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Impulse for animal welfare outside the experiment

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Abstract

Animal welfare is a growing societal concern and the well-being of animals used for experimental purposes is under particular scrutiny. The vast majority of laboratory animals are mice living in small cages that do not offer very much variety. Moreover, the experimental procedure often takes very little time compared to the time these animals have been bred to the desired age or are being held available for animal experimentation. However, for the assessment of animal welfare, the time spent waiting for an experiment or the time spent after finishing an experiment has also to be taken into account. In addition to experimental animals, many additional animals (e.g. for breeding and maintenance of genetic lines, surplus animals) are related to animal experimentation and usually face similar living conditions. Therefore, in terms of improving the overall welfare of laboratory animals, there is not only a need for refinement of experimental conditions but especially for improving living conditions outside the experiment. The improvement of animal welfare thus depends to a large extent on the housing and maintenance conditions of all animals related to experimentation. Given the current state of animal welfare research there is indeed a great potential for improving the overall welfare of laboratory animals.

Keywords

3Rs, animal use, environmental enrichment, housing, laboratory animal welfare

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Introduction

There is no reliable, let alone official, number of laboratory animals used worldwide. Even for highly regulated areas like the EU, comprehensive data is published with a considerable delay. Moreover, the data available comprises a fuzziness as there is no uniform convention on what exactly to count. The latest numbers available for the EU are for the year 2017, with 9.4 million animals used for animal experimentation.[1] Many countries provide yearly statistics on animal use, allowing some general conclusions to be drawn and enabling more current estimates. For example, the numbers for 2018 published by the German Federal Ministry of Food and Agriculture,[2] as well as the numbers of procedures in the UK in 2018,[3] can help to conclude some general directions. Overall, the latest numbers published were comparable to preceding years, and again, the most widely used species was the mouse with roughly 1.54 million individuals in Germany and 2.57 million procedures carried out with mice in the UK. For the year 2017, for the first time, not only the number of experimental animals but also the number of animals used for breeding and maintenance as well as the number of

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animals bred but not used was assessed throughout the EU. Overall almost 14 million additional animals were counted in 28 EU countries indicating that for every two experimental animals additionally three surplus animals have to be counted.[1] Assuming that the majority of the additional animals are mice as well, we will focus on mice for the most part of this impulse paper, but the discussion that is being fostered here will of course also apply to other experimental animal species.

Additional animals are held available for breeding and maintenance of certain genetic lines, are killed for organ or tissue samples, or are considered surplus animals, which will not be used for experimental purposes due to wrong sex, age, or genotype (Table 1). In principle, the same legislative rules for housing and maintenance apply for the additional animals as for the experimental animals. Animal experimentation is conducted for a wide range of different scientific purposes,[4] and in many studies animals spend the longest time of their lives not in the respective experiment itself. This is especially true for laboratory mice which are often considered as ''disposable goods'' in science,[5] and new experiments are usually carried out with new animals being bred in sufficient numbers in local facilities as well as by commercial breeders. While waiting for the experiment or after finishing a non-lethal experiment, laboratory mice are usually living in customary standardized laboratory housing conditions. In most countries these housing conditions fall under a variety of restrictions with regard to meeting the minimum requirements (e.g. for mice in the EU the minimum cage floor size is 330 cm^2, bedding, nesting material, and social company shall be provided; see EU guidelines 2010/63/EU). Above the minimum requirements, according to the 3Rs – which are anchored in many statutory provisions – refinement of living conditions shall be taken into consideration. Therefore, maximizing potential welfare by improving living conditions of experimental animals is not limited by legislations, but rather by experimental and economic reasons.

What is animal welfare?

Animal welfare much alike human welfare is a term that is notably hard to access and disentangle and there is no unambiguous consensus.[6–10] An early approach in defining animal welfare was raised by a press release of the Farm Animal Welfare Council in 1979, tracing back to the ''Brambell Committee 1965,''[11] and is referred to as the five freedoms (i.e. freedom from 1. hunger and thirst, 2. discomfort, 3. pain, injury, and disease, 4. fear and distress, and 5. restrictions to express normal behavior). The five freedoms, however, state what has to be avoided in order to prevent poor animal welfare rather than defining what constitutes animal welfare *per se*. Consequently, the later literature emphasizes subjectivity for animal welfare and incorporates the view of animals as perceived animal welfare.[12,13] The five freedoms lately have been advanced to the ''five provisions'' focusing on what should be provided to achieve good welfare.[10] It was also recognized that animal welfare is not static and thus concepts include adaptive capabilities in terms of coping with environmental challenges and/or being able to achieve certain goals.[9,14–16] Today's view on animal welfare also largely includes a quality of living approach,[17,18] focusing on good living rather than mere avoidance of unfavorable conditions. Quality of living inherently reflects a much more holistic view over an animal's life and is thus less affected by short timed events (e.g. pleasurable moments, few minutes of fear).[17] Our definition of animal welfare is based on the current literature and deliberately reflects the difficulties that come along with defining as well as with assessing animal welfare.

Animal welfare describes (objectively verifiable) the status of a subjectively perceived quality of life of an individual at a given period and is measured on an ordinal (nonlinear), multidimensional scale.

The core unit of animal welfare is the subjective perception of an individual. This makes welfare especially hard to measure, as individual perception seems to notoriously elude scientific quantification. However, recent advances in theoretical concepts and methodology increasingly allow to quantify for example affective states.[16,19–21] The multidimensionality results from the different levels on which animal welfare can be affected: An individual might suffer from an injury (an obvious indicator for bad welfare) but might be engaged in positive social interaction (indicator for positive welfare) at the same time. Naturally, this complicates the assessment of animal welfare as calculation of potential compensatory and/or additive effects between different dimensions is inherently difficult. Moreover, the difference between categories such as poor and very poor welfare is not necessarily the same as the difference between good and moderate welfare, thus the scale has to be considered ordinal. In the same vein, nonlinearity owes to the fact that physical and physiological parameters as well as descriptors of affective states do not follow simple mathematical additive rules in relation to their impact on animal welfare. Although physiological parameters like heart rate or stress hormonal levels are measured on an interval scale they are not linearly related to animal welfare.[15,22]

Although the status of animal welfare is usually assessed at a given point in time, the measurement reflects a period of unknown length preceding the assessment. In addition, preceding lifetime events

Table 1. Subjects categorized with regard to their relation to animal experimentation (rows) and different measures and constraints related to animal welfare (columns) that might be applicable.

Category	Description	Minimum food, water, bedding, hygiene status, health monitoring, etc.	Nesting nesting material, shelter, a place to sleep comfortable	Social providing "positive" social contact in social species	Enrichment e.g. climbing frames, toys, objects to manipulate	Space providing additional space	Treats providing special treats (e.g. fruits, seeds, sweets, juice, almond milk)	Maximum maximizing welfare without limitations related to an experiment	Constraints constraints related to planned experiment
Breeding stock	Breeding pairs, pregnant females, males used for breeding that are being separated from their breeding partner	yes	yes	yes	yes	yes	yes (restrictions might apply)	no	yes (e.g. separation, weaning age, attempts to standardize parental influences)
Breeding reserve	Animals held available as breeding reserve but not currently being paired	yes	yes	yes	yes	yes	yes	yes	no
Biological surplus	Animals of wrong sex or genotype for the experimental purpose	yes	yes	yes	yes	yes	yes	yes	no
Managed surplus	Animals of wrong age (too old) or weight for the experimental purpose	yes	yes	yes	yes	yes	yes	yes	no
Sentinel	Sentinel animals for health monitoring	yes	yes	yes	yes	yes	yes/no (same conditions as animals being monitored)	yes/no (restricted by the purpose and mode of use of the sentinels)	yes (e.g. co-housing for direct contact sentinels, exposure to dirty bedding, or air exhaust in IVCs, social restrictions)
Accompanying animals	E.g. castrated males or ovariectomized females used as social interaction partners	yes	yes (if not conflicting with experimental procedure)	yes	yes (if not conflicting with experimental procedures)	yes (if not conflicting with experimental procedures)	yes (if not conflicting with experimental procedures)	no	yes (same housing conditions as experimental animals)
Waiting	(Young) experimental animals waiting for reaching the desired age of experimentation	yes	yes	yes (if not conflicting with experimental procedures)	yes	yes	yes (if not conflicting with experimental procedures)	no	yes
Experimental animals	Experimental animals currently in an ongoing experiment	yes (certain restrictions might apply)	yes (if not conflicting with experimental procedures)	yes (certain restrictions might apply)	yes (certain restrictions might apply)	yes (certain restrictions might apply)	no	no	yes
Post-experimental animals	Animals not being killed after finishing the experiment; no subsequent experiments planned	yes	yes	yes (should be monitored if switching from single to social housing)	yes	yes	yes	yes	no

affect a current state of animal welfare differentially depending on frequency of occurrence, length, and intensity, for example.

Assessing animal welfare

It is obvious from the above that measuring animal welfare is not an easy endeavor. It is, however, feasible to measure animal welfare on an ordinal scale and to annotate labels ranging from very poor to very good welfare with reasonable precision. Poor welfare can be measured by evaluating to what extent the first four freedoms are met. In a broad sense, being free from pain, discomfort, hunger and thirst, fear, and disease can be considered a minimum standard that should be expected to be the normal state a laboratory animal is in. Although not always overly trivial, these parameters are generally considered to be measurable reasonably well.[10,14,23] Above obvious signs for poor welfare like sickness behavior, wounds, signs of starvation or dehydration, physiological parameters (e.g. stress hormones, heart rate) may be indicative for how well an animal is able to cope with the challenges introduced by the environment provided under laboratory conditions. The fifth freedom to be free to show normal behavior is far more difficult to assess. A wide spectrum of species specific behavior is related to coping with challenging situations in the wild that one can reasonably assume not to be applicable for laboratory animals (e.g. extensive foraging, predator avoidance, exaggerate aggressive encounters). Therefore, it is not unequivocally established what constitutes "normal behavior" in a laboratory animal. Nevertheless, monitoring day-to-day behavior of laboratory animals and comparing time budgets allocated to different behavioral domains is a feasible approach to analyze normal behavior in laboratory animals. In a similar vein, disturbed circadian rhythm or other behavioral deviations such as stereotypic behavior or hair pulling are considered to be associated with impaired animal welfare.[24–27] Finally, post mortem analysis (e.g. ulcers, adrenal weights) can also help to retrospectively assess poor animal welfare.[28]

Measuring good animal welfare on the other hand, is generally considered to be more complicated although not impossible.[29] Play behavior and affiliative behaviors, as well as some vocalizations,[30] appear to be promising measurable indicators for assessing positive animal welfare.[31] In addition, recently newly developed approaches in human animal interaction were also related to positive emotions, e.g. clicker-training and tunnel handling might indeed be perceived as positive interactions by the animals.[32,33] Finally, with regard to the quality of living, which would reflect a more holistic view of animal welfare, an ideal assessment should take into account that welfare throughout an animal's life (within and outside the experiment) has to be considered as well.

Specific conditions in animal experiments

For many years, it has been fostered to try keeping external physical, social, and internal physiological states as constant as possible. This was meant not only in order to standardize experimental conditions but also to guarantee the fulfillment of animal needs. Unfortunately, this approach falls short in regard to animal welfare as biological systems have evolved to cope with transience of external stimuli and therefore allostasis ("stability through change") rather than homeostasis is a key element of animal welfare.[15,34] This has been partially addressed by improving housing conditions especially by introducing environmental enrichment over the last decades. On the other hand, experimental set ups naturally require a standardization strategy (including, e.g., systematic variation to increase external validity[35]) to minimize animal use and maximize test sensitivity. Still, boredom as a natural consequence of under stimulation should be considered a major concern with regard to animal welfare of laboratory animals.[36] Sensation seeking is reflecting such a need for change and has been measured for example as proneness to sensory stimuli in mice,[37] self-administration of glucocorticoids in rats,[38] or seeking even aversive stimuli in mink.[39] Consequently, balancing standardization against boredom along with the animals' "need for change" will remain a challenge in future experimental designs. It would be fallacious to expect that any individual animal (or human) could be in a superior welfare state at all times. Thus fluctuation in welfare states is an inherent part of an animal's life and also contributes to a life worth living.[14] Overall, transience between welfare states within the range of very good, good, neutral, and even lightly aversive is most likely part of an interesting life worth living. This, however, is not at all easy to be realized for laboratory animals. Even if we assume that there were no restrictions with regard to financial shortage, qualified personnel, and available space, at least some categories of laboratory animals will be less eligible for the full range of possible welfare enhancement (see Table 1).

Enhancing animal welfare

Although assessing animal welfare is coming along with a number of problems with regard to accuracy, specificity, and generalizability, there is also a pragmatic approach when the goal is to increase animal welfare of laboratory animals. A positive welfare state can be derived by being able to engage in activities that are perceived as rewarding. Such behaviors are expected to

be capable to elicit positive affects which are related to anticipation of achieving goals, achieving the goal itself, and retrospectively eliciting the memory of having previously achieved a goal.[10] Consequently, any measures that enable laboratory animals to engage in rewarding activities, as well as states associated with anticipation or memory of rewarding activities are likely to enhance animal welfare. A classical reward is the provision of treats, which is very common, e.g. in companion animals. In laboratory animals, however, treats are often restricted to experiments of operant and classical conditioning where special food items are provided as a reward to increase their performance. If paying attention to nutritional needs, there should be no principle objections against providing special treats to other laboratory animals as well. However, one should bear in mind that if anticipated rewards are suspended the mismatch between expected reward and the reality check possibly leads to frustration.[40] Therefore, withholding treats or other positive stimuli that previously have been granted can also negatively affect animal welfare.

Positive affective states are also elicited in positive social interactions. Social interactions concern the entire life of social mammals and incisive experiences in early life also affect later social behavior. For example, it has been shown that delayed weaning increased social behavior later in life.[41] However, the weaning age is usually designed to maximize breeding success and does not necessarily correspond to the natural breeding behavior of the species. Social housing for laboratory animals later in life is generally recommended except for solitary species. However, group housing for animals that frequently engage in aggressive encounters, e.g. as observed in male groups of many mouse strains,[42,43] is sometimes not feasible. This is something that has to be taken into account when planning experiments and choosing the right model species, strain, or sex. As already outlined above, boredom due to a lack of stimuli and missing opportunities to engage in rewarding activities in laboratory housing systems is a growing concern.[36] This can be partially ameliorated by means of environmental enrichment and providing materials to perform species typical behavior (e.g. for rodents, nesting material, burrowing and gnawing substrate). For laboratory mice nesting material and shelters were slowly introduced over the last three decades and can nowadays be found in almost all European animal facilities as this is required by the EU directive 2010/63/EU. Still there is much room for improvement with regard to entertaining enrichment and providing opportunities to engage in rewarding behaviors. This can be realized by providing novel stimuli (e.g. new enrichment items that can be explored[44]), by introducing cognitive training (e.g. puzzle boxes, clicker training[32]) into the home environment, or by measures of occupational therapy (e.g. running wheels, or letting the animals work in order to get access to water or food). In addition, home environments could be improved by providing better opportunities for play behavior. Although play behavior is most prominent in juveniles and adolescents, adults of many species, including mice and rats,[45–47] do also play. Play behavior is usually considered to be an indicator for positive animal welfare,[48] but sometimes even elicited when coping with negative affective states.[49] Nevertheless, the absence of play behavior in an otherwise playful species certainly is an example for a deviation from "normal" behavior and thus should generally considered to be an indicator for disturbed animal welfare. Adult mice engage frequently in locomotor play if provided with enough space.[45,46] Indeed, more than 85% of play behavior in mice involves locomotor play.[50] Therefore providing more space (e.g. larger cages, connecting several small cages with tubes) or other opportunities to engage in locomotory activity should be taken into account to improve housing conditions for laboratory mice. Noteworthy, there is an ongoing debate with regard to the costs and benefits of changing "established" housing conditions with regard to size, type of nesting and bedding material, or different forms of enrichment. For example, excessive usage of running wheels might resemble stereotypic behavior in some individuals,[51,52] but in group housed mice no signs of stereotypic running wheel behavior were found.[53] Moreover, several behavioral as well as morphological, and physiological parameters can be affected by introducing environmental enrichment.[54] Also it is known that housing conditions can have interaction effects with pharmacological treatments.[55] However, concerns that enrichment generally increase variation in experimental results could not be substantiated.[56] Overall, possible interferences of improved as well as of restricted housing conditions with the experimental design, reproducibility, and external validity should be kept in mind. Enrichment is generally thought to enhance animal welfare although sex differences might apply (i.e. aggressive behavior[42]), and it is not always clear how different items are perceived by the animals themselves and thus animal centric strategies like preference tests will help to assess and rate different items.[57]

Improving animal welfare in- and outside the experiment

Generally speaking, we should aim to maximize animal welfare of laboratory animals owing to the fact that we are responsible for their well-being. As animal experimentation is under special scrutiny there is a high ethical standard ruling animal experimentation and it has become mandatory to consider refinement measures in the experimental design. Moreover, it is widely accepted that above the ethical concerns there is also

a scientific need for improving the welfare of laboratory animals.[58] However, restrictions affecting the welfare of experimental animals cannot always be overcome if they are directly related to the experimental aims. In our view, relating to historical data or established housing conditions alone does not suffice to refuse enhancing the living conditions. One of the main lessons to be learnt from the reproducibility crisis should be that only data that can be replicated in other contexts are truly biologically meaningful.[35] Experimental animals spend much of their lives outside the experiment and a large number of animals are not even used for experiments but held available for breeding or other maintenance related purposes. Table 1 summarizes the potential of enhancing animal welfare for different categories of laboratory animals. For each category of animals one should ask what can reasonably be done to maximize their welfare. Experimental animals and animals waiting for an experiment are probably more restricted with regard to maximizing their welfare as many measures potentially counteract the experimental purpose. Nevertheless, quality and size of measures to increase welfare depend on the experimental design and should be evaluated accordingly. On the other hand, for post-experimental animals there is basically no limit on what could be done to increase their welfare, even if it might only be for a short time compared to the life expectancy.[5] All in all, the time outside the experiment can be considered a special opportunity to improve the overall welfare of laboratory animals.

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References

1. European Commission. 2019 report on the statistics on the use of animals for scientific purposes in the Member States of the European Union in 2015-2017, https://ec.europa.eu/transparency/regdoc/rep/1/2020/EN/COM-2020-16-F1-EN-MAIN-PART-1.PDF (2020, accessed 6 February 2020).
2. BMEL. BMEL - Übersicht: BMEL informiert über Tierschutz - Verwendung von Versuchstieren im Jahr 2018, https://www.bmel.de/DE/Tier/Tierschutz/_texte/Versuchstierzahlen2018.html (2019, accessed 2 January 2020).
3. Fire, Licensing and Public Order Analysis Unit of the HOU. Annual statistics of scientific procedures on living animals in Great Britain 2018, https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/835935/annual-statistics-scientific-procedures-living-animals-2018.pdf (2019, accessed 27 November, 2019).
4. Bert B, Dörendahl A, Leich N, et al. Rethinking 3R strategies: digging deeper into AnimalTestInfo promotes transparency in in vivo biomedical research. *PLoS Biol* 2017; 15: e2003217.
5. Brust V, Schindler PM and Lewejohann L. Lifetime development of behavioural phenotype in the house mouse (*Mus musculus*). *Front Zool* 2015; 12: S17.
6. Fraser D. Science, values and animal welfare: exploring the 'inextricable connection'. *Anim Welf* 1995; 4: 103–117.
7. Stafleu F, Grommers F and Vorstenbosch J. Animal welfare: evolution and erosion of a moral concept. *Anim Welf* 1996; 5: 225–234.
8. Fisher MW. Defining animal welfare: does consistency matter? *NZ Vet J* 2009; 57: 71–73.
9. Ohl F and van der Staay FJ. Animal welfare: at the interface between science and society. *Vet J* 2012; 192: 13–19.
10. Mellor DJ. Updating animal welfare thinking: moving beyond the "five freedoms" towards "a life worth living". *Animals* 2016; 6: 21.
11. Brambell F. Report of the technical committee to enquire into the welfare of animals kept under intensive livestock husbandry systems, https://www.worldcat.org/title/report-of-the-technical-committee-to-enquire-into-the-welfare-of-animals-kept-under-intensive-livestock-husbandry-systems/oclc/475844139 (1965, accessed 1 March 2019).
12. Dawkins MS. From an animal's point of view: motivation, fitness, and animal welfare. *Behav Brain Sci* 1990; 13: 1–9.
13. Bracke MBM and Hopster H. Assessing the importance of natural behavior for animal welfare. *J Agric Environ Ethics* 2006; 19: 77–89.
14. Broom DM. Indicators of poor welfare. *Br Vet J* 1986; 142: 524–526.
15. Korte SM, Olivier B and Koolhaas JM. A new animal welfare concept based on allostasis. *Physiol Behav* 2007; 92: 422–428.
16. Gygax L. Wanting, liking and welfare: the role of affective states in proximate control of behaviour in vertebrates. *Ethology* 2017; 123: 689–704.
17. Broom DM. Quality of life means welfare: how is it related to other concepts and assessed? *Anim Welf* 2007; 16: 45–53.
18. Green TC and Mellor DJ. Extending ideas about animal welfare assessment to include 'quality of life' and related concepts. *NZ Vet J* 2011; 59: 263–271.

19. Paul ES, Harding EJ and Mendl M. Measuring emotional processes in animals: the utility of a cognitive approach. *Neurosci Biobehav Rev* 2005; 29: 469–491.
20. Bethell EJ, Holmes A, MacLarnon A, et al. Cognitive bias in a non-human primate: Husbandry procedures influence cognitive indicators of psychological well-being in captive rhesus macaques. *Anim Welf* 2012; 21: 185–195.
21. Kloke V, Schreiber RS, Bodden C, et al. Hope for the best or prepare for the worst? Towards a spatial cognitive bias test for mice. *PLoS One* 2014; 9: e105431.
22. Hau M and Goymann W. Endocrine mechanisms, behavioral phenotypes and plasticity: known relationships and open questions. *Front Zool* 2015; 12: S7.
23. Broom DM. Assessing welfare and suffering. *Behav Processes* 1991; 25: 117–123.
24. Späni D, Arras M, König B, et al. Higher heart rate of laboratory mice housed individually vs in pairs. *Lab Anim* 2003; 37: 54–62.
25. Reinhardt V. Hair pulling: a review. *Lab Anim* 2005; 39: 361–369.
26. Mason G and Latham N. Can't stop, won't stop: is stereotypy a reliable animal welfare indicator? *Anim Welf* 2004; 13: 57–69.
27. Würbel H, Stauffacher M and Holst D. Stereotypies in laboratory mice: quantitative and qualitative description of the ontogeny of 'wire-gnawing' and 'jumping' in Zur:ICR and Zur:ICR nu. *Ethology* 1996; 102: 371–385.
28. David JM, Knowles S, Lamkin DM, et al. Individually ventilated cages impose cold stress on laboratory mice: a source of systemic experimental variability. *J Am Assoc Lab Anim Sci* 2013; 52: 738–744.
29. Scott E, Nolan A, Reid J, et al. Can we really measure animal quality of life? Methodologies for measuring quality of life in people and other animals. *Anim Welf* 2007; 16(Suppl): 17–24.
30. Panksepp J and Burgdorf J. 'Laughing' rats and the evolutionary antecedents of human joy? *Physiol Behav* 2003; 79: 533–547.
31. Boissy A, Manteuffel G, Jensen MB, et al. Assessment of positive emotions in animals to improve their welfare. *Physiol Behav* 2007; 92: 375–397.
32. Leidinger C, Herrmann F, Thöne-Reineke C, et al. Introducing clicker training as a cognitive enrichment for laboratory mice. *J Vis Exp* 2017; 121: e55415.
33. Clarkson JM, Dwyer DM, Flecknell PA, et al. Handling method alters the hedonic value of reward in laboratory mice. *Sci Rep* 2018; 8: 2448.
34. McEwen BS and Wingfield JC. The concept of allostasis in biology and biomedicine. *Horm Behav* 2003; 43: 2–15.
35. Richter SH, Garner JP, Zipser B, et al. Effect of population heterogenization on the reproducibility of mouse behavior: a multi-laboratory study. *PLoS One* 2011; 6: e16461.
36. Burn CC. Bestial boredom: a biological perspective on animal boredom and suggestions for its scientific investigation. *Anim Behav* 2017; 130: 141–151.
37. Olsen CM and Winder DG. Operant sensation seeking engages similar neural substrates to operant drug seeking in C57 mice. *Neuropsychopharmacology* 2009; 34: 1685.
38. Piazza PV, Deroche V, Deminière JM, et al. Corticosterone in the range of stress-induced levels possesses reinforcing properties: implications for sensation-seeking behaviors. *Proc Natl Acad Sci* 1993; 90: 11738–11742.
39. Meagher RK and Mason GJ. Environmental enrichment reduces signs of boredom in caged mink. *PLoS One* 2012; 7: e49180.
40. Burokas A, Gutiérrez-Cuesta J, Martín-García E, et al. Operant model of frustrated expected reward in mice. *Addict Biol* 2012; 17: 770–782.
41. Curley JP, Jordan ER, Swaney WT, et al. The meaning of weaning: influence of the weaning period on behavioral development in mice. *Dev Neurosci* 2009; 31: 318–331.
42. Kappel S, Hawkins P and Mendl M. To group or not to group? good practice for housing male laboratory mice. *Animals* 2017; 7: 88.
43. Weber EM, Dallaire JA, Gaskill BN, et al. Aggression in group-housed laboratory mice: why can't we solve the problem? *Lab Anim* 2017; 46: 157–161.
44. Herring A, Lewejohann L, Panzer AL, et al. Preventive and therapeutic types of environmental enrichment counteract beta amyloid pathology by different molecular mechanisms. *Neurobiol Dis* 2011; 42: 530–538.
45. Marashi V, Barnekow A, Ossendorf E, et al. Effects of different forms of environmental enrichment on behavioral, endocrinological, and immunological parameters in male mice. *Horm Behav* 2003; 43: 281–292.
46. Freund J, Brandmaier AM, Lewejohann L, et al. Association between exploratory activity and social individuality in genetically identical mice living in the same enriched environment. *Neuroscience* 2015; 309: 140–152.
47. Reinhold AS, Sanguinetti-Scheck JI, Hartmann K, et al. Behavioral and neural correlates of hide-and-seek in rats. *Science* 2019; 365: 1180–1183.
48. Held SDE and Špinka M. Animal play and animal welfare. *Anim Behav* 2011; 81: 891–899.
49. Ahloy-Dallaire J, Espinosa J and Mason G. Play and optimal welfare: does play indicate the presence of positive affective states? *Behav Processes* 2018; 156: 3–15.
50. Pellis SM and Pasztor TJ. The developmental onset of a rudimentary form of play fighting in C57 mice. *Dev Psychobiol* 1999; 34: 175–182.
51. Sherwin CM. Voluntary wheel running: a review and novel interpretation. *Anim Behav* 1998; 56: 11–27.
52. Richter SH, Gass P and Fuss J. Resting is rusting: a critical view on rodent wheel-running behavior. *Neuroscience* 2014; 20: 313–325.
53. Weegh N, Füner J, Jahnke O, et al. Wheel running behaviour in group-housed female mice indicates disturbed wellbeing due to DSS colitis. *Lab Anim*. Epub ahead of

print 1 November 2019. DOI: 10.1177/0023677219879455).
54. Bayne K. Environmental enrichment and mouse models: current perspectives. *Anim Model Exp Med* 2018; 1: 82–90.
55. Hoffmann LC, Schütte SRM, Koch M, et al. Effect of ''enriched environment'' during development on adult rat behavior and response to the dopamine receptor agonist apomorphine. *Neuroscience* 2009; 158: 1589–1598.
56. Bailoo JD, Murphy E, Boada-Saña M, et al. Effects of cage enrichment on behavior, welfare and outcome variability in female mice. *Front Behav Neurosci* 2018; 12: 232.
57. Habedank A, Kahnau P, Diederich K, et al. Severity assessment from an animal's point of view. *Berl Munch Tierarztl Wochenschr* 2018; 18007.
58. Poole T. Happy animals make good science. *Lab Anim* 1997; 31: 116–124.

Résumé

Le bien-être des animaux est une préoccupation sociétale croissante et le bien-être des animaux utilisés à des fins expérimentales fait l'objet d'une attention particulière. La grande majorité des animaux de laboratoire sont des souris qui vivent dans de petites cages n'offrant pas beaucoup de variété. En outre, la procédure expérimentale prend souvent très peu de temps par rapport à la période d'élevage de ces animaux jusqu'à l'âge désiré ou leur mise à disposition pour l'expérimentation animale. Toutefois, pour l'évaluation du bien-être animal, le temps passé en attente d'une expérience ou le temps passé après avoir terminé une expérience doit également être pris en compte. En plus des animaux de laboratoire, de nombreux animaux (par exemple, pour l'élevage et l'entretien des lignes génétiques, les animaux excédentaires) sont liés à l'expérimentation animale et font généralement face à des conditions de vie similaires. Par conséquent, en termes d'amélioration du bien-être général des animaux de laboratoire, il n'existe pas seulement un besoin d'amélioration des conditions expérimentales, mais surtout d'amélioration des conditions de vie en dehors de l'expérience. L'amélioration du bien-être des animaux dépend donc dans une large mesure des conditions de logement et d'entretien de tous les animaux liés à l'expérimentation animale. Étant donné l'état actuel de la recherche sur le bien-être des animaux, il existe en effet un grand potentiel d'amélioration du bien-être général des animaux de laboratoire.

Abstract

Der Tierschutz ist ein zunehmend wichtiges gesellschaftliches Anliegen, und das Wohlergehen von für Versuchszwecke dienenden Tieren muss besonders strenger Überprüfung unterzogen werden. Die überwiegende Mehrheit von Versuchstieren sind Mäuse, die in kleinen Käfigen ohne viel Abwechslung leben. Hinzu kommt, dass die Dauer der Züchtung der Tiere bis zum erforderlichen Alter bzw. der Haltung in Vorbereitung auf Versuche oft lang ist, während die Versuche selbst nur sehr wenig Zeit in Anspruch nehmen. Bei der Bewertung des Tierschutzes ist jedoch auch die den eigentlichen Versuchen vorausgehende Zeit ebenso wie jene nach Abschluss eines Experiments zu berücksichtigen. Neben den Versuchstieren selbst sind viele weitere Tiere (z. B. solche zur Züchtung und Erhaltung von genetischen Linien, überzählige Tiere) mit Tierversuchen verbunden, die in der Regel unter ähnlichen Lebensbedingungen gehalten werden. Im Hinblick auf die Verbesserung des allgemeinen Wohlergehens von Versuchstieren besteht daher nicht nur die Notwendigkeit einer Verbesserung der Versuchsbedingungen, sondern insbesondere auch der Lebensbedingungen außerhalb der Versuche. Die Verbesserung des Tierschutzes hängt daher in hohem Maße von den Haltungs- und Unterbringungsbedingungen aller im Zusammenhang mit Versuchen stehenden Tieren ab. Nach dem derzeitigen Stand der Tierschutzforschung gibt es in der Tat großes Potenzial, das zur Verbesserung des allgemeinen Wohlergehens von Versuchstieren ausgeschöpft werden sollte.

Resumen

El bienestar animal es una creciente preocupación social y el bienestar de los animales utilizados para experimentos está siendo analizado detenidamente. La gran mayoría de animales de laboratorio son roedores que viven en jaulas pequeñas que no ofrecen gran variedad. Asimismo, el procedimiento experimental a menudo es de poca duración en comparación con el tiempo en que estos animales han sido criados hasta alcanzar la edad deseada o están disponibles para experimentar con ellos. Sin embargo, para la evaluación del bienestar animal, el tiempo de espera para un experimento o el tiempo transcurrido tras finalizar un

experimento son factores que también tienen que considerarse. Además de los animales para experimentos, muchos otros animales (p. ej., para criar y mantener líneas genéticas o para tener un excedente de ejemplares) están relacionados con la experimentación animal y a menudo viven en condiciones similares. Por tanto, en lo referente a la mejora del bienestar general de los animales de laboratorio, no solo hay una necesidad de refinar las condiciones experimentales sino especialmente de mejorar las condiciones de vida más allá del experimento. La mejora del bienestar animal, por tanto, depende en gran medida de las condiciones de mantenimiento y de las jaulas de los animales de experimentación. Dado el estado actual de la investigación sobre el bienestar animal, existe gran potencial para mejorar el bienestar general de los animales de laboratorio.