

Using home-cage monitoring to determine the impact of repeated timed mating on male mouse welfare



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All animal studies were ethically reviewed and carried out in accordance with Animals (Scientific Procedures) Act 1986 and the GSK Policy on the Care, Welfare and Treatment of Animals

Introduction

Some of our Genetically Altered mouse breeding programmes include the use of strain of sterile Prr1 male mice. These males are used to induce pseudopregnancy in female mice and are often kept for up to nine months under singly housed conditions. One refinement we previously made is to house these males with a companion female. During the timed mating period the companion is swapped for a naive female. We wanted to determine whether there was a significant impact on their welfare when their stable pair was disrupted.

We hypothesized that the impact in cage activity is significantly increased when a companion female is replaced with a new female, rather than when the companion female is left with the male. We used an established home-cage monitoring system to determine how much disruption is created to the activity pattern in cages when a companion female is swapped compared to when she is just removed and replaced in the pair's home-cage.

Method

We allocated 20 pairs of established and proven sterile *Prr1 males with their companion females and 20 naive females that were weight matched to the companion they would be exchanged with. On arrival to the animal room the mice were checked carefully and acclimatised for five days prior to the start of the study. Mice were kept on a 14:10 light:dark cycle.

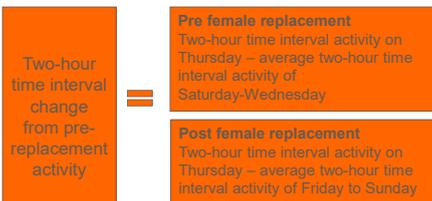
*Prr1 Genetically Sterile Protamine-1 (Prr1) EGFP Transgenic mouse obtained under licence from Dr Pawel Pelczar, University of Zurich, Switzerland (Hauster et al, 2010)

| Date of activity | Activity to be completed |
|---|--|
| Friday 6 th December | All selected cages were cage changed. |
| Monday 9 th December | The cages were randomised by naive female weight to the Group One Companion. |
| Thursday 12 th December 07:00-08:00hrs | Each male mouse in group one had his companion female replaced with a similarly matched by weight female. A note of the time the last cage was replaced on the rack was made. <ul style="list-style-type: none"> Group 1: the cage was removed from the rack and the companion female replaced with a naive female Group 2: the cage was removed from the rack, each female was removed from the cage then put back with the male. |
| Monday 16 th December | All females were replaced with the original companion female. Study ends. |

Table 1: Outline of study protocol

Activity sampling

We focused on the activity during four x two-hour intervals per comparison day; 8am-10am, 10am-12pm, 12pm-14.00hrs and 20.00-22.00hrs. For each time interval we calculated the change from pre female replacement for each cage to determine the activity increase or decrease on the day of female replacement compared to the previous days in the same time frame.



Results

The analysis focused on the pre-female and post-female replacement. Comparing:

1. Activity for each cage on the day of female replacement (Thursday) to the average activity of the five previous days.
2. Activity for each cage on the Thursday to three following days.

Pre female replacement

There was more variability in the activity data sampled between 8am-10am. Figure 1 shows a slight increase in activity for Group 1 during 10am-12pm on the Thursday compared to previous days (see Figure 1).

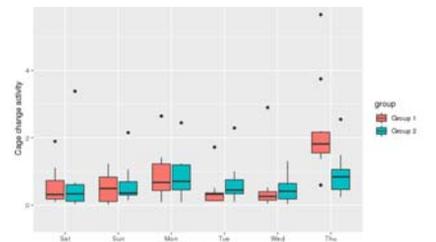


Figure 1: Average activity per day and cage between 20.00-22.00hrs

We completed a one-way factorial ANOVA on the change from baseline measurement for each time interval comparing the average activity of the previous days in the same timeframe. We found no significant difference in activity for the 8-10am time frame or the 12.00-14.00hrs and 20.000-22.00hrs time frame. There was a significant increase in activity (P=0.0198) between the groups during the 10.00am-12.00pm time frame (see Figure 2).

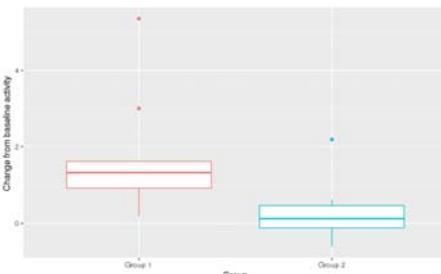


Figure 2: Change from baseline between 10.00am-12.00pm

Post-female replacement

There was more variability in the activity data sampled between 8am-10am. Figure 3 shows decreasing activity for Group 1 between 10am-12pm for each subsequent day (see Figure 1).

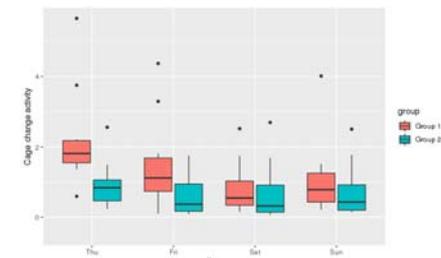


Figure 3: Average activity from 10am-12pm per day

We completed a one-way factorial ANOVA on the change from baseline measurement for each time interval comparing the average activity of the following days in the same timeframe. We found no significant difference in activity for the 8-10am time frame or 20.000-22.00hrs time frame. There was a significant increase in activity between the groups during the 10.00am-12.00pm time frame (P=0.0036), (see Figure 4) and 12.00-14.00hrs (P=0.023), (See Figure 5).

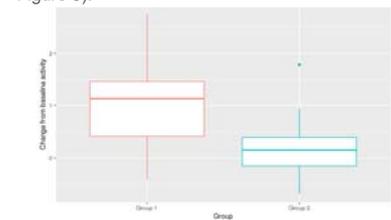


Figure 4: Change from the baseline between 10.00am-12.00pm

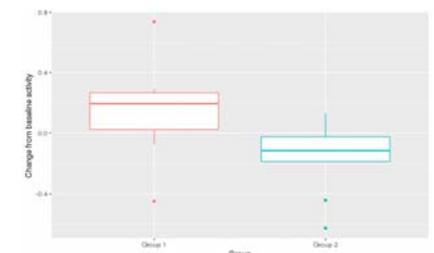


Figure 5: Change from the baseline between 12.00pm-14.00hrs

Discussion

When time mating animals (females are left overnight with a male then removed to accurately assess stage of pregnancy), the male is often individually housed for up to nine months. Using the sterile male mice we are already able to house them with a companion. During our initial study the activity caused by the replacement female was still visible when completed at the same time as cage changing (Unpublished data) in the two hours directly after the activity which is in agreement with the results of this study. We found more variability in the activity data sampled between 8am-10am likely due to staff presence in the room. Between 20.00-22.00hrs the decrease in activity from group one compared to group two (after female replacement) is likely to the mice being more active during the light phase and possibly fatigued during the dark phase. Regardless of the impact of timed mating itself on male mouse welfare (it could be seen as a positive), the disruptions caused by the intense activity seen in group where female were replaced, during their usually inactive hours followed by periods fatigue during active hours, is likely to have an effect on their circadian rhythm. This effect likely leads to poor welfare in the replacement group versus the group where the companion was left with the male. It would be interesting to see if the increase in activity was mirrored when the companion female is replaced or if timed mating was carried out at the end of the working day, nearer to the active time of the mice. Home cage activity monitoring gives us the unique ability to increase our understanding of how the work we do can impact the welfare of animals, thus giving us an opportunity to refine our processes to further meet their needs.

Acknowledgements

Guido Gottardo, Fabio Iannello, Techniplast S.p.A
Kay Dewar, IVSD, GSK
Steve Barrett, Research Statistics, GSK
Steve Wilson, IVSD, GSK

Reference

Hauster et al. Overexpression of Prr1-EGFP fusion protein in elongating spermatids causes dominant male sterility in mice. 2010. Genesis. 48 (3): 151-160. doi.org/10.1002/dvg.20598