Automated Home-Cage Monitoring Promotes Reproducibility and Data Capture

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Although mice are the cornerstone of animal experimental systems, they are fraught with challenges. When using mice, researchers must ensure good husbandry practices and document animal welfare on a daily basis, all while trying to generate reliable reproducible data for the scientific community. These tasks can prove particularly challenging because the animal handling required during routine cage changes for proper husbandry or experiments held outside of the cage can influence animal behavior and ultimately the results. In addition, the environment in animal rooms exposes the animals to a variety of disturbances, such as the presence of humans, noise, and lights. These environmental factors differ across facilities and impact animal behavior and activity patterns.

Automated home-cage monitoring systems can help address these issues because husbandry conditions are continuously monitored with nondisrupting technology, thus avoiding unnecessary cage changes and animal handling. In addition, such technology can help quantify potential impacts of environmental-related disturbances. In fact, a study recently published in *PLoS One* demonstrated how automated home-cage monitoring systems not only reduced the amount of animal handling and improved reproducibility of experiments but also ultimately captured valuable data about animal behavior that typically is not possible with conventional cage setups.

"The study provides new insights into the undisrupted home-cage behaviors of group-held mice," says senior study author Brun Ulfhake, MD, PhD, Professor of Anatomy, Department of Neuroscience, Karolinska Insititutet, in Sweden. "We learned how mice respond to care-taking events, such as cage-change, and other events, such as transitions between day and night." Dr. Ulfhake explains that more detailed knowledge of the spontaneous behaviors in the home cage will assist in welfare surveillance and help improve husbandry, as well as improve experimental design and monitoring of ongoing experiments.

The study was designed to keep animals in their normal husbandry conditions and then perform routine tasks, such as cage change, all while capturing continuous data 24/7 with the digital individually ventilated cage system (DVC®) from Tecniplast. Female C57BL/6J mice were housed in DVC systems at three facility locations: Consiglio Nazionale delle Ricerche in Rome, Italy; The Jackson Laboratory in Bar Harbor; and Karolinska Insititutet in Stockholm, Sweden. To observe gender differences, a fourth group of male C57BL/6J mice were housed in DVC systems at Karolinska Insititutet.

All DVC systems used a nondisrupting capacitive-based sensor board externally located under the standard individually ventilated home cage to collect data on animal activity within the cage every 250 ms, 24/7. The sensor board was made up of 12 capacitive-based planar sensing electrodes that measured changes in capacitance as animals moved across the cages and generated an activity metric for overall cage activity.

Mice were aged 6 to 8 weeks at the beginning of the study and activity was recorded with the DVC system until 25 weeks of age. Fifteen home cages were set up at each site, and each cage housed five mice. Cages contained standard bedding, food, and cage enrichments, and the vivarium light cycles were set to 12 h on to simulate day and 12 h off to simulate night.

By continuously monitoring activity across several weeks, the DVC system captured an abundance of data, such as the expected diurnal patterns of cage life. The data showed a gradual increase in mouse activity ~2 h after lights off followed by a high level of activity that varied over the next 4 to 5 h. This was followed by a decline in activity and a subsequent burst of activity before lights on. Mice remained active for a short duration after lights on and then returned to their resting state. Overall, these findings suggest that the transition between day-to-night and night-to-day yields different responses in activity.

The DVC system also elucidated considerable effects that normal procedures, such as handling, weighing, and cage change, can have on activity patterns. For instance, cage change led to an increase in activity that lasted for several hours for both female and male mice.

An evaluation of the activity across several weeks between two of the facility sites revealed statistically significant differences in the average activity and duration of activity. In addition, differences in peak activity, average activity, and duration of activity were seen among cages at the same site. Activity differences on the basis of gender were again observed, with female mice showing greater week-to-week variability in activity than male mice. Altogether, these variations underscore the complexity and sensitivity of animal behavior and indicate that activity is affected not only by site-specific factors, but also by group dynamics within each cage.

"The paper is a very clear example of the benefit that DVC can have on the scientific community," says study coauthor Fabio Iannello, principal data scientist at Tecniplast SpA. He explained that under normal husbandry conditions, a cage-change operation is performed and no data are collected during this process. "If you had DVC installed in every cage, you can actually perform a normal operation and collect the data and analyze the data, basically in real time," he says.

In addition, the DVC system can extract continuous information when a researcher is running an experiment, and the data capture is quantitative metrics, not subjective observations. Such quantitative data capture is valuable for a wide variety of locomotion experimental tests. For example, a researcher conducing oncology-related experiments to understand the effect of tumors on mouse locomotion could collect these data during experimental tests as well as around the clock with the DVC system without the need for animal handling. Furthermore, these data could be collected at night, when mice are naturally active. Dr. Ulfhake says, "You can really capture activity of the mice that otherwise you would not have."

Other monitoring systems can collect real-time information like DVC does, but they lack scalability. For example, video camera-based systems can be installed on only a limited number of cages, whereas the DVC system can be installed on a low number of cages as well as upward of thousands of cages. "There are no other tools that are as scalable as DVC," says Mr. Iannello. "It's really a scalable system that can collect real-time information from thousands of cages."

In addition to being scalable, DVC generates data with very low computational complexity, thus requiring minimal storage space. Video camera-based systems generate recordings that require significant storage space, limiting its utility. DVC also has the advantage of being fully integrated into the facility management process and can be washed and autoclaved. Having these features, the authors explain, means DVC does not change any of the conventional maintenance operations performed in a facility.

"Our results so far indicate that much remains to be done to harmonize the conditions of an experiment. If we make good use of this, the complementary data generated by the DVC system will likely contribute to improved reproducibility of animal testing," says Dr. Ulfhake. "With a deepened understanding of how the DVC data is best interpreted, I am convinced that more advanced behavioral testing will be done in the home-cage of the mice. This would be a highly significant refinement of the testing conditions."