

Results of mouse studies deeply affected by the way the animals are handled

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A laboratory mouse is being encouraged into a handling tunnel. Credit: Jane Hurst, University of Liverpool

A new study shows that how mice are picked up by the experimenter can

substantially change their behaviour in cognitive tests. The work, by Dr Kelly Gouveia and Professor Jane Hurst from the University of Liverpool, was published in *Scientific Reports* today.

The researchers discovered that mice handled by a 'mouse-friendly' [tunnel](#) for transfer to the [test](#) arena showed much more active exploration during testing than those picked up by the [tail](#), which had a major positive impact on test performance.

In the tests, mice were placed near a new attractive stimulus (urine from the opposite sex) that should stimulate approach and investigation, especially during the first contact. This was repeated in three sessions, to get animals familiar with the new scent. Throughout all the sessions, mice picked by the tail showed very little willingness to explore the test arena and therefore investigate the new stimulus. Many animals failed to sniff the stimulus even once, making it challenging to compare the sessions and to collect enough data to reach statistical significance. By contrast, mice picked up in a tunnel explored their environment readily, showed a strong interest in the new stimulus, and a clear effect of becoming familiar with it in the consecutive sessions.

To test discrimination between two different scents, the mice were then placed near a different urine stimulus. Because the performance of mice picked up by the tail was so poor from the start, they did not discriminate between the known and new scents. Those handled by a tunnel showed robust discrimination, making them much more reliable experimental subjects.

The traditional way to pick up a mouse from the cage is by grasping the base of the tail, although this has no scientific validation. This method, although fast and not painful, is known to be aversive to mice and to cause stress and anxiety.

In their previous work, the team from Liverpool developed alternative methods of handling mice that are much more animal-friendly and just as quick once the handlers are trained (2,3). This involves picking up mice by guiding them into an open tunnel that is inexpensive and autoclavable (see photo). Professor Hurst showed that this technique makes a big difference to how mice respond to the handler - while mice picked up by the tail show caution and are reluctant to approach the handler, mice used to the tunnel interact with the tunnel and with the person handling them much more willingly.

Mice are the most common animal used in research and handling is an important part of both routine husbandry and experimental procedures. Handling stress could therefore impact the welfare of millions of mice used in research world-wide.

But minimising the stress associated with handling is key not only to the animal's well-being; it has scientific importance as well. It is well established that anxiety in rodents correlates with reduced exploration. Unnecessary stress or anxiety due to handling before testing is likely to shift the animal's attention away from a particular test and make it less able to learn and/or solve specific tasks. Avoiding this by using a better handling method could improve the reliability of a wide range of behavioural tests used to understand learning and memory, assess gene function, test sensory deficits, or for drug discovery, for example.

Use of a non-aversive handling can remove the requirement for prior familiarisation with the handling procedure and test environment, as animals that are not anxious will readily explore the novel environment. This could save valuable time during testing, as well as substantially improve the reliability of behavioural responses to test stimuli that are not confounded by handling-induced anxiety.

Commenting on the work, Professor Hurst said: 'The method used to

pick up [laboratory mice](#) has a surprisingly strong influence on their anxiety, and our study shows that this has a major impact on the reliability of their behavioural response to test stimuli. A simple change to picking up mice up in a tunnel rather than by the tail could have a really positive impact on the wide range of research that relies on behavioural testing, as well as improving the well-being of test animals.'

Dr Mark Prescott, NC3Rs said: 'This study provides further evidence for the need to shift away from tail handling of laboratory [mice](#), this time for scientific reasons. Tunnel handling should be the method of choice for researchers conducting behavioural tests with these animals.'

To help train handlers in the tunnel method, Professor Hurst's team, in collaboration with the NC3Rs, have created a [mouse handling video tutorial](#).

More information: 1. Gouveia K, Hurst JL (2017) Optimising reliability of mouse performance in behavioural testing: the major role of non-aversive handling. *Scientific Reports* 7: 44999. [DOI: 10.1038/srep44999](#)

2. Hurst JL, West RS (2010) Taming anxiety in laboratory mice. *Nature Methods*. Oct;7(10): 825-6. [DOI: 10.1038/nmeth.1500](#)

3. Gouveia K, Hurst JL (2013) Reducing mouse anxiety during handling: Effect of experience with handling tunnels. *PLoS ONE* 8(6): e66401. [DOI: 10.1371/journal.pone.0066401](#)

Provided by NC3Rs

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