Reducing Aggressive Behavior in Mice with the Addition of Cage Dividers

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Introduction

Reducing aggressive behavior in mice has long been the goal of institutions and investigators. The consequence of identified aggressive behavior is single housing, which impacts animal social behavior and welfare, and increases research costs. Our goal was to develop a method to reduce aggression in group-housed mice, which maintained social housing and avoided drugs or techniques that modified behavior from "normal". Additionally, the solution could not incur undue costs (research or resources) or work for laboratory animal staff.

Mice reared in a complex cage system that emulates a burrow-like environment will lead to healthier, less reactive mice (Chamove, 1989). Few publications evaluate the effects of cage dividers or complex caging in mice. Of those that do, the modifications include a much larger cage, or caging system, that varied in the complexity of customization to cages. No simple, cost effective home-cage interventions are available to reduce aggression and maintain animal welfare. Therefore, we conducted an observational study of group-housed mice within standard disposable individually ventilated mouse cages with the addition of custom built dividers.

Hypothesis

Cage dividers, which provide burrows and common access to food/water for mice in their home-cage, reduce aggressive behavior in group-housed mice.

Methods

- 18 Balb/c male mice at ~ 8 weeks of age were divided into two groups upon arrival: non-divided, standard caging; and divided, standard caging.
- Each group's (n=9) cage density was 3 mice per cage (3 cages per group).
- The dividers provided access to a 'common area' (wherein water is located) and 3 burrow-like structures (each with food access).
- A camera was positioned at the rear of each cage to record mouse behavior in 12 hour increments (6 hours of light cycle, light:dark transition, 6 hours of dark cycle).
- Recordings occurred on the day of receipt (introduction to the new environment), 24 hours later, and 7 days later.
- Recordings on days 1 and 2 represent the animals' acclimation to the new environment, and recordings on day 7 represent post-acclimation and the establishment of a hierarchy.
- Videos were reviewed for behavior, aggression, and group dynamic, and were scored on an Animal Activity Score Sheet developed for this study. For each cage, the number and severity of each event was recorded over one hour intervals. Each aggressive behavior event received a score from 1 to 5.
  - 1 - Posturing: mounting, pouncing, chasing, barking, and tail twitch
  - 2 - Scuffling
  - 3 - Unprovoked biting
  - 4 - Blood being drawn
  - 5 - Injury that results in veterinary attention

The Cage Divider*

- Custom made from a single piece of corrugated plastic.
- Held in place by the hanging feed hopper, without restricting access.
- Fits inside existing cages without modification to the enclosure.
- Provides three isolation "burrows" and a common room.
- Makes the cage appear to be psychologically larger (Chamove, 1989).
- Does not decrease floor space.
- Permits line-of-sight observation of cohabitants.
- Does not impair airflow in individually ventilated caging (IVC).

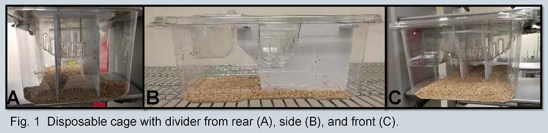

Fig. 1 Disposable cage with divider from rear (A), side (B), and front (C).

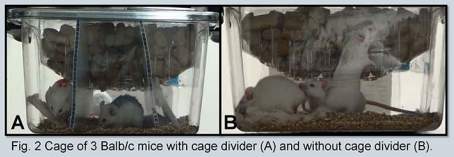

Fig. 2 Cage of 3 Balb/c mice with cage divider (A) and without cage divider (B).

* U.S. Patent Pending

Cage dividers decrease aggressive behavior in light and dark cycles

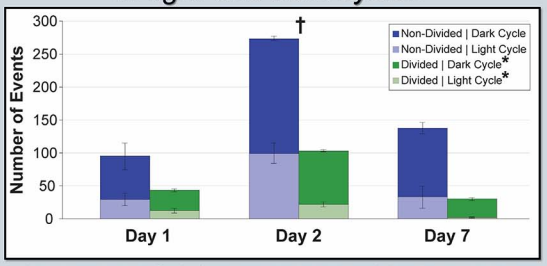

Fig. 3 Divided cages had significantly fewer aggressive behavior events than the non-divided cages, in terms of total number of events ($F(1,4) = 280.189$, $p=0.000$, *), events in the light cycle ($F(1,4) = 38.822$, $p=0.003$, *), and events in the dark cycle ($F(1,4) = 289.053$, $p=0.000$, *). For total events ($F(2,8) = 19.840$, $p=0.001$, *), light cycle events ($F(2,8) = 8.915$, $p=0.009$, *), and dark cycle events ($F(2,8) = 31.255$, $p=0.000$, *), the number of aggressive behavior events on day 2 were significantly greater than on day 1 and day 7 (post-hoc, †). There were no interactions regarding the total number of events between divided and non-divided cages over time ($F(1,4) = 280.189$, $p=0.000$).

Cage dividers decrease aggressive behavior over days and time

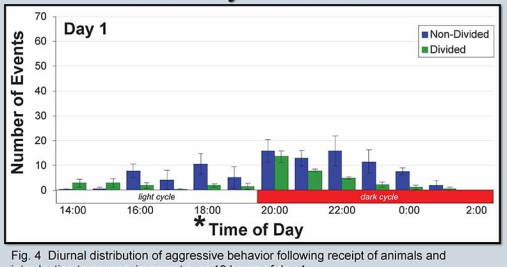

Fig. 4 Diurnal distribution of aggressive behavior following receipt of animals and introduction to new environment over 12 hours of day 1.

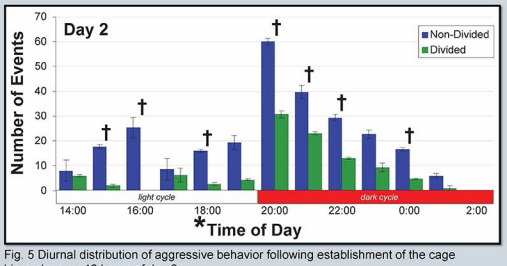

Fig. 5 Diurnal distribution of aggressive behavior following establishment of the cage hierarchy over 12 hours of day 2.

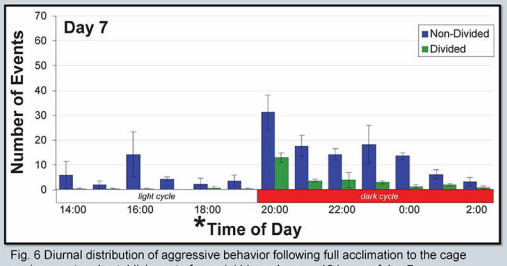

Fig. 6 Diurnal distribution of aggressive behavior following full acclimation to the cage environment and establishment of a social hierarchy over 12 hours of day 7.

As expected, the number of aggressive behavior events significantly differs over the time of day at day 1 ($F(12,48) = 8.982$, $p=0.000$, *), day 2 ($F(12,48) = 96.437$, $p=0.000$, *), and day 7($F(12,48) = 7.017$, $p=0.000$, *). Divided cages significantly reduced aggressive behavior events on day 2 ($F(12,48) = 96.437$, $p=0.000$), with significance at individual hours shown (post-hoc, †).Significant interactions regarding the total number of events between divided and non-divided cages over hours were observed on day 1 ($F(12,48)=2.143$, $p=0.031$) and day 2 ($F(12,48)=12.429$, $p=0.000$).

Cage dividers decrease the incidence of aggressive behavior severities

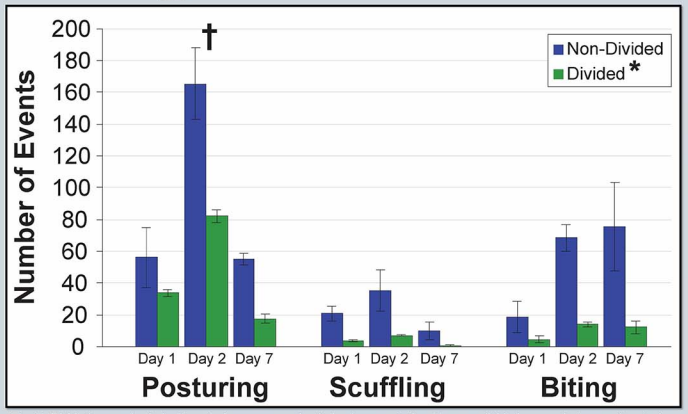

Fig. 7 Divided cages had significantly fewer aggressive behavior events than the non-divided cages, in terms of posturing ($F(1,4) = 44.330$, $p=0.003$, *), scuffling ($F(1,4) = 20.360$, $p=0.011$, *), and unprovoked biting ($F(1,4) = 23.710$, $p=0.002$, *). On day 2, more posturing was counted in comparison to day 1 and day 7 ($F(2,8) = 24.301$, $p=0.000$, †). No events of blood drawn or veterinarian intervention were observed. Comparisons between severities were not conducted. There were no interactions regarding the total number of posturing events between divided and non-divided cages over time ($F(2,8)=2.632$, $p=0.132$).

Conclusions

- The use of cage dividers showed significant reductions in aggressive behavior in group-housed Balb/c male mice. This included the number and severity of aggressive behavior over days and time.
- Cage dividers led to fewer aggressive interactions when compared to standard housing, and could improve animal welfare and serve as environmental enrichment.
- Cage dividers can be considered as an intervention for mice that show aggressive behavior, or during studies that experimentally increase aggressive behavior.
- The reduction of aggressive behavior may reduce injuries that require separation of animals and increase research costs
- Cage dividers may collapse the social hierarchy and control environmental stressors, thereby reducing variability between animals and improving scientific rigor.

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Reference

1. A.S. Chamove. 1989. Cage design reduces emotionality in mice. Laboratory Animals **23:**215-219.

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