Animal Welfare Beyond the Cage ... and Beyond the Evidence?

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Animal Welfare Beyond the Cage . . .
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In “Laboratory Rodent Welfare: Thinking Outside the Cage,” Balcombe (2010/this issue) suggests that laboratory cage housing is damaging to rats and mice because it does not meet their evolved needs and may damage their psychological and physical health. The article also indicates that larger and more enriched spaces reduce aggression and mortality and improve the health and friendliness of rodents in the laboratory. Remarkably, many of the studies cited as supporting these assertions fail to provide data bearing on the issues involved or may even report findings opposite to those described by Balcombe, whereas many studies that are highly relevant to these issues are not cited or described. Moreover, although the “evolved needs” of rats and mice are presented as the basis for an analysis of rodent welfare, the important and well-documented changes in needs- or motivation-related behaviors of a rodent in the laboratory (due to human selection over hundreds of generations) is ignored. This pattern of disconnections between data and conclusions is so pervasive as to demolish the scientific value of the exposition.

In “Laboratory Rodent Welfare: Thinking Outside the Cage,” Balcombe (2010/this issue) presents a case that rats and mice should not be housed in laboratory cages because a range of their evolved needs are not met there. A core issue to this conclusion is the empirical basis on which standard laboratory housing is to be interpreted as damaging. An array of studies are cited to indicate that rats and mice are sentient and emotional creatures, a view with which few researchers of animal behavior would disagree, although there is a far more parsimonious explanation—fear—for most of the studies interpreted as indicating that rats
show consideration or empathy for other rats. The issue is not whether these animals are capable of being damaged but whether standard caging damages them.

**PSYCHOLOGICAL HEALTH**

Only a single study (Zhu et al., 2006) is specifically cited as indicating that the psychological health of rodents may be adversely affected by standard laboratory caging. They compared mice living in such cages with those in larger cages containing a number of objects that were changed weekly, reporting significant differences in behaviors in the elevated plus maze (EPM), open field, and food neophobia tests between the groups. All these tests provide measures of anxiety; one, the EPM, is the single most commonly used measure of anxiety, reported in more than 7,000 articles in the past 2 decades (Canteras & Blanchard, 2008). However, Zhu et al. reported that animals from the “enriched” caging group were consistently more, rather than less, anxious than those maintained in standard housing. They also noted that some of these findings replicated earlier work from the same lab. Unless greater anxiety is indicative of improved psychological health, these results are the diametric opposite of how they are described in the Balcombe (2010/this issue) article.

**PHYSICAL HEALTH**

Another issue that is obviously involved in analysis of the health consequences of laboratory caging is that of the physical health of the nonhuman animals involved. This is only briefly mentioned in the context of a hope (Morrison, 2001) that animals living in larger and more enriched housing conditions might live longer, but the topic deserves additional consideration. How long do mice and rats live in nature, the environment(s) in which they (and their panoply of needs) have evolved and in which there is certainly some chance that these needs will be satisfied?

Although there is no direct evidence on rodent longevity in nature, age of onset of reproduction, gestation times, and litter-size data suggest that a breeding pair of mice and their offspring can produce 100,000 or more individuals in a single year. That this is indeed possible may be seen in the population explosions labeled “mouse plagues.” These may follow periods—such as wet periods in Australia—of unusual food supply (Singleton et al., 2005). They involve the sudden appearance of millions of animals in areas where rodent populations are typically low or moderate and rodent predators correspondingly sparse. This suggests that inadequate food supplies, leading to starvation of both adult and
young animals, and predation (along with human intervention in the form of traps and poisons) are usually major factors in rodent mortality in nature. In fact, mortality prior to breeding would have to exceed 95% for freely breeding rodents to fail to show an explosive increase in numbers; the means of death, in nature, are uniformly unpleasant. In contrast, moderation of reproduction in laboratory settings is generally achieved through a denial of breeding opportunities, whereas death, when it comes, is achieved through methodologies that are selected as minimally painful or stressful for the animal.

THE BEHAVIORAL ADVANTAGES OF LARGER CAGES

It might be argued that nature is an inappropriate control group and that the force of the Balcombe (2010/this issue) treatment is to show advantages of larger and more enriched cages. Although there is an enormous literature that is potentially relevant, with PubMed providing nearly 5,000 citations for a combination of “rodent” and “enrichment,” what is cited in the Balcombe article is sparse and selective. Morrison (2001) and Boice (1977) are reported as showing reduced aggression for rats in larger cages. Both studies are interesting in different ways, but neither provides any actual data on aggression, whereas there is a relatively extensive literature on rats and mice in larger cages that does provide such data. This tends to indicate very high and enduring levels of aggression, particularly among males, for mixed-sex rodent groups in larger cages (Blanchard, Flannelly, & Blanchard, 1988) and population boom-bust cycles for both wild-trapped and laboratory mice and rats in very large cages over extended periods (Van Oortmerssen & Busser, 1989).

In contrast, the Morrison (2001) report was of 2-male rat groups in a 1.7 × 9 m enclosure; notably, rat aggression is very low in groups without breeding females. Although the Boice (1977) study did include females as well as males, their data-free comment that “serious fights were probably absent . . .” requires further examination. The single 12 × 7 × 1 m outdoor cage used in that study provided protection from predators and ample food (around 100 lb/week). The animals constructed subsoil burrows and utilized them freely. In this seemingly ideal habitat, initial placement of 5 male and 5 female pairs resulted in a population that quickly rose to about 50 and remained at this level for the next 2 years.

And now this question: Why did this population, in contrast to the long-term rodent population of Van Oortmerssen and Busser (1989) fail to expand? Litters are noted, especially in the spring and fall, but somehow there were no more rats than the 50 noted as “quickly” appearing. The statement that there were few deaths is apparently based on finding only a few bodies of young animals. However, this was a study of burrow-system effects, and the burrows were checked only once a year. Did animals dying in the extensive burrow systems
escape detection? Were dead pups eaten? Although it cannot be certain why they died or what happened to the bodies, new litters but no additional animals flatly contradict this statement (for which no additional evidence was given): “These animals showed better health and lower mortality than did a control group of rats housed in typical wire cages” (Balcombe, 2010/this issue, p. 83).

The Morrison (2001) article is also cited as indicating that cage enrichment makes rats more inquisitive and friendly and less fearful of personnel than rats housed in standard cages. Although data are again not presented, there seems little reason to question whether the rats in this study were inquisitive/friendly and less fearful, as the Morrison article itself also notes that “the pens attracted people to visit the rats and feed them” (p. 34), a relevant factor not noted in the Balcombe (2010/this issue) article.

**THE ISSUE OF “EVOLVED NEEDS”**

An important statement in the Balcombe (2010/this issue) article explains that “laboratory animals’ is being used here as shorthand for animals in the laboratories and should not be taken to imply anything about the animals’ nature or purpose” (p. 78). In fact, when the term “laboratory” is applied to rats or mice, it does indeed mean something about the animals’ nature. Laboratory rodents are the products of well over 100 years and several hundred generations of selection for some specific behavioral traits (D. C. Blanchard, Arakawa, Crawley, & Blanchard, in press). Laboratory rats, more extensively studied in this context than mice, show sharply reduced defensiveness to human approach and handling compared to wild *Rattus norvegicus*, even when the latter have been fostered onto lab-rat dams and reared in standard caging (R. J. Blanchard, Flannelly, & Blanchard, 1986).

The process and results of selection of rats in the wild for a lack of defensiveness to human handling have been replicated, and their neurobiological correlates investigated, in a remarkable long-term program at the Institute for Cytology and Genetics, Novosibirsk, Siberia (Plyusnina, Oskina, Tibeikina, & Popova, 2009; Popova, Nikulina, & Kulikov, 1993). Does this process result in laboratory rats and mice with “evolved needs” that are more amenable to life in cages than are those of wild rats and mice? Although there is at present no comprehensive empirical basis for answering this question, it is certain that the process of domestication has produced striking changes in at least one evolved need: Laboratory rodents breed freely under laboratory conditions, whereas only about 10% of wild, trapped *R. norvegicus* do so (unreported observations from this laboratory), a difference that likely reflects the role of fear in suppressing hormonal and behavioral aspects of reproduction. That fecundity and survival of offspring to adulthood—both clearly adaptive traits—
are strong in laboratory rodents in laboratory conditions indicates that the social and ecological characteristics or preferences of the wild congenors of these animals in nature do not necessarily describe evolved needs for their laboratory descendents.

THE BROADER ISSUE: ANIMALS IN LABORATORIES

This brief analysis suggests serious defects in the empirical basis given in the Balcombe (2010/this issue) article for a view that standard laboratory caging is damaging to laboratory rats and mice. There are indications that the Balcombe critique also extends to noncaging aspects of maintenance of animals in laboratory conditions: Laboratory features described as potentially damaging to rodents include “computing equipment, cage washers, hoses, running taps, squeaky chairs, and some fluorescent lighting.” In addition, “Cleaning agents, perfumes, and companion animal scents on human handlers are also aversive to rodents” (p. 82). Here again, the empirical basis for statements concerning potential damage to animals may be questionable.

Three articles are cited in support of the statement about cleaning agents, perfumes, and companion animal scents on human handlers. Two of these articles, R. J. Blanchard et al. (1998) and Williams (1999), did not deal with cage cleaning or perfume and are of questionable relevance to the issue of companion animal scents on human handlers. Although both Blanchard et al. (1998) and Williams investigated predator odor effects on rodents, neither involved a human intermediary; it seems unlikely that temperature-dependent, relatively nonvolatile predator fur/skin odors on human handlers in laboratory settings are likely to cause as much rodent distress as are actual predator odors in the real world. The third citation (Burn, Peters, & Mason, 2006) did not mention either perfumes or companion animal scents on human handlers but specifically reported, “no evidence that cage cleaning caused rats any acute decrease in welfare” (p. 161)—a very different conclusion from what is claimed in the text to which this citation is attached.

SUMMARY

Are laboratory conditions deleterious to laboratory rats and mice? In comparison with what? If longevity is the criterion, the standard laboratory situation is far superior to the wild, where the vast majority of rodents die prior to reproductive maturity. There is no indication that longevity would be enhanced by larger and more complex cages; studies not cited in the Balcombe (2010/this issue) treatment suggest high levels of aggression and/or mortality from intraspecific
fighting when rat or mouse populations are unregulated for long periods in seminatural settings.

Moreover, in terms of the evidence presented in the Balcombe (2010/this issue) article, standard caging appears to be not equivalent but superior to the “enriched” variety with reference to psychological health as indexed by standard measures of anxiety. In addition, both standard and enriched caging situations are almost certainly less anxiogenic than the real world, in which rats and mice must contend with predators, starvation, and human attempts to kill them. In sum, the conclusions of this article are not supported and, on several important points, are directly contradicted by the findings cited in support of them.

CONCLUSION

This is no peripheral matter. The business of research in general (and of science in particular) is to base conclusions upon evidence, not the other way around. Acceptance of a view that current laboratory conditions do not meet the evolved needs of laboratory rats and mice represents a potential threat—one of many—to the integrity of biomedical science. To accept this view on the basis of evidence that simply does not support it would represent a shocking deviation from the standards of logic by which both scientists and medical practitioners attempt to act.

REFERENCES

ANIMAL WELFARE BEYOND THE CAGE


