Journal of the American Association for Laboratory Animal Science
Copyright 2015
by the American Association for Laboratory Animal Science

Vol 54, No 3
May 2015
Pages 267–272

Effects of Changing to Individually Ventilated Caging on Guinea Pigs (*Cavia porcellus*)

Marta Giral,[1,*] Clara Armengol,[2] Sonia Sánchez-Gómez,[2] and Amadeu Gavaldà[2]

The goal of this study was to evaluate the effect of changing to IVC housing on guinea pigs by recording several physiologic parameters in guinea pigs housed sequentially in open-top cages (OTC) and IVC. To register heart rate and locomotor activity, 10 male Dunkin–Hartley guinea pigs implanted with telemetric transmitters were moved from OTC to new, freshly prepared OTC or IVC and subsequently monitored by telemetry during the 4 d after the first cage change. Body weight and food consumption were measured twice during the study. Comparison of data from OTC- and IVC-housed guinea pigs showed no relevant differences in heart rate (mean ± 1 SD; 213 ± 10 bpm and 207 ± 9 bpm, respectively) at any time point. In contrast, locomotor activity varied: whereas activity during the first 4 h after the change of cage type was greater in IVC-housed animals, that during the following 24 h was greater in OTC but was similar between groups thereafter. Animals housed in OTC consumed more food than did those in IVC and, under both conditions, consumption was statistically related to body weight changes. Together, these results show that a change to IVC housing induced only transient increases in locomotor activity in guinea pigs without a marked increase in heart rate but with a decrease in food consumption. Because decreased food consumption was the only stress-associated sign during the 4-d observation, longer studies are needed to ascertain the importance of this finding.

Abbreviations: ACH, air changes per hour; OTC, open-top cage.

In the last 2 decades, IVC have become a common housing system for laboratory rodents. IVC systems have some well-known advantages over open-top cages (OTC), including decreased intracage humidity, reduced CO_2 and ammonia levels, protection against pathogens, decreased frequency of cage changes, reduced airborne allergens, and decreased costs associated with general ventilation and other parameters. However, some concerns regarding the potential harmful effects of IVC systems have arisen recently.[2,8-10]

Much research has been performed to study the housing preferences of mice and rats (for example bedding types, ventilation rates, and so forth) as well as factors that affect animal behavior and produce stress-related conditions.[2,4,7,9,10] In contrast, remarkably few studies address guinea pigs and their housing conditions.

Guinea pigs are used less frequently for research purposes than are other species, such as mice and rats. In 2011, guinea pigs represented only 1.5% of the total number of animals used in the European Union for experimental and scientific purposes, whereas mice (60.9%) and rats (13.9%) were by far the most common overall.[5]

Guinea pigs are easy to work. They are very docile animals and rarely bite or scratch. However, gentle handling is highly important because guinea pigs are easily excited by loud noises or sudden movements. In these situations, they often 'stampede,' that is, jump and race around the cage, which can result in self-injuries (especially of the eyes) that occur on contact with sharp objects (for example, feeders) or when their limbs become trapped in the holes of the perforated cage floor. This reaction -often occurs in OTC-housed guinea pigs when housing room doors are opened. However, in IVC, guinea pigs present different behaviors: the stampede reaction rarely occurs, and the animals appear relaxed and calm, even when caretakers make loud noises or sudden movements. Nonetheless, this apparent calm might be misleading because guinea pigs tend to freeze when they hear unfamiliar sounds,[12] and they may remain immobile for variable time periods (from several seconds to some minutes). This characteristic raises the question as to whether the behavior observed in IVC could also be a sign of fear.

To address this question, we designed the present study to compare the effects of 2 types of housing conditions, IVC and OTC, on telemetry-implanted guinea pigs in terms of several physiologic parameters related to the animals' wellbeing, including heart rate, locomotor activity, body weight, and food and water intake.

Materials and Methods

Animals. Male Dunkin–Hartley guinea pigs (n = 10; age, 10 to 12 mo; weight, 975 to 1500 g) were purchased from a commercial breeder (Charles River Laboratories, Barcelona, Spain) and housed at the Almirall animal facilities (Barcelona, Spain) throughout the study. The animals were bred in OTC at the supplier facilities. On arrival at our facility, the guinea pigs were housed in groups of 3 in ventilated cages (1500U Eurostandard Type IV S, Sealsafe IVC Blue Line, Tecniplast, Varese, Italy) with an inner floor area of 1500 cm^2 and kept in a room with controlled conditions of light (lights on from 0700 to 1900, with 30 min of dawn and dusk), ventilation (15 to 20 air changes per hour [ACH]), temperature (22 ± 2 °C), and humidity (55 ± 10%). These conditions were maintained during the 5-d acclimation period before the evaluation of the animals. A standard guinea pig diet (2040 Teklad Global Guinea Pig Diet, Harlan, Barcelona, Spain) and water were available ad libitum

Received: 04 Jun 2014. Revision requested: 02 Jul 2014. Accepted: 02 Sep 2014.
[1]Animal Research Facilities, and [2]Integrative Pharmacology Department, Almirall SA, Barcelona, Spain.
**Corresponding author. Email: marta.giral@almirall.com*

throughout the study. The diet was supplemented daily with a handful of irradiated hay (Harlan) that was introduced into each cage. A mixture of 2 types of aspen particles (3000 and C32/23, Souralit, Girona, Spain) was used as bedding. After the surgical implantation of the telemetric transmitters and during the study, the animals were housed singly in conventional OTC under the described environmental conditions. Data recording began more than 6 mo after the surgery.

The care of animals was undertaken in compliance with the European Commission Directive 2010/63/EU and the Spanish and autonomous Catalan laws (Real Decreto 53/2013 and Decret 214/1997). Experimental procedures were approved by the Animal Experimentation Ethics Committee of Almirall.

Surgical implantation of the transmitters. One week prior to the surgery, ascorbic acid (1 g/L; 95209-250G, Sigma Aldrich, Madrid, Spain) was added to the guinea pigs' drinking water to avoid vitamin C deficiency after surgery. On the day of the surgery, the guinea pigs were anesthetized with an intraperitoneal injection of a mixture of 50 mg/kg ketamine (Imalgene 500, Merial, Barcelona, Spain) and 8 mg/kg xylazine (Rompun 2%, Bayer Hispania, Barcelona, Spain). Analgesia (0.05 mg/kg SC; Buprex, Schering–Plough, Madrid, Spain) was administered immediately prior to surgery and once daily for the subsequent 2 d. Injectable ascorbic acid (30 mg/kg SC; 1 g injectable ascorbic acid solution, Bayer Hispania) and enrofloxacin (10 mg/kg SC; Baytril 2.5%, Bayer) were administered prior to and once daily for 3 d after the surgery.

The dorsal area of the guinea pigs was shaved and the skin prepared by using povidone–iodine in saline. The body temperature was maintained via the placement of a homeothermic blanket throughout the procedure. A radiotelemetry transmitter (PhysioTel CA-F40, Data Sciences International, St. Paul, MN) for measuring ECG and locomotor activity was implanted surgically into a subcutaneous pocket made on the back of each guinea pig.[13] Bipolar electrodes for ECG were implanted to record lead apex–base ECG; one lead (negative pole) was placed on the right front limb, and the other lead (positive pole) was positioned near the last left rib to obtain a clear lead II recording.[16]

After surgery, the guinea pigs were individually housed in conventional cages, and the surgical wound was checked daily and disinfected with povidone–iodine. The animals were weighed daily for 1 wk after surgery to monitor their recuperation. They were allowed to recover for at least for 3 wk before use in experimental studies. The animals were housed individually until the end of the study.

Telemetric system setup and data recording. A separate experimental room with the same environmental conditions as described earlier was used for the study. The room setup consisted of a single rack with conventional cages, with 2 more racks at the opposite side of the room. One of these racks was identical to the single rack, and the other was an IVC system. The ventilation for the IVC was supplied by an air unit (TouchSLIM-Line, Tecniplast) at positive pressure and 75 ACH.

Telemetry units from a commercially available system (Data Sciences International) were set up as follows. Two receivers (RPC-1) were placed under each guinea pig cage. A data exchange matrix (BCM 100), an ambient pressure reference (APR1), and Dataquest ART Gold version 2.3 software were used to record ECG and locomotor activity parameters. The ECG was analyzed by using ecgAUTO version 1.5.12.36 (EMKA Technologies, Paris, France).

ECG and locomotor activity data were collected at scheduled acquisition intervals. The acquisition software was programmed to record data at 5-min intervals, and the duration of each recording segment was 20 s for animals with heart rates of 170 to 220 bpm as the guinea pig; accordingly, 20 s provides approximately 60 beats, which we consider to be sufficient for reliable analysis of the ECG in light of our extensive previous experience. Heart rate (in bpm) was calculated directly from the ECG.

The data exchange matrix provided the activity counts. As a guinea pig moved in its cage, the telemetry signal transmitted to the receiver antennae varied in strength. When the signal strength changed by a specified amount, an activity count of 1 was generated as a measure of activity. The number of counts generated depended on both the distance moved and the movement speed. The activity data provided a strictly relative measure of locomotor activity and were not in any way related to absolute measurements of distance moved or spatial position. The system reported a value of 6 counts per minute for a single activity count within a 20-s sampling period.

Because the activity data were highly dispersed, we analyzed this parameter statistically by using a qualitative score (movement or absence of movement) that was described previously.[7] In brief, counts equal to 0 were assumed to be equivalent to the absence of movement, and values greater than 0 were defined as movement. For the comparison of activity, all samples (that is, all the readings recorded by the telemetry system) were taken into account.

Study design. At 3 d before the start of the experiment, the animals were moved from their maintenance room to the experimental room to allow acclimation to the new environment. They were weighed to establish the basal weight of each animal and then placed in clean conventional cages with free access to food and water, as previously described. Each cage was placed on top of 2 telemetric receivers (RPC-1).

All 10 guinea pigs were housed randomly under both housing conditions (OTC and IVC) for 4 d each. Thus, half of them were in the OTC and the other half in IVC, simultaneously.

The experimental protocol during the 4 d of data recording is shown in Figure 1. Briefly, 6 h before the change to the new rack (at 0900 h), telemetry transmitters were switched on bringing a magnet close to the subcutaneous pocket holding the transmitters and thus initiating data recording, which occurred from 1100 to 1500 h and was used as baseline data.

At 1500 h, the guinea pigs were changed to new clean cages, which contained 300 g of food and 500 mL of water, and moved to the assigned rack. The new cages were placed on top of the telemetry receivers. From this point on, cages were changed (for cleaning) every other day. During the change procedure, the guinea pigs, remaining food, and remaining water were weighed, and 300 g of food, a handful of hay and 500 mL of water were added. On the alternate days, only the water bottles were changed and hay was added, to minimize animal handling. The animals were always handled by the same caretaker.

Food consumption was calculated by weighing the feeders at the end of day 2 and at the end of the experiment. The difference in weight was considered to be the amount of consumed food. The same procedure was used to determine water consumption.

At 1500 h on day 4, all animals were moved to OTC and weighed, and the transmitters were switched off. Consumed food and water were measured as previously described.

The recording of data was stopped momentarily every 24 h (at 1500 h) to obtain the data and to evaluate the follow-up of the study.

To facilitate data analysis, each day of the study was divided into 6 phases of 4 h each, as follows: phase 1, last light period (1500 to 1900); phase 2, first dark period (1900 to 2300); phase

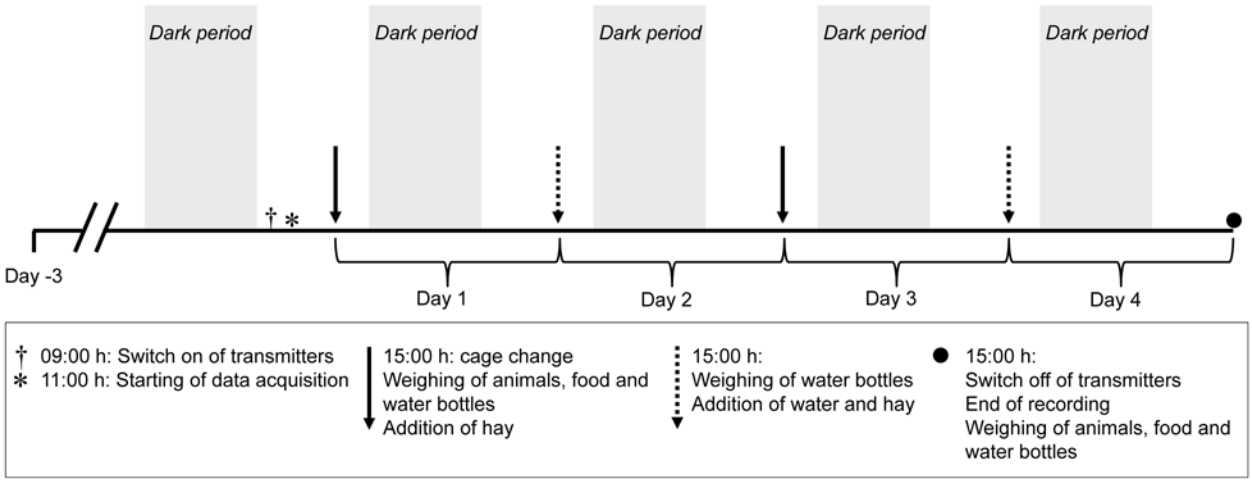

Figure 1. Experimental protocol.

3, intermediate dark period (2300 to 0300); phase 4, last dark period (0300 to 0700); phase 5, first light period (0700 to 1100); and phase 6, intermediate light period (1100 to 1500).

Statistical analysis. We calculated the mean values of all quantitative variables analyzed (heart rate, body weight, and food and water consumption). The means of heart rate values at each phase were calculated from all values obtained in all animals (that is, the raw data from all animals were pooled into a single mean).

Means were compared by using the Student *t* test for normally distributed data and the Kruskal–Wallis test for nonnormal distribution. A *P* value of less than 0.05 was accepted as evidence of statistical significance. Qualitative variables were compared by using the χ^2 test. Two-tailed *P* values of less than 0.05 were considered to be evidence of statistical significance. The relationship between food consumption and body weight changes was determined by Pearson correlation analysis. Power and effect sizes were calculated where appropriate; the effect size was measured by using the Cohen's d statistic.

Statistical analyses were performed by using GraphPad PRISM 5 for Windows (version 5.0; GraphPad Software, San Diego, CA), OpenEpi (Open Source Epidemiologic Statistics for Public Health, version 2.3.1, www.OpenEpi.com), and StatPlus version 2009 (AnalystSoft, Alexandria, VA).

Results

Heart rate. The mean heart rate from guinea pigs during each experimental phase is shown in Figure 2. Prior to the first cage change, the heart rate as measured by telemetry ranged from 188 to 229 bpm (mean ± 1 SD, 209 ± 7 bpm). After the first cage change and until the end of the experiment, the heart rate ranged from 184 to 258 bpm (213 ± 10 bpm) and 183 to 247 bpm (207 ± 9 bpm) for the OTC and IVC housing conditions, respectively.

Heart rate was analyzed every 5 min, and all values were compared individually between the 2 conditions at each time point. Only transient significant differences between OTC and IVC conditions were observed at sporadic measurement points. Of the total of 1152 measurement points, only 68 presented a statistically significant difference ($P < 0.05$). For this parameter, the power size ranged from 81.0% to 100%, and the effect size (Cohen d value) ranged from –0.22 to 0.34.

Locomotor activity. The evolution of the locomotor activity in the guinea pigs throughout the study is shown in Figure 2. The locomotor activity profile followed a circadian pattern, with higher activity during the night (mainly during the first half of the dark period) and lower activity during the second half of the dark period and throughout the light period.

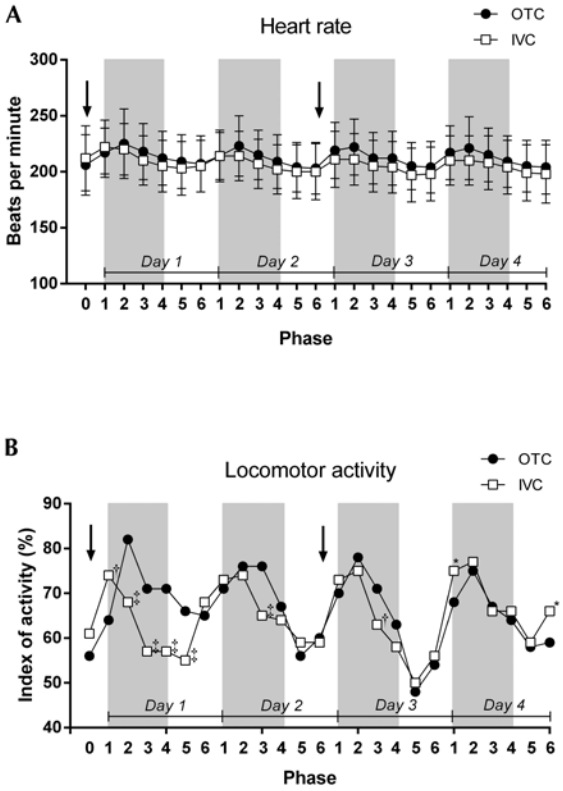

Figure 2. (A) Heart rate (mean ± 1 SD) and (B) locomotor activity recorded throughout the experiment from guinea pigs housed in OTC or IVC cages ($n = 10$). Arrows indicate when cages were changed. Differences (‡, $P < 0.001$; †, $P < 0.01$; and *, $P < 0.05$; Student *t* test) between groups are indicated.

Before the first cage change, the activity index was similar under both housing conditions, with values of 56% and 61% for OTC and IVC, respectively. After this cage change, the activity index was higher in IVC (74%) than in the conventional cages (64%), and the difference was statistically significant ($P = 0.001$). In contrast, throughout the dark period, the activity index was markedly lower in the guinea pigs housed in IVC than in OTC ($P < 0.0001$ in all cases). During the first light phase, there was

even less activity in the guinea pigs housed in IVC than OTC (55% compared with 66%; $P = 0.0005$).

During days 2 and 3, the only phase presenting a significant difference between housing conditions was phase 3 ($P = 0.0003$ and $P = 0.006$, respectively), with lower activity in the guinea pigs in IVC. On day 4, only transient significant differences were present, with slightly higher activity in the IVC (Figure 2).

The guinea pigs housed in IVC showed a daily activity pattern that was repeated almost identically throughout the experiment. However, the pattern was not always the same when the animals were housed in OTC. Specifically, when the guinea pigs were moved to a new conventional rack, the activity index remained high (71%) during the last part of the dark period (phase 4) and even during the light period (phases 5 and 6; activity indexes of 66% and 65%, respectively). However, after the following cage change, the locomotor activity was lower in all 3 phases (63%, 48%, and 54%, respectively), with statistically significant differences compared with the first cage change ($P = 0.02$, $P < 0.0001$, and $P = 0.0004$, respectively). The power size ranged from 90.8% to 99.9%.

Body weight. There were no significant differences in mean body weight throughout the experiment. However, when analyzing the results in terms of weight gain or loss, we found an extremely high standard deviation of the data, such that the means were nearly constant across the experimental time period because the body weight gains of some animals were compensated by losses in others. In OTC, only 1 of the 10 guinea pigs showed a slight decrease in body weight at the end of the experiment (3% relative to the initial body weight), whereas in IVC, 4 guinea pigs showed decreases in body weights, which ranged from 3% to 8% (Figure 3).

Food consumption. Food consumption was evaluated as indicated previously, and the amount consumed was expressed as grams of food per 100 grams of body weight.

Statistically significant differences between the 2 housing conditions occurred on days 2 and 4, with guinea pigs housed in IVC appearing to consume less food than guinea pigs housed in OTC ($P = 0.005$ and $P = 0.01$, respectively; Figure 4). In addition, food consumption and body weight change were positively statistically correlated in OTC ($P = 0.03$) and in IVC ($P = 0.02$). The power size ranged from 84.5% to 90.4%, and the effect size (Cohen d value) ranged from 1.38 to 1.50.

Water consumption. There was no statistically significant variation in water consumption during the course of the study. The guinea pigs housed in OTC presented a mean consumption ranging from 204 ± 113 to 230 ± 111 mL/day, whereas the animals housed in IVC consumed from 251 ± 168 to 284 ± 150 mL/day.

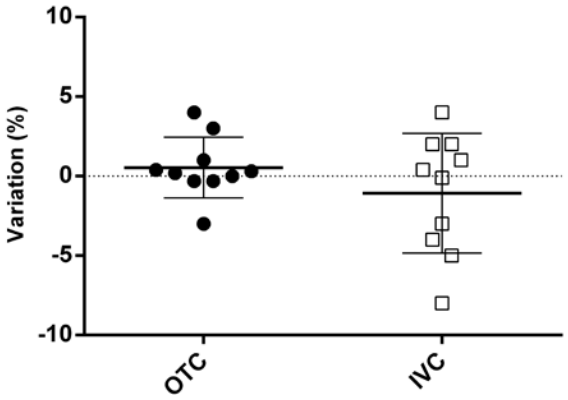

Figure 3. Variations in body weight of guinea pigs at the end of the study (day 4) relative to the initial values under the 2 housing conditions. The horizontal bars indicate the mean ± 1 SD.

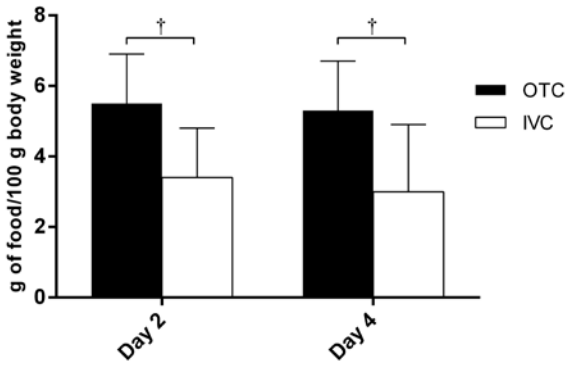

Figure 4. Food consumption (including pellet spillage; mean ± 1 SD) of guinea pigs housed in conventional and in ventilated cages ($n = 10$). Food consumption differed ($P < 0.01$, Student t test) between the guinea pigs assigned to OTC compared with IVC.

Discussion

Guinea pigs are very sensitive animals. Their typical response to potential danger, sudden movements, or loud noise is an explosive stampede, which can cause self-injuries. Alternatively, when these animals are approached or placed in an unfamiliar environment, they tend to become immobile (that is, display freezing behavior).[14]

In our facilities, we have observed that guinea pigs housed in IVCs do not stampede in reaction to sudden stimuli, including noise and unexpected movements inside the room. However, in rooms where the animals are housed in OTC, even slight or slow movements can provoke explosive reactions.

The present study used telemetry to evaluate the effects of IVC systems on several general physiologic parameters in guinea pigs, and the results from this evaluation were used to draw conclusions about animal well-being under these particular housing conditions.

Preference tests in rats and mice have addressed several ventilation parameters, such as air velocity or number of ACH in the IVC. In these preference tests, rats seemed to prefer cages with an ACH below 80.[10] A range between 60 to 80 ACH is considered acceptable for removing polluted gases and for adequately drying bedding surfaces.[15] The number of air changes seems to be less important for mice, because they showed no preference for any of the different conditions studied (40, 80, or 120 ACH).[9] In contrast, mice seem to be very sensitive to drafts that can occur with air speeds higher than 0.2 m/s.[9] A ventilation air speed of less than 0.5 m/s appears to be acceptable for rats.[10] To our knowledge, no preference tests have been performed under similar conditions for guinea pigs. For the present study, we used 75 ACH, and the IVC cage-change schedule was the same as that usually followed when using OTC for guinea pigs (that is, 3 times per week). Guinea pigs are quite messy and tend to scatter food and water all around their cages, so that these animals require more frequent cage changes as compared with rats or mice.

In general, changes in heart rate are considered to be an indicator for measuring animal wellbeing and distress.[7,17] In guinea pigs, this indicator has not been fully validated, although some studies have used heart rate with other parameters (for example, locomotor activity and body weight) to assess the effect of a stressful stimulus, such as transportation.[17] In addition, our own preliminary observations showed that an unequivocally stressful environment (that is, wire-bottom caging) led to a marked increase in guinea pig heart rate (data not shown). In the

present study, the guinea pigs did not show any marked increase in heart rate, perhaps suggesting that, despite the novelty of the housing, guinea pigs coped quite well with the new IVC environment. Moreover, when we considered individual heart rate recordings, this parameter seemed to follow a circadian rhythm in all of the animals in our study, with higher rates during the dark period. However, some authors have reported that guinea pigs may have different individual rhythmicity characteristics[1] that are unlike those observed in other rodents such as rats and mice.[3,11] Nonetheless, stressful situations are generally reported to have a strong effect on the circadian rhythm of heart rate,[17] and we did not observe this effect in the present study.

Guinea pigs housed in OTC are potentially exposed to a variety of stimuli (odors, noise, and so forth) that might cause stressful responses, although which stimuli elicit freezing compared with stampede-type responses is unclear. Therefore measuring locomotor activity in these animals could lead to confounding results. However, it seems clear that during the dark period, when the animals exhibit their normal nocturnal behavior and there are no extraneous sounds or unfamiliar smells associated with caretakers, technicians, or equipment, the measurement of activity might be more valuable and could more precisely indicate real changes in guinea pig behavior.

We have previously used the activity index as a measure of locomotor activity.[7] This index compares the number of measurements during which there is movement (that is, the number of measurements in which the movement count is greater than 0) with the total number of measurements. In the present study during basal conditions (that is, guinea pigs housed in OTC), this index was around 57% to 59%. In the current experiment, we assumed that the IVC was a novel environment for the animals, because they had been always housed in OTC, except during the initial acclimation period (5 d) more than 6 mo earlier. When the animals were moved to a new environment (IVC), the activity index increased dramatically (by 74%) during the first 4 h after the cage change. These higher values could be a consequence of the normal exploratory behavior of the animals in a new environment. However, during the night, there was a tendency toward a decrease in activity, especially during the second part of the dark period (below 60%), which is in accordance with the fact that guinea pigs are a crepuscular rather than a nocturnal species.[6] This activity pattern was repeated almost identically over the following days. Therefore, the pattern observed during the first day–night period could be considered as normal, given that the same pattern was observed when the animals were not moved to new cages and left undisturbed.

When the guinea pigs were moved from one OTC to another, there was an initial slight increase in the activity index (near 65%). However, during the first part of the dark phase, the index reached a maximum of 82%, which coincides with the crepuscular behavior of guinea pigs. Interestingly, during the second part of the dark period, and even during the following light period, the activity index remained unexpectedly high, not only in comparison with the index from animals housed in IVC, but also regarding the following dark and light periods. This finding suggests that something unrelated to the new cage environment, perhaps a quality of the macroenvironment, affected the animals. Because the OTC are open to the environment, the animals could be influenced by external stimuli when they were moved to a different rack, and the effect may be related to the different location of those racks in the experimental room. For instance, because the top air diffusers in the room used in this study were not placed symmetrically on the ceiling, different airflow rates might influence some cages more than others. The activity levels of these animals were lower during the following days, suggesting some kind of habituation.

Food consumption was lower when the guinea pigs were housed in IVC. Calculating the exact amount of food eaten by guinea pigs can be difficult because, as mentioned earlier, this species tend to play with feeders, such that food counted as consumed might not be equivalent to that actually eaten. However, in the present study, weight loss was more frequent in IVC housing than in OTC, and this result was related to food consumption. Regarding water consumption, guinea pigs also find bottles very attractive and repeatedly manipulate and shake the bottle caps, allowing the water to flow onto the bedding. However, water consumption did not differ between housing conditions in the present study.

In conclusion, our results showed that housing guinea pigs in IVC systems did not lead to relevant alterations in heart rate or locomotor activity, whereas food consumption was reduced and body weight was slightly decreased in some animals. Our findings provide useful information about the effect of moving guinea pigs to IVC and its apparent lack of strong negative effects on the wellbeing of this species. These preliminary results require further and longer studies to ascertain the importance of changes in food consumption and the effects of IVC housing on other stress parameters, such as cortisol levels.

Acknowledgments

We thank Ms Laia Benavent for her invaluable technical assistance during the course of this study.

References

1. **Akita M, Ishii K, Kuwahara M, Tsubone H.** 2001. The daily pattern of heart rate, body temperature, and locomotor activity in guinea pigs. Exp Anim **50:**409–415.
2. **Baumans V, Schlingmann F, Vonck M, van Lith HA.** 2002. Individually ventilated cages: beneficial for mice and men? Contemp Top Lab Anim Sci **41:**13–19.
3. **Büttner D, Wollnik F.** 1982. Spontaneous short-term fluctuations in the daily pattern of heart rate, body temperature and locomotor activity in the laboratory rat. Lab Anim **16:**319–326.
4. **Castelhano-Carlos MJ, Baumans V.** 2009. The impact of light, noise, cage cleaning and in-house transport on welfare and stress of laboratory rats. Lab Anim **43:**311–327.
5. **European Commission.** 2013. Report from the Commission to the European Parliament and the Council on the overall operation of official controls on food safety, animal health, animal welfare, and plant health in member states. Brussels (Belgium): European Commission
6. **Fox JG, editor.** 2002. Laboratory animal medicine. 2nd ed. Amsterdam (NY): Academic Press.
7. **Giral M, García-Olmo DC, Kramer K.** 2011. Effects of wire-bottom caging on heart rate, activity, and body temperature in telemetry-implanted rats. Lab Anim **45:**247–253.
8. **Krohn TC, Hansen AK.** 2002. Carbon dioxide concentrations in unventilated IVC cages. Lab Anim **36:**209–212.
9. **Krohn TC, Hansen AK.** 2010. Mice prefer draught-free housing. Lab Anim **44:**370–372.
10. **Krohn TC, Hansen AK, Dragsted N.** 2003. The impact of cage ventilation on rats housed in IVC systems. Lab Anim **37:**85–93.
11. **Li P, Sur SH, Mistlberger RE, Morris M.** 1999. Circadian blood pressure and heart rate rhythms in mice. Am J Physiol **276:**R500–R504.
12. **Percy DH, Barthold SW.** 2007. Pathology of laboratory rodents and rabbits, 3rd ed. Ames, (IA): Blackwell Publishing Professional.
13. **Provan G, Stanton A, Sutton A, Rankin-Burkart A, Laycock SK.** 2005. Development of a surgical approach for telemetering guinea pigs as a model for screening QT interval effects. J Pharmacol Toxicol Methods **52:**223–228.

14. **Quesenberry KE, Carpenter JW.** 2004. Ferrets, rabbits and rodents: clinical medicine and surgery, 3rd ed. St. Louis (MO): WB Saunders Company.
15. **Reeb-Whitaker CK, Paigen B, Beamer WG, Bronson RT, Churchill GA, Schweitzer IB, Myers DD.** 2001. The impact of reduced frequency of cage changes on the health of mice housed in ventilated cages. Lab Anim **35:**58–73.
16. **Shiotani M, Harada T, Abe J, Sawada Y, Hashimoto K, Hamada Y, Horii I.** 2005. Practical application of guinea pig telemetry system for QT evaluation. J Toxicol Sci **30:**239–247.
17. **Stemkens-Sevens S, van Berkel K, de Greeuw I, Snoeijer B, Kramer K.** 2009. The use of radiotelemetry to assess the time needed to acclimatize guineapigs following several hours of ground transport. Lab Anim **43:**78–84.