burrow. Most importantly, we need to understand some basic facts about mouse biology and physiology. For instance, olfactory cues are very important and permit individual and group recognition. Reproductive cycle synchronization relies on pheromones. Many inbred strains of mice have vision impairments and rely on scent for nearly all of their environmental cues.

We also remind readers that “there is no consensus on how to define ‘environmental enrichment’” (Olsson and Dahlborn 2002, p. 265). A recent report by van de Weerd and colleagues (2002) defined enrichment, based on an earlier report by Newberry (1995), as modification to the environment. Thus, enrichment can be as simple as adding a tissue or a particular type of bedding material to the cage, or as complex as adding devices such as shelters, running wheels, blocks for chewing, or plastic tubes. Nevertheless, “it is important that the change results both in enhanced animal welfare and improved biological functioning of the animals, and it is in principle not correct to use the term ‘enrichment’ before such results have been shown” (Olsson and Dahlborn 2002, p. 245).

The literature on enrichment for rodents is difficult to assimilate and summarize easily, in part because different investigators may use very different paradigms. For instance, when Warren and colleagues (1982) studied the effects of enrichment on male B6 mice between the ages of 600 and 750 days, enrichment consisted of “structures to crawl through, over and under. . . . marbles, ping pong balls and 4 sexually receptive females that were removed and replaced as they became pregnant” (p. 15). This design is not frequently found in the literature so it is difficult to
compare it with other enrichment schemes. Similarly, the study by Moncek and colleagues (2004), mentioned above, included rather unusual variables.

There seems to be general agreement that any change to animals’ housing should “increase the frequency and diversity of positive natural behaviors, decrease the occurrence of abnormal behavior, maximize the utilization of the environment and increase the animal’s ability to cope with the challenges of captivity” (Olsson and Dahlborn 2002, p. 245). However, the entire issue becomes complicated when one considers that although aggression may be a natural, species-specific behavior, it is not desirable in the research environment. In addition, abnormal behavior may be a normal behavior that is practiced at increased frequency, intensity, or duration (Garner 2005). We add that change or enrichment should not yield experimental results that are so variable that significantly larger numbers of subjects are needed to reach conclusions.

According to Jennings and colleagues (1998), mice can exhibit more than 40 individual activities and postures. It must be kept in mind, however, that behavior is highly variable among inbred strains of mice. They may allocate different percentages of time to different behaviors. The light:dark cycle, age, sex, and social status of the animals also affect behaviors. Other factors such as the amount of hair coat and general level of aggression must also be taken into account. For instance, athymic nude mice need extra bedding to maintain body temperature, and male SJL mice should not be grouped housed because of their aggressive behavior.

Future Research

Several areas would benefit from additional research. For instance, most studies examining floor space needs of mice have been relatively short term. It would be useful to know the effects of longer exposure to relatively high-density housing of same-sex groups of adult mice as well as the effects of higher density housing on older or breeding rodents. Parameters other than those included in our own studies should also be measured. These parameters might include a variety of indices of immune function that could have an impact on several areas of biomedical research. It would also be helpful to evaluate floor space needs of rodents, specifically mice, in combination with different types of cost-effective enrichment, such as the presence of tissues or other nesting materials. One may speculate that these two inexpensive measures, when combined, could materially improve the lot of these very social and inquisitive animals because, as the title of Poole’s 1997 article states, “Happy Animals Make Good Science” (Poole 1997, p. 116).

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