Automated Homecage Behavioural Analysis and the Implementation of the Three Rs in Research Involving Mice

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DISCUSSIONS

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It is widely accepted that the Three Rs principles of replacement, reduction and refinement should be introduced into experimental procedures involving laboratory animals whenever possible. A range of behavioural analysis systems are now available, that can be used to automate the study of behaviour within animals’ homecages. Most of these systems are designed for studies on mice, which are the most widely-used laboratory animals, and they are frequently marketed as tools that can aid the implementation of the Three Rs. Here, the technology currently available to carry out automated homecage behavioural analysis of mice will be summarised, and the case that these systems have the potential to both refine scientific procedures (minimising pain and distress) and reduce the number of mice used experimentally, will be discussed.

Types of automated homecage behavioural analysis

The technology that underlies the automated homecage behavioural analysis of mice is reviewed in detail elsewhere. Briefly, the methods of automated homecage behavioural assessment include automated video analysis, radio-frequency identification (RFID) transponders, infrared beams, infrared sensors, telemetry, and the quantification of homecage vibration. Systems vary in the types of behaviours that can be detected, but they all have the capacity to measure some form of spontaneous behaviour. Some of the systems only measure activity (e.g. infrared-based systems), whilst others can detect simple behaviours, such as rearing (e.g. automated video analysis and vibration-based systems). Physiological parameters (e.g. heart-rate and blood pressure) can be measured, in addition to behavioural monitoring, by using telemetry, whilst some RFID transponder systems allow operant behavioural testing to be carried out.

Refinement

Automated homecage behavioural analysis is frequently advocated as a refinement to standardised behavioural testing. It is likely that the welfare of the mice can be improved by studying animals in their homecages, as this minimises the necessity for human handling, which may be stressful and can act as a potential source of experimental variability. Automated homecage behavioural testing also has many potential applications for mouse welfare assessment. One of the key limitations to implementing refinements to experimental studies involving mice, is the challenge of objectively identifying pain and/or distress. It can therefore be difficult to determine when refinements such as changes to husbandry or scientific procedures, should be introduced, and to then evaluate how these refinements affect animal welfare. Examples of how automated homecage technology can be used for welfare assessment include the use of automated video analysis and telemetry to objectively measure post-operative pain and to assess analgesic efficacy, as well as the use of RFID transponder systems to carry out preference testing. Automated homecage behavioural analysis systems have also been used successfully to detect subtle behavioural changes that correlate to disease progression in studies involving mouse models of chronic disease, and this capacity is likely to be useful in refining disease studies. If subtle behavioural changes can be detected, then further intensive monitoring can be carried out on specific individual animals, in study periods where pain and/or distress are likely to occur. The detection of behavioural changes that precede clinical disease also has applications in the implementation of appropriate humane endpoints, increasing the likelihood that mice can be killed prior to the onset of pain or distress, when the scientific objectives of the study have been met.

Although there are several ways that automated homecage behavioural analysis can potentially refine
experimental procedures involving mice, there could be some negative aspects of automated homecage behavioural analysis with respect to mouse welfare. The majority of the systems that are currently commercially available require that animals be individually housed, and there may also be limitations in the types of environmental enrichment that can be used. Implants are not required in many of the systems, but RFID-based systems require the implantation of small transponders under a brief general anaesthetic, and telemetry requires the surgical implantation of larger transmitters. As the animals are less frequently handled when automated homecage behavioural analysis systems are used, they are likely to be less acclimatized to humans. As a result, periods when handling is required (e.g. for cage cleaning) may be more stressful to them. Finally, while automation may be a very useful way to complement human observation of animals, it is critically important that it never replaces the direct assessment and care of animals by compassionate and experienced personnel.14

Reduction

The main argument that automated homecage behavioural analysis can help in reduction of the number of animals used experimentally, is that the more-effective use of animals decreases the overall number of animals required. Through the use of more-sensitive assessment techniques, fewer animals may be required to produce statistically-significant results than has been previously obtained by using conventional techniques (e.g. standardised behavioural testing). Scientifically, there is evidence that the standardisation typically carried out for individual behavioural tests may not always be effective in generating reproducible experimental studies between laboratories.19, 20 In contrast, studies carried out by using an automated homecage system show consistency, regardless of the laboratory concerned.21 Many automated techniques also permit investigators to examine several aspects of behaviour simultaneously, which minimises the necessity to carry out several studies examining different behaviours. However, there may be ways in which automated behavioural analysis promotes the use of mice in research, and thus increases the overall number of animals used. Many of these automated techniques are designed to support high-throughput phenotyping, typically involving large numbers of transgenic mice. The generation of genetically modified animals has generally led to increases in the number of animals used, with a 42% increase in animal procedures in the UK since 2001 — when technology to genetically modify animals was introduced.22 It is also possible that more animals may be required to validate
new automated assays, as a result of the necessity of their comparison with standardised behavioural techniques as part of the validation process.

Discussion and conclusion

On balance, there is now increasing evidence that automated homecage behavioural analysis can be useful with respect to the implementation of the Three Rs in research involving mice. However, there are some potential areas of concern with respect to the Three Rs that the laboratory animal community should continue to evaluate as this technology develops.

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