Published in final edited form as:

Lab Anim. 2017 December ; 51(6): 647–651. doi:10.1177/0023677217711966.

Locomotor effects of a low-frequency fire alarm on C57BL/6 male mice: a preliminary study

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Abstract

Maintaining appropriate acoustic conditions for animal welfare and data collection are crucial in biomedical research facilities. Negative impacts of disruptive sound are known and can include auditory damage, immune function changes, and behavioral alterations. One type of disruptive sound occurring in research facilities is that of fire alarms. To ameliorate this problem, many facilities have incorporated the use of low-frequency fire alarms that emit tones outside the rodent audible range. The impact of these devices has been assumed to be negligible. However, this has yet to be evaluated with controlled behavioral experiments. Thus, our objective was to investigate the impact of low-frequency fire alarm exposure on locomotor behavior in the open field, a test sensitive to acoustic stimuli disruption. Male mice were randomized to three alarm exposure groups (No-Alarm; Alarm-During; and Alarm-After) and placed in individual photobeam-activated locomotor chambers. The Alarm-During group displayed significantly reduced horizontal locomotion, with a trend towards reduced vertical locomotion. These data suggest that a low-frequency brief alarm tone can temporarily disrupt movement, a valuable insight should an alarm be deployed. Further, findings support close collaboration between researchers and institutional facility staff to ensure appropriate acoustic conditions are maintained, whenever possible, for research animals.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Abstract

Le maintien de conditions acoustiques appropriées pour le bien-être des animaux et la collecte de données est crucial au sein des infrastructures de recherche biomédicale. Les effets négatifs des bruits perturbateurs sont connus et peuvent causer des dommages auditifs, des modifications de la fonction immunitaire et des altérations comportementales. Les alarmes incendie sont un exemple de bruit perturbateur présent dans les infrastructures de recherche. Afin de remédier à ce problème, de nombreuses installations ont intégré l'utilisation d'alarmes incendie à basse fréquence qui émettent des tonalités en dehors de la plage audible des rongeurs. L'impact de ces dispositifs a été supposé négligeable. Cependant, cela n'a pas encore été évalué lors d'expériences comportementales contrôlées. Ainsi, notre objectif était d'étudier l'impact de l'exposition à l'alarme incendie à basse fréquence sur le comportement locomoteur en plein air, un test sensible aux perturbations des stimuli acoustiques. Des souris mâles ont été réparties de manière aléatoire dans trois groupes d'exposition à l'alarme (pas d'alarme ; pendant l'alarme ; après l'alarme) et placées dans des cages d'activités locomotrices individuelles activées par des faisceaux lumineux. Le groupe « pendant l'alarme » présentait une activité locomotrice horizontale nettement réduite et une tendance à la réduction de l'activité locomotrice verticale. Ces données suggèrent qu'une brève tonalité d'alarme à basse fréquence est susceptible de perturber temporairement le mouvement, information précieuse en cas de déclenchement d'une alarme. En outre, ces résultats encouragent une collaboration étroite entre les chercheurs et le personnel des infrastructures institutionnelles afin de garantir le maintien de conditions acoustiques appropriées pour les animaux de recherche à chaque fois que cela est possible.

Abstract

Die Wahrung geeigneter akustischer Bedingungen ist für Tierwohl und Datenerfassung in biomedizinischen Forschungseinrichtungen von höchster Bedeutung. Zu den bekannten negativen Auswirkungen störender Geräusche zählen Gehörschädigung sowie Immunfunktions- und Verhaltensänderungen. Ein in Forschungseinrichtungen auftretendes Störgeräusch ist das von Feuermeldern. Zur Behebung dieses Problems haben viele Einrichtungen Niederfrequenz-Feuermelder installiert, die Töne jenseits des Hörbereichs von Nagern ausgeben, in der Annahme, dass die Auswirkung dieser Geräte vernachlässigbar sei. Dies war allerdings noch anhand kontrollierter Verhaltensexperimente nachzuweisen. Ziel der vorliegenden Studie war daher die Untersuchung der Auswirkung von Geräuschbelastungen durch Niederfrequenz-Feuermelder auf lokomotorisches Verhalten im Freifeld, ein Test für akustische Reizstörung. Männliche Mäuse wurden randomisiert in drei Meldergeräuschen ausgesetzten Gruppen eingeteilt (kein Alarm, während des Alarms, nach dem Alarm) und in individuellen, Lichtstrahl-aktivierten Lokomotorkammern untergebracht. Bei der "während des Alarms" untersuchten Gruppe war eine wesentliche Abnahme horizontaler Bewegung und eine Tendenz zu reduzierter vertikaler Bewegung zu erkennen. Diese Daten legen nahe, dass ein kurzer Niederfrequenz-Alarmton zu vorübergehender Bewegungsstörung führen kann – eine wichtige Erkenntnis für den Einsatz von Meldegeräten. Außerdem stützen die Ergebnisse eine enge Zusammenarbeit zwischen Forschern und dem Personal von Einrichtungen im Interesse einer weitestgehenden Wahrung optimaler akustischer Bedingungen für Versuchstiere.

Abstract

Mantener unas condiciones acústicas adecuadas para el bienestar animal y la recopilación de datos es crucial en las instalaciones de investigación biomédica. Los impactos negativos de ruidos molestos son conocidos y pueden incluir daños auditivos, cambios en la función inmune y alteraciones del comportamiento. Uno de los ruidos molestos que se dan en las instalaciones de investigación son las alarmas contraincendios. Para mejorar este problema, muchas instalaciones han incorporado el uso de alarmas contraincendios de baja frecuencia que emiten tonos fuera del campo auditivo de los roedores. Se ha asumido que el impacto de estos dispositivos es insignificante. No obstante, esto todavía tiene que evaluarse con experimentos controlados del comportamiento. Por ello, nuestro objetivo era investigar el impacto de la exposición a alarmas contraincendios de baja frecuencia en el comportamiento locomotor en campo abierto, una prueba sensible a la perturbación de estímulos acústicos. Se aleatorizaron ratones macho en tres grupos que serían expuestos a distintas alarmas (no alarma; alarma-durante; alarma-posterior) que, asimismo, se colocarían en cámaras locomotoras individuales activadas mediante fotobeam. El grupo Alarma-durante mostró un locomovimiento horizontal reducido muy significativo con una tendencia a un locomovimiento vertical reducido. Estos datos sugieren que un tono de alarma breve de baja frecuencia puede perturbar temporalmente el movimiento, una conclusión valiosa en caso de que se utilice una alarma. Asimismo, otras conclusiones respaldan una colaboración estrecha entre investigadores y el personal de instalaciones institucionales para garantizar unas condiciones acústicas adecuadas para los animales de investigación en la medida de lo posible.

Keywords

noise; fire alarm; animal welfare; rodent behavior; locomotion

Ensuring appropriate environmental conditions in biomedical research facilities is crucial both for animal welfare and for scientific integrity of preclinical data. Of these conditions, acoustic disruption has the potential to adversely impact rodents housed within these facilities.^{1,2} These impacts can include an altered immune response, hearing loss, induction of seizures in some rodent strains, and behavior changes, all of which can have secondary effects on experimental variables.^{3–6} One of the many sounds heard by laboratory animals is from fire alarms. Unlike other types of acoustic disturbances (such as building construction) that can be scheduled to minimize negative impacts on laboratory animals through collaborative interaction among researchers veterinary/husbandry technicians, and facility staff, disturbances due to fire alarms are generally unpredictable. To attempt to reduce the negative impacts of fire alarm exposure on laboratory animals, many research facilities have incorporated the use of low-frequency fire alarms designed to emit sounds outside the audible range of rodents, but within the range of human audition.⁷ Functional assessment of laboratory animal behavior is highly sensitive to auditory disruption; yet, at present, the impact of low-frequency fire alarm disturbance on animal behavior has not been well-studied. Thus, the objective of this study was to characterize the behavioral impact of, and recovery from, exposure to low-frequency fire alarms in a typical experimental mouse model undergoing functional assessment.

The present study was conducted at West Virginia University, an institution accredited by AAALAC International (formerly the Association for Assessment and Accreditation of Laboratory Animal Care). All procedures were evaluated and approved by the West Virginia University Institutional Animal Care and Use Committee (IACUC). C57BL/6 (C57BL/6NCrl) specific pathogen-free (SPF) male mice ($n = 19$), aged five months, were purchased from Charles River Laboratories (Wilmington, MA, USA). The mice were maintained under typical laboratory conditions: 12 h light/dark cycle (light hours: 06:00 to 18:00 h), with an ambient room temperature of 20–26°C and a relative humidity of 30–70%. Animals were group-housed ($n = 4$ –5 per cage), in standard filter-topped, transparent cages, and provided with environmental enrichment in the form of crinkled paper strips (Uline Shipping Supplies, Allentown, PA, USA) and corncob bedding (Envigo, Indianapolis, IN, USA), as well as access to chow pellets and water ad libitum throughout the entire study. To test our hypothesis that a low-frequency fire alarm impacts rodent behavior, the mice were acclimatized to the testing room for 30 min and were then randomized to one of three fire alarm exposure groups (No-Alarm, $n = 6$; Alarm-During, $n = 7$; and Alarm-After, $n = 6$); $n = 6$ –7 per fire alarm exposure group allowed for the detection of trends, if not effects, in this preliminary study. Open field was the behavioral test chosen for the assessment as it is known to be sensitive to acoustic disruption in rodents.⁸ The animals were placed into individual 16×16×15 inch³ chambers (Photobeam Activity System; San Diego Instruments, San Diego, CA, USA) and were allowed to explore the arena for a 10 min trial; each trial was divided into four 2.5 min intervals. Horizontal and vertical movements were measured by determining the number of photo-beams disrupted by the animals. For animals in the Alarm-During group, the alarm (Silentone™; Paxton Processing, Charleston, IL, USA) was triggered immediately after the last animal was placed into its chamber (within the first interval for all mice). Animals in the Alarm-After group underwent testing approximately 15–25 min post-alarm exposure. Per the parameters of the Silentone™ fire alarm, a biphasic sound output of 97 dB was generated at a frequency of between 430 and 470 Hz.⁷ This range, well within the audible frequency range of humans (approximately 20–20,000 Hz),⁹ is outside the audible frequency range of mice (approximately 2000–96,000 Hz).^{7,9–11} The duration of alarm exposure was 60 s. The alarm unit, located within the same room where the behavior testing was conducted, was placed approximately 3±1.5 m from the multi-chamber set-up and approximately 4 m from the location in which the animals were placed prior to locomotor testing. After the study, animals were reallocated for other behavioral optimization purposes.

Locomotor data were analyzed using a repeated measures analysis of variance (ANOVA) with ‘Treatment’ as the between factor and ‘Interval’ as the repeated factor for each dependent variable (horizontal movement; vertical movement) separately. We were particularly interested in differences between the No-Alarm and Alarm-During or Alarm-After groups. Therefore, significant interactions or main effects were probed with hypothesis-driven, two-group planned comparisons set a priori. Data were analyzed using the Prism 7 software (GraphPad Inc, La Jolla, CA, USA) with alpha set to 0.05 as the threshold for significance. The results indicate that alarm exposure reduced movement (Figure 1). For horizontal movement, there was a significant Treatment main effect [$F(2,16)=3.684$, $P<0.05$]. Two-group planned comparisons probing this main effect revealed

a significant difference between the Alarm-During and No-Alarm groups [$t(11)=2.362$, $P<0.05$]. For vertical movement, there was a trend towards a Treatment main effect ($P=0.1$), with animals in the Alarm-During group appearing to move less than those in the No-Alarm group.

The results of this study demonstrate that mice that were briefly exposed to a low-frequency fire alarm exhibited changes in their locomotor behavior. Specifically, the animals in the Alarm-During group were less mobile than their No-Alarm group counterparts within the horizontal assessment. Marginal trends of locomotor reduction were also observed within the vertical assessment of the Alarm-During group relative to the controls. These findings could likely be attributed to the well-known acoustic startle response, in which animals exhibit freezing behavior in response to an aversive auditory stimuli.¹² Decreased locomotion due to the startle response could suggest that the animals are, in fact, able to hear the frequency range emitted by the fire alarm unit.

An alternative explanation to these findings could be that it is not the frequency, but rather one or more additional properties of sound that appear to be eliciting a response in the animals. Moreover, it is possible that the acoustic property of amplitude, or the sound pressure level (perceived as loudness; measured in decibels) of the alarm unit is such that it is capable of inducing sensory disturbance in our C57BL/6 N mice, as sensitivity to sound increases with increased sound pressure level.⁹ For example, animals may be responding to vibrations produced as a secondary effect of the alarm sound, rather than the alarm frequency itself. The direction of the sound is an additional acoustic property that could alter the response of the animals to the alarm unit. Indeed, sound direction dictates frequency discrimination in mice, as demonstrated by an increased sharpness of frequency tuning curves in mice that are associated with sound direction at an ipsilateral (rather than contralateral) angle.¹³

In addition to factors associated with the sound levels of fire alarm systems, behavioral responses to an unpredictable acoustic disruption could also be influenced by variables at an animal model level. For instance, age-related hearing loss in laboratory rodents is of particular concern given that some high-frequency hearing loss is documented in C57BL/6 N substrains around six months of age, with near deafness to high-frequencies among mice aged 18 months.¹⁴ Differences in frequency hearing capabilities among different age groups of mice (i.e. adolescent versus geriatric) in combination with distance of the alarm unit as a function of sound pressure level and/or sound direction could affect locomotor response to an acoustic disruption in laboratory animals.^{9,14} This situation is especially problematic should a disruption occur in studies involving animals of several different age groups. Given these factors, as well as the known sex differences on the impact of behavioral studies,¹⁵ future investigations should extend these findings to female mice as well as aging cohorts to better evaluate the gradations of hearing loss relative to age and sex.

Apart from the known sources of auditory disruption that can impact laboratory animals and induce startle responses,¹⁶ our data suggest that low-frequency fire alarms, designed specifically to minimize disruption of animals in research facilities, could also influence other laboratory rodents, such as rats, gerbils, and rabbits during locomotor behavior

characterization.^{17–19} Furthermore, the data presented here are likely to be an underestimation of the impact of alarm testing on the animals. Indeed, effect size and power calculations (G*Power, Version 3.0.10) from the current findings revealed a large effect size ($d = 1.293$) but low observed power (56%) for horizontal movement comparison of the No-Alarm and Alarm-During groups. This indicates that the current study was likely underpowered, and was susceptible to an increased likelihood of making a type II error (not detecting a significant effect of the alarm, when in fact, one exists in the population).²⁰ Moreover, although some evidence of behavioral recovery (Figure 1: No-Alarm versus Alarm-After groups) was found following the brief alarm deployment used here, longer durations typical of emergency situations could exacerbate the impact of, and prolong recovery from, alarm exposure.

In conclusion, prioritization of animal welfare and data integrity in research facilities, given the necessity of fire alarms which may nonetheless impact locomotor behavior among laboratory animals, can be achieved through the cooperative and collaborative efforts of research scientists, veterinary and animal husbandry staff, and facility employees. This can be done by working together to minimize non-emergency alarm conditions (e.g. alarm testing) in order to ensure that appropriate acoustic conditions are present wherever possible.

Acknowledgement

We wish to thank James W Simpkins, PhD, for his insightful feedback during the preparation of this manuscript.

Funding

The author(s) received financial support for the research, authorship, and/or publication of this article from GM109098 and GM104942 as well as WVU intramural funds awarded to EBE-C and James W Simpkins, PhD.

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Figure 1.

Open field locomotion (mean $\pm$ SEM, number of beam breaks). (a) Repeated measures analysis of variance (ANOVA) of horizontal movement revealed a main effect of Treatment ($P < 0.05$). (b) T-tests probing the Treatment main effect (a) revealed a significant reduction in horizontal movement in the Alarm-During versus the No-Alarm groups ($P < 0.05$). (c) Repeated measures ANOVA of vertical movement revealed a trend towards a main effect of Treatment ($P < 0.1$). (d) Visual inspection of the graph suggests that alarm exposure during the trial tends to reduce movement relative to the No-Alarm group. ■ No-Alarm; ■ Alarm-During; ■ Alarm-After.