

Richer Data and More Effective Analysis with Reduced and Refined Rodent Testing

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Introduction

Everyone is familiar with the importance of the 3Rs, particularly for CROs. However, continually abiding by them can present a challenge. Ensuring that licensing requirements are consistently met is difficult enough without trying to adjust trials to meet 3Rs requirements. There is always the risk that you will sacrifice data for the sake of compliance, leading to more rodents being used in the long run anyway.

Fortunately, there is a solution. Actual Analytics has designed the Actual Home Cage Analysis system (known as ActualHCA) with the express purpose of simplifying 3Rs compliance and generating richer, better data. Read on for information about how to reduce the amount of rodents you use, refine your experimental designs, and still collect much more data than ever before.

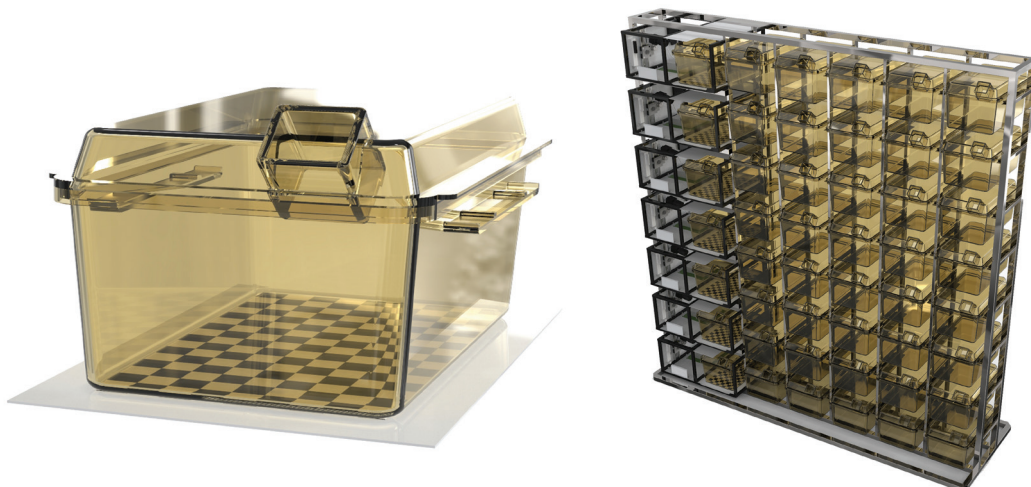
ActualHCA and Cost

In pre-clinical trials, the collection and analysis of useful and reproducible data is paramount. An individual rodent does not produce a significant amount of data; therefore, each trial requires a large amount of rodents to succeed.

Rodents, as it is well known, are at their least active during daylight hours when we can observe them, and at their most active at night when we can't. This means that a vast amount of important data is lost. Early phenotypes and neurodegenerative stressors may occur only once a day in the very early stages; they could happen in the dark periods.

The ability to monitor and quickly collect data that we previously could not results in a refinement of disease models, because intervention can occur earlier. Even having a camera monitoring rodents 24/7 isn't hugely effective, as it takes around five days for three people to comb through all the footage looking for significant activity. As a result, even more time is wasted and study lengths are extended, leaving clients unhappy and costs mounting.

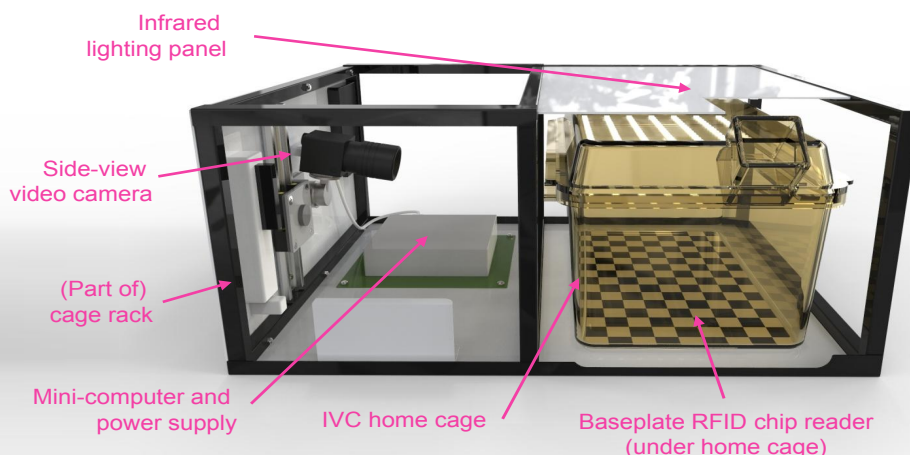
ActualHCA provides a solution to all of these cost problems. The system obtains the richest data currently possible from each rodent, drastically reducing rodent throughput and minimising waste.



Features of the home cage 24 h monitoring system

BASEPLATE READER

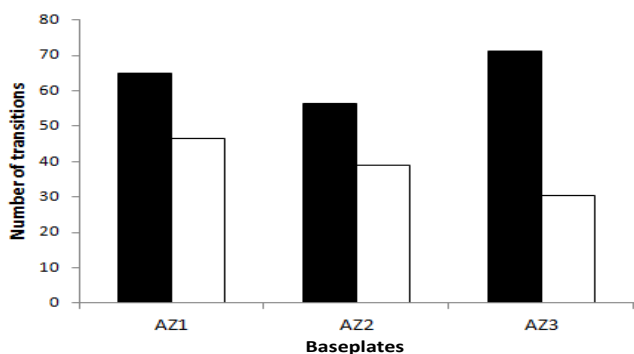
- Automated acquisition of ambulatory activity
- Automated acquisition of subcutaneous temperature
- RFID data used to 'ID tag' each animal in the video



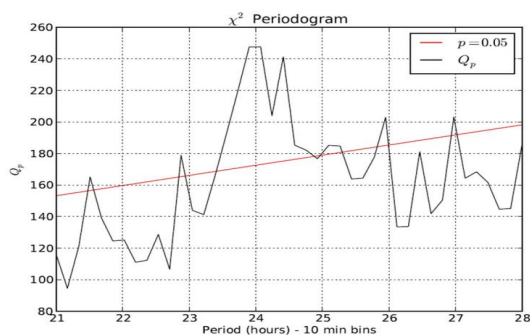
The camera is trained on the home cage enclosure 24 hours a day, and the baseplate reads data from the subcutaneously-inserted RFID chip in each rodent. This setup allows for each rodent's identity to be retained throughout every study. Infrared lighting ensures that no matter the time of day, data can be consistently collected.

So how is this different from standard monitoring? ActualHCA software will look out for unusual activity for you. Months of dedicated annotation and software "training" have resulted in a program that is loaded with algorithms designed to pick up on and flag any kind of unusual behaviour. If rearing, fighting, or social isolation is taking place, the software will detect it. The rest of the time, the footage will be standard. You can select the flagged time periods and watch them for an instant insight into what specifically happened surrounding unusual events.

24 h Periodicity of activity data



Differences between dark phase and light phase group mean activity for 3 baseplates (n = 5 rats).



Periodogram showing peak in frequency distribution of activity at a 24 h frequency

It's clear how this system is beneficial from a cost, data and welfare perspective. When richer data can be obtained from each rodent, fewer are needed and trials take far less time. The analysis of the camera footage starts right away, with the first results available within 15 minutes.

The 3Rs

Replacement

Currently, full replacement of rodents within drug discovery is not yet possible. Rodent research is essential to ensuring safety related attrition is kept down as much as possible during clinical stages. However, it is possible to reduce and refine this process greatly thanks to new technology.

Reduction

Using rodents in experiments is a fraught issue outside the world of science, and within it there has been an ongoing effort to avoid “wasting” animals by using too many for experimental purposes. As we've discussed above, using ActualHCA means a smaller number of rodents is needed. By recording fewer animals more often, we increase the statistical power of longitudinal studies. In certain studies, separate treatment groups could be mixed into the different cages, giving you a data point per cage per animal and reducing the number of animals needed whilst using the same statistical power.

ActualHCA is also designed to store all of the raw data from studies, meaning that in some cases, instead of repeating experiments, you can apply new analysis algorithms. This can eventually lead to the replacement of rodents in some studies. Reducing the number of animals used is not only beneficial from a cost perspective, but is also excellent for data and 3Rs compliance.

Refinement

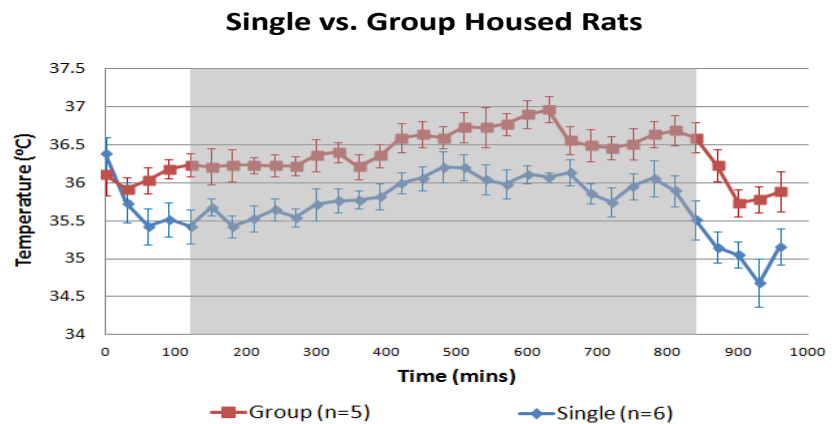
Organisations such as the NC3Rs are consistently working with CROs and pharmaceutical companies to ensure the consistent refinement of animal research. The ultimate aim is to find out how to make the process less stressful and painful for the animals, without allowing the research to suffer.

ActualHCA is almost entirely non-invasive, with the exception of the subcutaneous injection needed to implant the RFID chip. Rats and mice are social creatures: being housed alone or removed from their social environment causes restlessness and anxiety. These signs of distress are easily confused with signs of neurobehavioral, CNS, or drug- or disease-related symptoms, and vice versa. Without the issue of social isolation or discomfort in a new environment, a far more accurate baseline of “normal” behaviour can be established. This allows us to more accurately gauge the likelihood that the rodents are suffering from symptoms. ActualHCA ensures the amount of negative variables that commonly lead to safety related attrition in later phases is greatly reduced.

In addition to the higher-quality data generated by reducing behavioural variables, ActualHCA also offers the opportunity to obtain data previously inaccessible without disturbing the home cage. For the first time, it is possible to obtain data on rat temperature when they are group housed.

Effects of single-housing on subcutaneous temperature

- Decrease in subcutaneous temperature immediately upon housing singly after being housed in groups of 3
- Possible causes: group housing or rats enables intermittent 'huddling' with two cage mates, and may achieve a higher ambient temperature (with two additional rats generating heat)
- Illustrates just one of several physiological stressors associated with single housing (not to mention the psychological stressors).



As you can see, there is a considerable difference in terms of body temperature between rats that have been housed singly and group-housed rodents, possibly because of stress. This kind of information would not be accessible without the RFID chip-baseplate combination offered by ActualHCA.

Conclusion

When you combine the ability to view rodents as individuals, the access to previously inaccessible data, and the capacity to pick up on unusual activity early, the amount of information accessible using ActualHCA is impressive to say the least. It has remarkable potential for advancement both in terms of its own development and the ongoing drive to improve the way clinical trials are conducted.

Using this system guarantees improved 3Rs compliance, access to richer, more refined data, and a reduction in costs in terms of both finances and resources. For more details on this product, or to learn more about how it works, visit the Actual Analytics website at actualanalytics.com.

How to buy ActualHCA

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