

Implementation of the 3Rs in research: “Recommendations for handling experimental mice in research”

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The Animal Welfare Body at Karolinska Institutet



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Recommendations from the Animal Welfare Body at Karolinska Institutet to the Research community for implementation of the 3Rs in research

Recommendation for handling mice: Handle mice with a tunnel or a cupped hand.

Laboratory mice handled during daily routines, like cage changes, and scientific procedures are traditionally picked up by the base of the tail. Research shows that picking up mice by the tail induces aversion and anxiety, which can be reduced by using a tunnel or a cupped hand instead. Therefore, the Animal Welfare Body recommends, when possible, to handle mice using tunnel or cup handling methods.

Humane handling of mice used in research benefits animal welfare and scientific outcomes.

Recently, it has been proposed that the handling technique used by researchers and laboratory staff influences both the welfare of mice and the data obtained from experimental studies (*Hurst and West 2010, Gouveia and Hurst 2013, Ghosal et al., 2015, Gouveia and Hurst 2017, Clarkson et al., 2018*). The standard procedure for handling mice is to pick up the mouse by its tail, but alternative methods such as using a tunnel or a cupped hand may be preferable. Research shows that lifting mice by the tail induces aversion and anxiety and unfortunately repeated tail lifting does not seem to habituate mice to this procedure (*Hurst and West 2010*). Mice lifted by a tunnel or a cupped hand spend more time voluntarily interacting with a handler, and they show reduced anxiety-related behaviour in standardised behavioural tests of anxiety such as the elevated plus maze, compared to mice lifted by the tail (*Hurst and West 2010, Gouveia and Hurst 2013, Gouveia and Hurst 2017*). Furthermore, it has been shown that restraining mice by the scruff of the neck was more accepted and less stressful for mice picked up by a tunnel or cupped hand compared to tail-lifted mice (*Hurst and West 2010*). Thus, methods such as tunnel or cup handling are beneficial as they are less stressful for the mice and have the added benefit of promoting a positive response to human contact (*Hurst and West 2010, Gouveia and Hurst 2013*).

Many laboratory mice are at some point subjected to an experimental setting when they are lifted by a human hand and some type of procedure is carried out. Handling mice by a tunnel or a cupped hand during cage changes could thus be considered as part of the handling habituation. Studies have demonstrated that mice handled by tunnel or cupping methods, compared to tail-handled mice, show improved performance in different behavioural tests e.g. larger consumption of sucrose solution (amount and licking cluster size) as a test of sensitivity to reward (*Clarkson et al., 2018*) and increased motivation to investigate attractive stimuli (*Gouveia and Hurst 2017*). It should be noted that in one study there was no difference between cupped hand and tail-lifted mice in the radial maze cognitive bias test (*Novak et al. 2015*). However, cup handling has also been shown to reduce the confounding contribution of stress to evaluation of metabolic measures, such as glucose tolerance tests (*Ghosal et al., 2015*). Thus, stress-induced influence on data interpretation could be reduced by cup or tunnel handling methods. These handling methods are also recommended by the National Center of the 3Rs (<https://www.nc3rs.org.uk/how-to-pick-up-a-mouse>) and the Swedish Center for Animal Welfare (SCAW, *Spangenberg and Cvek, 2017*).



Benefits of the tunnel and cup handling methods

- Mice are less anxious
- Mice show more reliable behavioural and physiological responses
- Mice only need brief experience of tunnel or cup handling to habituate
- Once familiar with the methods you can pick up the mice just as quickly as by the tail

Advice for successful implementation of tunnel and cup handling

- Start slowly – select one or two cages for initial implementation to gain confidence in the technique prior to adopting it more broadly.
- Consider leaving a tunnel in the cage for at least five days to habituate the mice to the tunnels before starting to use the tunnel technique.
- Adjust your method to the strains you are working with. For example, C57BL/6 mice appear to easier adapt to handling by a tunnel than hand cupping while BALB/c and outbred ICR (CD-1) strains habituate quickly to both methods.

Video tutorials:

<https://www.nc3rs.org.uk/news/new-video-tutorial-released-mouse-handling-made-easier>

<https://www.nc3rs.org.uk/how-to-pick-up-a-mouse>

<https://vimeo.com/nc3rs>

Conclusion

Tail lift should be avoided when possible and replaced by hand cupping or tunnel handling.

References

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