



Vigilant little creatures:
The law stipulates compliance
with the so-called '3Rs'.

Mouse welfare principle

Over 60 years ago, two British researchers drew up basic principles for working with laboratory animals. Their thinking has now become a key concept of research in the form of the '3Rs principles'.

Mice can be mice here – would be a fitting inscription on the room-sized enclosure. In the semi-darkness, the rodents scurry through the area, squeeze curiously through narrow corridors and sniff each other with interest. The small mammals' spacious 'adventure playground' is located at the German Centre for the Protection of Laboratory Animals at the German Federal Institute for Risk Assessment (BfR) in Berlin-Marienfelde. Professor Dr. Lars Lewejohann and his team are researching how mice behave in different environments. A major aim of the work is to improve living conditions before, during and after experiments involving animals. The technical terms for this is 'Refinement'.

Together with the basic approaches of 'Replacement' and 'Reduction', 'Refinement' forms the basis of the ethically responsible treatment of laboratory animals. These '3R principles' were first formulated by the zoologist William Russell and the microbiologist Rex Burch in their 1959 paper 'The Principles of Humane Experimental Technique'.

It was the start of a quiet revolution in research using animals. Over 60 years later, it is bearing fruits: '3Rs' has gained worldwide recognition and must be considered in scientific projects. German law also requires these guiding principles to be taken into account in animal experiments. For example, if there is an animal-free method for the same research approach, this is to be adopted by preference.

Animal husbandry: room for improvement

"For the public, the main focus is on reducing animal experiments or replacing them," says BfR scientist Lewejohann. "But despite considerable progress, we will not be able to banish them just yet, for example in the development of medicines and vaccines." Instead of an either-or, the biologist focuses on a pragmatic, step-by-step approach to improving the welfare of laboratory animals. "There is potential for further developments, for example in the housing conditions of the animals."

Lewejohann demonstrates this on the subject of keeping mice (they make up two-thirds of the laboratory animals in Germany). They enjoy the greatest possible freedom in their spacious enclosure and enjoy better conditions than in the wild because they have a constant supply of food. "The animals have ideal conditions here, they are not bored and even the older mice play", explains Lewejohann. "Of course, research facilities can't adopt something like this on a one-to-one for space reasons alone, but there are good compromise solutions."

The cages come to life at night

One possibility is to connect several cages with tubes to give the animals greater opportunity to move around. "During the day, mice sleep," says the scientist. "That gives the wrong impression that they are inactive – but they come to life at night and are quite vigilant."



Professor Lars Lewejohann looks after the welfare of the animals in the laboratory and makes sure that they don't get bored in their cages.

To accommodate their urge to move, Lewejohann's team has installed running discs in the cages. The animals can exercise on them without having to bend their backs – as they would on a running wheel. Using smart trial and error, they can open 'puzzle boxes' and grab a small reward such as oat flakes or millet seeds. "Already with this form of 'enriched' husbandry, apathy and stereotypical behaviour in the mice declines considerably," Lewejohann has observed.

Prospects are also opening up for replacing animal experiments. These include organoids, the subject of intriguing discussions right now. These are three-dimensional microscopic 'miniature versions' of organs such as the liver, kidneys, brain or skin. In Berlin-Marienfelde, a BfR team is working on a bone organoid. "Advances in stem cell research have enabled this development," says Professor Dr. Gilbert Schönfelder, head of the German Centre for the Protection of Laboratory Animals at the BfR.

Fruit flies and roundworms

Another approach that has been tested is research on invertebrates such as the fruit fly *Drosophila melanogaster* or the roundworm *C. elegans*. "Basic principles of biology apply to humans as well as to these organisms – therefore they can be studied and understood very well on them," explains Schönfelder.

The fact that the 3R principles and good science sit happily side by side is evidenced in the principle of 'reduce'. Put the other way: poor research is at the expense of

the animals. Because the results are meaningless, for example, and animals were used unnecessarily.

Good animal welfare, good research

Scientific research should be meaningful and allow for statistically robust results, for example, but at the same time comply with the 3R principles. Many scientific journals now require compliance with these principles for publications submitted to them, and have also introduced common guidance known as the ARRIVE guidelines. "3R is part of the planning of an experiment from the very beginning," emphasises Schönfelder.

Another possibility is to enter the design of a study involving animals in the Animal Study Registry database at the Bf3R before it begins. "That is an important step in enabling scientific quality and transparency, and avoiding unnecessary animal experiments," explains Schönfelder.

But the most important thing is to remember that 3R is more than a bureaucratic body of rules. At its core is an idea. A guiding principle that was first introduced by William Russell and Rex Burch, and that continues to evolve today: in the minds of scientists who conduct research using animals. ■

More information:
www.bfr.bund.de/en > German Centre for the Protection of Laboratory Animals (Bf3R)