

At the German Centre for the Protection of Laboratory Animals at the BfR Professor Dr. Lars Lewejohann is investigating how the living conditions of laboratory animals can be improved. The scientist is also a professor at the Institute of Animal Welfare, Animal Behavior and Laboratory Animal Science at Freie Universität Berlin.



Understanding Mice

Professor Dr. Lars Lewejohann conducts research into the behaviour of laboratory animals at the BfR. His goal is better living conditions for the animals – and better science at the same time.

It's all go in the cage. A ball of fur the size of a chestnut crawls through a length of transparent plastic pipe to a higher-level platform, another one is drinking at the water trough. These are house mice, scientific name *Mus musculus*, with black fur, long tail, erect ears and cute little button eyes.

In the dim light, the mice scurry through the two by two metre cage with its high plateaus, tunnels, boxes and separated areas, all of which the animals find interesting. "The mice live here almost as they do in the wild," says behavioural biologist Lars Lewejohann about the large enclosure. "They can explore their surroundings without having to worry about predators and they are provided with food – a mouse's paradise."

This paradise isn't just for the mere sake of it, however, it's part of a research project by Professor Lewejohann and his team. The scientist works at the German Centre for the Protection of Laboratory Animals at the BfR. At the Institute's Marienfelde location, he examines how the living conditions of laboratory animals can be improved. Refinement is the term used for this.

Replacement, Reduction, Refinement

Refinement is one of the three pillars of the 3R principle along with the replacement and reduction of experiments with animals. With "3R" – replace, refine, reduce – microbiologist Rex Burch and zoologist William Russell drew attention to the situation of laboratory animals around 60 years ago. "We've already achieved a lot for the animals," is how Lewejohann

describes the current situation, "but we are still not where we could and should be".

The greatest possible gain in findings with the lowest possible level of animal suffering is the researcher's credo. "Better animal husbandry is not a contradiction to good research," says Lewejohann. For the biologist, one does not exclude the other, they complement each other. Good conditions for laboratory animals lead to natural behaviour and thereby to realistic scientific results.

Early death in the wild

The scientist does not succumb to illusions about the animals leading a pleasant life in freedom. "It would be naïve to assume that all wild animals are 'happy', because the stress of survival is extreme," explains Lewejohann. "Parasites, disease and predators are constant dangers and most mice die prematurely in the wild. There is a reason why they produce so many young!" As the keepers of the animals in captivity, however, humans have to accept responsibility.

What does the mouse want? This question has been driving Lewejohann ever since he embarked on his scientific career. He tries to understand the rodents and see things from their point of view. This can only be done by closely studying their behaviour and thereby their decisions and then subjecting these to scientific interpretation. Does the animal prefer coarse or fine nesting material, does it want to be "challenged", how is boredom expressed and how can it be prevented? And do mice have something resembling a personality?

If you can answer these questions, the animals' living conditions can be improved specifically.

The nature of the mouse

House mice are sociable; the nocturnal rodents snuggle up closely together in their nests and groom one another. The little mammals are still individuals, however, and Lars Lewejohann even attributes a kind of individual personality to the animals. This is all the more astonishing as the mice used in the experiments are practically identical from a genetic point of view. It would therefore seem obvious that the rodents would not only be as identical as two peas in a pod with regard to their genetic make-up but also with regard to their character. This does not appear to be the case, however.

Biologists and psychologists have discovered some amazing things in recent years about the animals' abilities, intelligence, memory and even their moral behaviour. The idea that mice could have an individual nature is no longer all that unusual (and already an established fact for fans of Tom and Jerry or Mickey Mouse).

Discoverers and laggards

The animals can be distinguished by their behaviour inside their large enclosure. The mice, which are tagged with transponders (small transmitters), are registered

via a system of antennae which provides information on where they are and which routes they have taken. There are mice which "get around a lot", as Lewejohann says. They patrol the terrain, presumably driven by a desire for adventure and the fun of playing as they slide almost recklessly down through plastic pipes. Others are more reserved; cautiously and apparently ready for whatever might happen, they cover a comparatively small area.

A further experiment deals with the animals' mentality. An acoustic signal at the water dispenser indicates reward, another punishment. Once the mice have learnt this, they are confronted with mixed tone sequences. This is an ambivalent signal which has to be interpreted by the animals. The rodents react in different ways. The "optimists" can't be held back and head for the dispenser, whereas the "pessimists" fear the worst and stay away from it. Both of these behaviours have their advantages and may have evolved as strategies for this reason. What the animals experience immediately before they hear the ambivalent signal can also contribute towards whether they tend to react optimistically or pessimistically, however. "In this way, we can 'ask' the mice how stressful they find certain experiments, for instance," says Lewejohann, whose research is also sponsored by the German Research Foundation (DFG).

Another project is dedicated to the research of boredom. Stereotypes – always the same behavioural patterns –, a disturbed day-night rhythm (house mice are normally





99
Some mice are driven by a desire for adventure and the fun of playing.

active at night) and “eating attacks” are interpreted as signs of dulling and disinterest. Lars Lewejohann and his team have come up with some ideas here to disperse the animals’ lethargy. Tricky “problem boxes”, for example, which can only be opened with skill in order to relinquish the reward they contain. Along with swings, exercise games and little houses with rotatable roofs. Some of these toys are self-built or originate from a 3D printer. Video games for mice are also being tested in the meanwhile, Lewejohann reports.

The pivotal question: What does the animal want?

The scientist’s motivation is almost tangible – to find out what the animal wants. His approach combines the topic “Improvement of animal tests” with psychology, brain research and medicine in its attempt to find out more about mental deterioration (dementia) and isolation, which mice can presumably suffer from too.

An example of the bandwidth of his scientific work is Lewejohann’s involvement in the Berlin research project “Science of Intelligence” in which he participates as a professor of Freie Universität Berlin. In this cluster of excellence sponsored since recently by the German Research Foundation, scientists from very different areas of specialisation have got together to dedicate themselves jointly to the subject of intelligence, be it animal, human – or artificial. Many disciplines are represented, from philosophy, psychology and biology to robotics and computer science. Understanding intelligence is in their view one of the great challenges of the present, and the overcoming of interdisciplinary boundaries an important step towards meeting them together.

It may appear paradox to conduct animal tests while taking a very critical view of them at the same time, but Lewejohann is enough of a realist to know that tests in the development of drugs, for example, will continue to be indispensable for quite some time. “Testing drugs directly on humans before trying them out on animals is not a road we can go down,” he says. “Our goal is to structure tests which cannot yet be replaced in such a way that they benefit the animals if this is at all possible. What also applies here is that the people who conduct animal tests must also review their own actions again and again – a great demand.” ■

More information:

Habedank et al. 2018. Severity assessment from an animal's point of view. *Berl Münch Tierärztl Wochenschr* doi 10.2376/0005-9366-18007