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The Ethical Implications of Using Mice in Biomedical Research: A Critical Welfare and Policy Review from an RSPCA Perspective

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Abstract

Mice (*Mus musculus*) are widely used as a mammalian animal model in biomedical studies because they are genetically related to humans, which implies that their use requires stringent ethical and welfare considerations. This review examines the ethical issue of mouse experimentation as an RSPCA concern, focusing on the dilemma between scientific utility and the moral sentience of mice as sentient creatures. There is evidence that mice have complicated emotional abilities, such as empathy -like behaviors and vulnerability to stress contagion. Nevertheless, the physiological and behavioral needs of people are not usually addressed in the traditional laboratory environments, which results in chronic stress and low experimental validity. In this paper, the Five Domains Model is used to identify severe welfare gaps in the normative housing and handling procedures. The moral permissibility of such research is determined by the use of the following ethical frameworks: Utilitarianism, Animal Rights Theory, and the Capabilities Approach. In addition, the article criticizes the practical use of the Animals (Scientific Procedures) Act 1986 by finding that the regulation lacks compliance and harm and benefit evaluation. To solve these problems, the review suggests obligatory environmental enrichment, non-aversive handling, and more focused investment in the non-animal technologies. Finally, empirical welfare science must be combined with the

ethical theory to improve the research practice and respect the moral duties of sentient research participants.

Introduction

Mice (*Mus musculus*) are the most common mammalian model in biomedical research (Suresh, 2025), accounting for 80 percent to 90 percent of animals used in NIH-sponsored studies. This is because of the ease of handling in laboratories, ease of care, and a substantial genetic similarity to humans (Standley et al., 2024; Hickman et al., 2017). According to the National Research Council, mice and rats represent a prominent portion of research animals that are not significantly reported in U.S. animal use reports under the Animal Welfare Act. More than 99 percent of the mouse genome is shared with that of humans (Rosenthal & Brown, 2007), with approximately 85 percent similarity in protein-coding regions (National Human Research Institute, 2010), which makes mice indispensable as models of human diseases. Moreover, some of the genes and their functionality are very conserved between the two species (Eppig et al., 2015). They have a high reproductive rate and can be modified genetically, genetically modified mouse models that have been very useful in complex disease studies such as cancer, diabetes, and neurodegenerative conditions like Alzheimer's (Jucker, 2020; Day et al., 2015).

Although they are very important in research, ethical issues revolve around the well-being and moral integrity of testing mice in a laboratory set-up (Ormandy et al., 2013). The justifications for their use depend on medical progress and scientific advancement (Festing & Wilkinson, 2007), but increasingly, the main focus is on the quality of life that mice are subjected to in the laboratories. Normal housing, which tends to be sterile, does not allow them to freely express their innate behaviors, like nesting and associating, a factor that contributes to lifelong stress and dysfunctional behaviors (Makowska & Weary, 2016). Also, mice are very often subjected to painful surgeries where appropriate anesthesia is not provided. The ethical duty to take account not only of the scientific value, but also the moral status of sentient beings is strengthened by their legal definition under UK legislation, in the Animal Welfare Act 2006 and Animals (Scientific Procedures) Act 1986, as sentient beings. (UK Government, 2006; Carbone, 2021).

Moral Status of Mice

There is growing scientific evidence that mice are sentient beings capable of feeling a diverse array of emotions and sensations, including pain, pleasure, fear, and anxiety (Mogil, 2019). The mice exhibit behavioral and physiological factors consistent with emotional sophistication, and their ability to suffer (Carbone, 2011). It is documented that mice have empathy-like behaviors. Research has shown that when mice are exposed to a conspecific in pain, they experience heightened stress themselves, a process called stress contagion (Piriyaprasath et al., 2023). Mice also enjoy social suffering in which the companionship reactions reduced the stress reactions (Langford et al., 2006).

Mice tend to experience anxiety, depressive symptoms, and stress when exposed to unfavorable housing conditions, which proves that they are sentient beings that need to be considered and afforded ethical attention (Clarkson et al., 2018). Sentience is a proxy that is used as a moral concern on a philosophical level. Singer (1977) demonstrated that the mice's capacity to suffer poses moral obligations to consider the interests of animals equally. Thus, mice sufferings cannot be ignored only because of human progress.

From a deontological perspective, animals have intrinsic value due to their perceptual and emotional ability (Regan, 2008). In turn, they should not be used solely as a means of scientific advancement. This is also supported by the capabilities approach as a part of justice, which demands that animals should be given the chance to show their species-specific behavior (Nussbaum, 2007). In the case of mice, it would entail the ability to burrow, nest, huddle, and socialize, most of which is extremely limited in the traditional laboratory setting (Olsson et al., 2012).

Mentally, mice are not a small organization. They have high levels of learning, memory, spatial orientation, and behavioural adjustment (Whishaw & Kolb, 2004; Shettleworth, 2010). These characteristics make it even stronger that mice can have meaningful experiences and cannot be treated as biological test-tube animals.

According to the law, the UK statutes perceive mice as sentient beings. They require their ethical treatment in certain environments, stipulated by the Animal Welfare Act 2006 and the Animals (Scientific Procedures) Act 1986 (ASPA) (UK Government,

1986). Such laws provide additional reinforcement of the moral duty to reevaluate the housing, handling, and use of mice in research and to promote better ethical practices.

Welfare Implications in Laboratory Use

Although mice are widely used in biomedical research, the conditions where they are confined usually fail to meet their physiological requirements. Not only does it raise serious ethical issues, but it also reduces the validity of experimental data. Mice are highly sentient, social, and curious animals, so behaviors like nesting, climbing, foraging, and burrowing seem natural to them (Barbee & Turner, 2019). Conventionally, laboratory cages do not provide enough environmental enrichment, which causes the development of abnormal behavior like stereotypy and barbering in prolonged stress (Bailoo et al., 2018).

These welfare problems are highlighted by multiple procedural stressors of laboratories:

- **Social Stress** is a major issue. Improper housing, especially in young males, may result in aggression or social isolation, and isolation may cause depression and loneliness (Kappel et al., 2017).
- **A deprivation of enrichment**, e.g., nesting material, hinders vital behavior and physiological processes like thermoregulation, sleep, and maternal care. It is shown that enriched environments reducce corticosterone, a biomarker of physiological stress (Gaskill, 2017; Ratuski & Weary, 2022).
- **Handling work** also influences the welfare. Tail handling makes animals more anxious and avoidant, whereas the tunnel or cupping procedures led to less anxious and more exploring behavior (Hurst & West, 2010; Clarkson et al., 2018).
- **The treatment of pain** is erratic. Mice are mostly exposed to procedures with minimal or no analgesia, largely due to long-lasting fear that analgesia would impair the experimental outcomes (Jirkof & Potschka, 2021).

To structure these welfare issues, the Five Domains Model is a multidimensional assessment tool that contains the domains of Nutrition, Environment, Health, Behavior, and Mental state (Mellor & Beausoleil, 2015). When measured in traditional laboratory housing, the deficits are often observed in all five categories, indicating poor welfare (Cait et al., 2022). The core of this model is to evaluate the positive experience, or effects

that unite both internal circumstances and environmental surroundings to determine well-being (McGreevy et al., 2018). The model can be applied to practice the planning of enrichment plans, distress monitoring, and humane endpoint assessment (Mellor, 2017).

The RSPCA advocates integrating these structures into ongoing ethical reviews of projects, the project planning, and its implementation, and the publication phase. The beneficial/harm analysis conducted by Animal Welfare and Ethical Review Bodies (AWERBs) is essential to ensure that the benefit of scientific or societal value of animal welfare needs to outweigh the harm when used to justify animal suffering (RSPCA, 2025). Poor welfare is not only an ethical problem, but a scientific one too. Stress, pain, and anxiety affect immune, endocrine, and behavioral systems; due to biological variability, they reduce reproducibility and translational relevance of experimental work (Balcombe et al., 2004; Gaskill et al., 2009). So, one of the 3Rs principles becomes necessary: Refinement. It entails improved housing, husbandry, and procedural care to reduce distress and increase the well-being of animals (RSPCA, 2025). Enriched cages, social housing matching strain compatibility, humane handling, and effective pain relief not only lead to higher standards of welfare but also to stronger and replicable science (NC3Rs, 2025). RSPCA uses evidence-based refinements as a priority to implement within the institution because they start the work of institution-wide implementation immediately and cover a vast area (RSPCA, 2025).

Comparison with other Species

The welfare of mice is less considered than that of rats (*Rattus norvegicus*), even though both species have comparable sentience, social lives, and susceptibility to pain (de Boer & Koolhaas, 2024). Effects of the enriched, multi-level cages to which rats are commonly kept include shelves, tunnels, and chewable materials, which allow natural behaviors and minimize stress (Abou-Ismail et al., 2010). But mice normally exist in standard shoebox cages, without much enrichment, causing aberrations and anxiety (Olsson & Dahlborn, 2002; Van de Weerd et al., 1997). That is an implication that welfare choices are more convenient and traditional than scientific. A constant trait-based approach would be more fruitful for animal welfare.

Ethical Frameworks

To weigh the moral validity of subjecting mice to biomedical research, it would be necessary to critically consider the main theories of morality. Utilitarianism, Animal Rights Theory, and the Capabilities Approach: 3 popular theories of ethics that present a valuable argument with respect to animal experimentation ethics.

Utilitarianism, a theory proposed by Jeremy Bentham, later developed by Peter Singer, focuses on the outcomes of the action and holds that morally right actions are those that yield the maximum and the minimum stress (Singer, 1975). Within this framework, the use of mice in research might be deemed ethically acceptable if the projected benefits to human health significantly outweigh the harm inflicted on the animals. But utilitarian ethics also carry with them a strong obligation to do all we can to reduce the suffering of animals. The 3Rs: Replacement, Reduction, and Refinement proposed by Russell & Burch (1959) rely on this principle. The interpretation of this view by organizations such as the RSPCA emphasizes the need to limit the use of animals to cases where there is no alternative and to take every measure to minimize distress (RSPCA, 2025).

Contrarily, Animal Rights Theory, proposed by Tom Regan, suggests that sentient beings are not mere means of human service, but moral subjects and that they have moral rights. These animals exist as "subjects of a life," they can experience pain, and they can form a relationship, as well as have agency (Jamieson, 1990). Based on this approach, using mice in research is logically unjustifiable insofar as possible human benefit is concerned. Such behavioral evidence that mice are complex and emotional supports this theory further, and it is not reform, but a total end to the use of animals in research (Walker & Eggel, 2020).

A subtler picture is the Capabilities Approach developed by Martha Nussbaum. The approach to justice suggested by this theory is not to experience as little suffering as possible, but to be able to go forward with species-specific possibilities (Nussbaum, 2007). In mice, flourishing means a capacity to live natural lives, including nesting, burrowing, socializing, and living without unwarranted pains. Such principles are hardly upheld in laboratories, but they are strikingly like the contemporary welfare instruments such as the Five Domains Model, considering both physical and emotional states (Mellor & Beausoleil, 2015).

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Legal and Policy Review

In the UK, legislation covering the use of mice in certain research is amended by the Animals Act 1986 (Scientific Procedures) Regulations 2012 to bring it into compliance with EU Directive 2010/63/EU. This regulation states that any procedure which is likely to inflict pain, suffering, distress, or lasting harm must be licensed under a licensing system that involves an ethical review, justification to use a particular species, and assessment of the harm and benefit (Home Office, 2023; European Parliament & Council of the European Union, 2010). Central to ASPA is the legal integration of the 3Rs framework, Replacement, Reduction, and Refinement, which aims to limit animal use and suffering (Russell & Burch, 1992; NC3Rs, 2023).

Although this is a stronger legal structure, practical application is a problem. Critics contend that the ethical review processes serve as formality instead of evaluative moral processes. According to several researchers, these reviews are interpreted as administrative duties as opposed to legitimate moral examination (Ferdowsian & Beck, 2011; Pound & Nicol, 2018). Research has shown that harm-benefit tests will often incorrectly weigh the potential benefits of a scientific project, as well as downplaying the actual or available pain and suffering that animals go through (Schuppli, 2011). Carbone (2014) claims that the word necessary is usually treated too broadly, which means that it will be normal to perform experiments on mice even in situations where alternative means are available.

Monitoring and compliance are also the main issues. Concerns about the frequency and effectiveness of institutional inspection occur for 50 inspectors monitoring licensed from over 200 licensed facilities RSPCA, 2025). A culture of regulatory forgiveness is present since non-compliance or violating procedures rarely have meaningful consequences (Hawkins, 2014). There is an institutional discrepancy in the interpretation of welfare standards, resulting in varying levels of care and protection provided by laboratory mice (Diaz et al., 2020).

Recommendations

Following useful and scientific interventions, justify the use of mice in biomedical research.

Require Environmental Enrichment: Mice should have the enriched environments put in place with the materials to use as a nest, shelter, and vertical space to alter natural behavior. This enrichment enhances cognitivity by reducing anxiety and repetitive behaviors (Olsson & Dahlborn, 2002; Baumans, 2005). Some studies showed mild enrichment, which adversely affects not only the welfare but also the uniformity of scientific outcomes (Swaisgood & Shepherdson, 2005).

End Stressful Handling Protocols: In mice, tail holding is a stressful procedure that influences research outcomes and animal welfare. Tunnel handling or hand cupping are non-aversive practices and thus should be the norm, because they have been shown to minimize stress and increase behavioral reactivity considerably (Hurst & West, 2010; Gouveia & Hurst, 2017).

Strengthen Pain Management Practices: The use of analgesics is not uniform in research facilities, and some processes are still conducted without proper pain management (Herrmann & Flecknell, 2018). The analgesic protocol must be optimized and be species-specific and procedure-specific indicators (Carbone, 2021; Flecknell, 2008).

Adopt Comprehensive Welfare Assessment Models: The systematic evaluation procedure should apply the Five Domain Model of welfare assessment that considers nutrition, environment, health, behavior, and mental state (Mellor & Beausoleil, 2015). This solution enables active and comprehensive welfare oversight required by regulations.

Boost Investment in Animal-Free Technologies: Additional investment in replacements that are biologically relevant, such as organoids, microfluidic devices, and computer modelling, should be increased to replace the use of animals (Marx et al., 2016; Ingber, 2022).

Promote Transparency in Animal Welfare Practices: Research institutions should openly share data on animal welfare, licensing, and inspections. Public access to such information fosters accountability and encourages better practices across the sector (Pound & Nicol, 2018).

Conclusion

Although mice are still core to the innovations in the biomedical sciences, their extensive use poses serious ethical issues. Being sentient beings who suffer pain, distress,

and have emotional depth, mice are morally worthy individuals whose interests go beyond the utilitarian value in research. Unluckily, the current laboratory environment often does not pay attention to their behavioral and psychological needs, which could be the reason to raise not only welfare issues but also the scientific validity of derived data.

It is important to bring together ethical theory and empirical welfare science to deal with such concerns. Utilitarianism, Animal Rights Theory, and the Capabilities Approach frameworks would make significant contributions to the analysis of whether using mice in research is morally permissible. Moreover, stricter enforcement of legal frameworks, including the Animals (Scientific Procedures) Act 1986, explains that ethical considerations are practically applied rather than theoretically.

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