

REVIEW ARTICLE

Vibration in mice: A review of comparative effects and use in translational research

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Abstract

Sound pressure waves surround individuals in everyday life and are perceived by animals and humans primarily through sound or vibration. When sound pressure waves traverse through a solid medium, vibration will result. Vibration has long been considered an unwanted variable in animal research and may confound scientific endeavors using animals. Understanding the characteristics of vibration is required to determine whether effects in animals are likely to be therapeutic or result in adverse biological effects. The eighth edition of the “Guide for the Care and Use of Laboratory Animals” highlights the importance of considering vibration and its effects on animals in the research setting, but knowledge of the level of vibration for eliciting these effects was unknown. The literature provides information regarding therapeutic use of vibration in humans, but the range of conditions to be of therapeutic benefit is varied and without clarity. Understanding the characteristics of vibration (eg, frequency and magnitude) necessary to cause various effects will ultimately assist in the evaluation of this environmental factor and its role on a number of potential therapeutic regimens for use in humans. This paper will review the principles of vibration, sources within a research setting, comparative physiological effects in various species, and the relative potential use of vibration in the mouse as a translational research model.

KEYWORDS

animal models, mice, translational, vibration

1 | INTRODUCTION

Translational research is commonly referred to as the combining of various scientific disciplines and using the expertise of individuals working within those disciplines to accelerate basic scientific findings into advances for novel therapeutics, medical devices, and treatment regimens for human patients.¹ Basic scientific endeavors may use various in vitro methodologies, but prior to clinical use in humans, studies in animals are imperative to fully assess diagnostic or therapeutic modalities. Animals and humans share the same organ

systems, and many therapeutics and procedural regimens are comparable as well. These similarities lead to the use of animals as translational models of human disease. The animal model is selected because it is predictive of the specific disease in humans and in whole or part, the animal model will respond to medical intervention similar to humans.

Novel therapeutics require assessment of efficacy in animals, but the lack of validation of the animal model can result in erroneous interpretation of data from the model and lead to lack of predictability during extrapolation to humans.² Success rates of novel

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therapeutics in humans during clinical development remain low due to the lack of relative levels of efficacy in preclinical testing, including animal models and in humans during clinical trials.^{2,3} Careful attention to the assessment of a proposed animal model is critical to ensure species differences are identified and considered in the process. Similarly, reproducibility and transparency of published research using animals is imperative to ensure characterization of a model that will be predictive of human biology and disease.^{4,5} Thus, it is critical to define the criteria being assessed within the animal model to ensure translational success in humans.

This paper reviews the current understanding of vibration in the research setting. The most recent revision of the “Guide for the Care and Use of Laboratory Animals” highlights the importance of considering vibration and its effects on animals in research.⁶ Vibration likely elicits stress-mediated effects, as reported in the literature, but scant information is available on the level of vibration (threshold) that will cause effects or on the nature of the effects in animals. Understanding the threshold effects of vibration ultimately will assist in the evaluation of this environmental factor and its potential role in a number of therapeutic regimens in humans. This paper summarizes the basic principles of vibration, sources within a research setting, comparative physiological effects in various species and the potential use of vibration in the mouse, relative to other species, as a translational research model.

2 | PRINCIPLES OF VIBRATION

Sound and vibration are forms of energy that travel in waves with sound being perceived by what we hear and vibration by what we feel. In fact, sound is comprised of pressure waves caused by movement of air particles that can be detected by either a human or animal. These waves are oscillatory in nature and have both an amplitude and frequency. The amplitude contributes to the intensity of the sound or vibration and is represented by how far the peak of the wave moves past the position of equilibrium. Frequency is the amount of time that it takes to complete one cycle from a point on one wave to the same point on the next wave. The term “Hertz” is used as a unit of measure for frequency and is the number of cycles per second. One Hertz (Hz) is one cycle per second.⁷ The magnitude or loudness of sound is measured in decibels, whereas the magnitude of vibration can be measured in relation to the amplitude by displacement from the point of equilibrium (often measured in millimeters), the velocity of wave movement (quantified in meters per second) or acceleration past the neutral point measured in meters per second squared (m/s^2).^{8,9}

Both the magnitude and frequency of sound and vibration are important in the perception and potential adverse or therapeutic effects in humans and animals. For example, the human hearing range is from 20 Hz to 20 kHz and the mouse hearing range is from about 1 kHz to 100 kHz.¹⁰ Likewise, an object will vibrate differentially based on its physical composition and will also tend to vibrate at some frequencies more than others. The frequency where

vibration occurs most readily and can amplify the vibration is called the resonance frequency. The resonance frequency is located within the resonance frequency range (RFR), where the vibration would become greater at frequencies closer to the resonance frequency and somewhat less at the ends of the range. These frequency ranges are unique to an animal, a body region, or any other object and are dependent on that subject's physical composition with regard to “stiffness” and mass. Any object or part of an animal's body has a resonance frequency (F_n), which is calculated by the formula $F_n = 1/(2\pi) \times \sqrt{k/m}$, where k is the stiffness constant, and m is the mass.^{11,12} Knowledge of resonance frequencies is important because vibration near these frequencies, compared with other frequencies, will be perceived more strongly and ultimately will induce more physiological effects, including those considered harmful.¹³ Therefore, different species or size of animals may perceive vibration to a lesser or greater degree depending on the frequency of the vibration. In addition to the frequency of vibration, other factors that will determine the effects on animals include magnitude, duration, whether the vibration is directed at the whole body or is localized, and potentially individual variation in perception across species or within the same species.

Because both frequency and magnitude impact the exposure level of vibration, the interpretation of the literature with regard to both beneficial and adverse effects of vibration can be difficult. Until recently, only the resonance frequency of the liver had been determined in mice, which is 2-7 Hz.¹⁴ The predicted resonance frequency for the mouse was calculated^{11(p655)} and then studied by performing measurements in both rats and mice.¹⁵ Importantly, the resonance frequency for a single organ is quite different than the vibrating frequency of the entire body in cumulative. Similarly, different body regions of a human or animal will have different RFRs. For example, the human abdomen has a resonance frequency of 4-8 Hz, the thorax of 5-10 Hz, and the head from 20 to 30 Hz.¹⁶ In rats, the RFR was 27-29 Hz for the abdomen, 225-230 Hz for the thorax, and 75-80 Hz for the head.¹⁷ Although resonance frequencies had not been reported for mouse anatomical regions, the predicted RFRs for mice were 85-92 Hz for the abdomen, 711-727 Hz for the thorax, and 237 to 253 Hz for the head when assuming equivalent inherent stiffness of tissue is similar in mice and humans.^{11(p655)} Anesthetized mice that were exposed to vibration generally attenuated vibration that would have been detected by a mounted accelerometer on their back, except for vibration in the ranges of 30-100 Hz. Instead, the magnitude of the vibration in these ranges was either equal to or greater than the applied vibration, indicating that the RFR for these animals lie within these ranges.^{15(p1963)} Mice that were exposed to vibration at 80 and 90 Hz showed increases in blood pressure and/or heart rate, whereas no increases were observed with frequencies 70 Hz or less or with 100 Hz or greater.¹⁸ A recent study has demonstrated that mice show more behavioral alterations due to whole-body vibration (WBV) predominantly between the frequencies of 70-100 Hz.¹⁹ Therefore, mice appear to be the most sensitive to vibration between frequencies of 70-100 Hz. Within this RFR, mice should be most susceptible to low

level vibration, which would likely most affect an animal's normal physiological and behavioral functions.

3 | SOURCES OF VIBRATION IN RESEARCH SETTING

Because the care of animals requires the use of mechanical systems and equipment, vibration will be present in the animal facility to some degree. There are three general sources of vibration: vibration produced from mechanical systems or procedures within the animal facility; vibration produced outside, but near the animal facility; and vibration resulting from the transportation of animals from the vendor or to locations within an animal program. Sources of vibration that occur within the animal facility include ventilation systems, husbandry-associated cleaning and sterilizing equipment, ventilated racks, and cage change stations.^{11(p656),20} There are several studies regarding the numerous effects of construction noise and vibration on rodents that have detailed effects such as increases in corticosterone levels and other alterations in biochemical parameters or reproductive efficiency.²¹⁻²⁸ Recently, studies have begun to separate the effects of construction noise vs vibration. In one study, dams of two strains of mice were exposed to vibration levels comparable to that produced in an animal facility from proximal construction.^{23(p3)} While no changes in overall fertility were noted, nursing dams did show some alterations in normal maternal behavior. The study raised several important points to consider with regard to construction-induced vibration. Specifically, vibration from outside sources (ie, construction, trains) is often produced in sudden, intermittent bursts in contrast to vibration produced over long continuous time periods. Intermittent vibration is thought to produce more adverse effects than continuous vibration due to its unpredictability.^{23(p3)} While no changes in fertility were detected in this study, other research has demonstrated increased rates of abortion, cannibalism, and resorptions following construction procedures in proximity to animal facilities.²⁹ High rates of cannibalism were also observed in a mouse housing room located near an active railroad.^{22(p737)} Measurements were taken to adequately characterize the frequency and magnitude of both the sound and vibration produced by the passing train. While most sound that was produced was outside the range of mouse hearing, significant vibration of up to 0.25 m/s^2 was generated. In addition, the exposed female mice exhibited higher corticosterone levels relative to female mice that were not vibrated.^{22(p737)} Lastly, the transportation of animals by vehicle, by a hand-pushed cart, or by hand has been shown to produce a relatively high degree of vibration exposure.^{30,31} Using an accelerometer placed inside a standard polycarbonate mouse cage, vibration was measured during transportation by either hand-carrying or with several types of carts. With transport of the cage along a set pathway, vibration within the cage varied by as much as 35 m/s^2 between the transportation methods, suggesting that movement of animals even between rooms and buildings, which is common in many research environments, can

subject animals to considerable vibration.^{31(p544)} For this reason, animals should be provided with an opportunity to recover from vibration exposure before being used in scientific experiments. Mice that were transferred from their housing room to another room across the hall and placed on a shaker apparatus, with no vibration administered, took between 1.5 hours to approximately 24 hours for their active behaviors (eg, locomotion, rearing, sniffing) and inactive/maintenance behaviors (eg, sleeping, grooming, eating) to return to pre-transport levels.¹⁹

While it is not always possible to completely mitigate vibration from sources such as trains, subways or proximal construction, these factors should be taken into consideration during the design and location site planning for animal facilities. In addition, care should be taken to reduce vibration from cage movement and disturbances within the animal room or between locations within an institution. Even when rodents are exposed to movement from opening cages for routine experiments or normal husbandry activities, animals may be stressed. For example, rats have been shown to have higher corticoid metabolites in their feces following husbandry procedures.³² Appropriate training of research personnel and staff can help mitigate some of these effects with proper handling. Even simple measures and policies, such as limiting cell phone use in animal facilities can have an effect. In a study with rats, exposure to intermittent noise and vibration from cell phones increased anxiety-like behavior during plus maze testing.³³ Vibration-induced effects should also be considered when obtaining materials and equipment for animal facilities. For instance, most modern individually ventilated racks have a heavy construction with clips to hold cages in place. Such racks may be better at dampening short bursts of vibration compared to other types of racks. In addition, in one study that looked at vibration produced by common transport carts used in a facility, metal carts with large wheels helped to decrease vibration at the cage level. Using padding on the carts also helped to further dampen vibration's accelerative forces.^{31(p546)}

4 | ADVERSE VIBRATION EFFECTS AND POTENTIAL BENEFITS IN ANIMALS AND HUMANS

In humans excessive vibration can cause effects on bone, joints, nerves, muscles, and blood vessels that can be profound and debilitating.^{34,35} Because of these effects, regulations and standards have been employed to limit vibration exposure in humans.^{36,37} Similarly, animal studies have shown that vibration can have a myriad of adverse effects in many different species, including altering the normal physiology and even cell structure. Information regarding the adverse effects of vibration in animals and humans is summarized in Table 1.

Stress as a result of vibration, not unexpectedly, causes increases in heart rate in mice and humans. Conscious mice exposed to vibration can exhibit increases in heart rate (HR) and mean arterial blood pressure (MAP). When mice were anesthetized and unconscious,

TABLE 1 Adverse effects of vibration in various species

Species	Adverse effect	References
Mouse	Decreased the number of litters born relative the number bred	22(p737)
Mouse	Nursing dams exhibited noticeable agitation and disruption in nursing	23(p8-10)
Mouse	Increased both heart rate and mean arterial blood pressure	18(p374,375)
Mouse	Decreased the number of blood vessels per muscle fiber in the soleus muscle	66
Mouse	Startle response and fear-related behaviors	19
Mouse	Increased blood levels of corticosterone	22(p737)
Mouse, Pig	Changes in reproduction associated with hormonal changes with an increase in stress hormones	Mouse ^{22(p737)} , Pig ⁶⁷
Rat	Disrupted myelin in axons, decreased the arterial lumen size, and an increased arterial smooth muscle vacuolization in the tail	68,69
Rat	Altered serotonin levels in the brain	70(p15)
Rat, Dog	Caused stress leukograms	Rat ⁷¹ , Dog ⁷²
Dog	Increased aortic flow rate and pulse pressure during anesthesia	40
Rabbit	Altered neuropeptides in the dorsal root ganglion associated with ultrastructural changes in cellular structure	73

neither HR nor MAP were elevated under the same vibratory conditions, suggesting that consciousness is a requisite for these cardiovascular effects in mice.^{18(p374,375)} To assess the effect of noise and vibration on heart rate in humans, study participants were exposed to experimentally induced vibration, equivalent to that produced from a train, during sleep. In 79% of participants subjected to the high-vibration condition, an average increase of at least 3 beats per minute per train was observed and cardiac responses were generally higher in the high-vibration condition than in the low vibration condition.³⁸ The increased HR in humans was characterized by an initial and then a delayed response, indicating that a startle response was associated with awakening and a more conscious response ensued as the vibration continued. Similarly, the HR of participants receiving vibration during squat training had higher HR than individuals not receiving vibration. The HR of individuals that received vibration was increased on the initial training day and declined during subsequent training days, showing a rapid cardiovascular adaptation to the vibration stimulus.³⁹ Therefore, both humans and mice may perceive vibration as a psychological stressor and subsequently undergo increases in HR. However, vibration may have other cardiovascular effects that do not require consciousness since vibration at very high magnitudes (9.8-29.4 m/s²) caused an increase in aortic blood flow and pressure during anesthesia in dogs and pigs.^{40(p386)}

In larger species, vibration associated with transportation is considered one of the factors involved in transportation stress.⁴¹ Exposure of swine to WBV, to mimic transportation stress, caused behavioral avoidance of the vibration produced.⁴² Transportation-induced vibration in poultry causes stressed-induced behaviors and the stress-related effects of increased heart rate and blood circulation.⁴³ Vibration levels during transport can become high, which may contribute to observed behavioral alterations. The vibration levels produced from routine animal facility transport methods such as carts and hand carrying have been measured.^{31(p544)} In some instances, vibration magnitudes reached as high as 17.31 m/s² for

some of the carts tested.^{31(p546)} These levels are much higher than ambient vibration levels of approximately 0.024 m/s² measured in animal rooms.^{11(p655)}

Some studies have shown potential benefits of vibration on bone, muscle, fat accumulation, metabolism, and in wound healing (Table 2). The studies demonstrating the positive effects of vibration point to exciting potential for vibration to be used in the therapy for conditions that affect humans as well as areas for future translational studies using animal models. Because of the potential positive effects, vibration has been used to treat musculoskeletal diseases as well as to increase athletic performance in humans. Work still needs to be done, however, to determine the accelerations and frequencies that are most beneficial.^{44,45} As discussed below, because the frequency, magnitude, and duration of exposure can determine if vibration will have negative, positive or no effects, animal models will be important in developing these therapeutic uses.

5 | CHALLENGES IN ANIMAL STUDY DESIGN

Because of the varied nature of experimental design applied to WBV studies reported in the literature, it is challenging to determine which vibration protocol is likely to have the greatest benefit, adverse effects, or no effects at all. For example, in studies to use vibration exposure for promoting bone growth or maintenance, there were acceleration ranges between 2.94 and 29.43 m/s², frequency ranges between 8 and 90 Hz, varied durations of exposure, as well as animal age and species.^{46(p1059),47(p349),44-46,48,49} Higher magnitude WBV of 19.62 and 29.43 m/s² was only osteogenic in ovariectomized rats,^{50(p316)} whereas low magnitude vibration applied to osteoporotic (ovariectomized) rats at approximately 2 m/s² reversed some of the negative effects of osteoporosis and accelerated early peri-implant osseointegration.⁵¹ An evaluation of WBV effects on

TABLE 2 Potentially beneficial effects of vibration in various species

Species	Potentially beneficial effects	References
<i>Bone</i>		
Mouse	Increased bone formation on the endocortical surface of the metaphysis during skeletal growth	74
Mouse	Increased cortical bone area and cortical thickness in the femur and tibia diaphysis	75
Mouse	Increased trabecular metaphyseal bone formation and percentage of mineralizing surfaces	76
Mouse	Increased trabecular bone volume of the proximal tibial metaphysis	77
Rat	Mitigated negative effects of bone repair and bone callus formation due to ovariectomy	78
Rat	Improved fracture callus density, enlarged callus area and width, accelerated osteotomy bridging, upregulated osteocalcin expression and suppressed osteoclast activity after ovariectomy	79
Rat	Improved stiffness and increased endosteal and trabecular bone densities during fracture repair after pharmacological induction of osteoporosis and ovariectomy	80
Rat	Attenuated the loss of bone mass and trabecular bone microstructure after spinal cord injury	81
Rat	Promoted migration of mesenchymal stem cells and fracture healing, upregulation of several osteogenic proteins, up-regulation of the expression of chondrogenesis-, osteogenesis-, and remodeling-related genes	82-84
Sheep	Increased femoral trabecular bone formation	47,85
<i>Muscle</i>		
Humans	Prevented a shift in myofiber type during extended bed rest	86
Humans	Increased isometric muscle strength, explosive muscle strength, and muscle mass in men older than 60 y of age	87
Human	Caused muscle relaxation in the neck and back	88
<i>Other effects</i>		
Mouse (diabetic)	Attenuated hyperglycemia and insulin resistance, reduced body weight, normalized muscle fiber diameter, mitigated adipocyte hypertrophy in visceral adipose tissue, and reduced hepatic lipid content	89
Mouse (diabetic)	Decreased skin wound healing time, increased wound-associated angiogenesis and granulation tissue formation, accelerated wound closure and re-epithelialization, and increased expression of insulin-like growth factor-1, vascular endothelial growth factor and monocyte chemoattractant protein-1 in the wounds	48
Humans	Increased the oxygen carrying capacity of the blood during exercise	49

bone formation in healthy rats using a constant acceleration and 45 or 90 Hz demonstrated that only a frequency of 90 Hz stimulated bone formation,⁴⁶ indicating that studies performed only at the low frequencies would have yielded a different conclusion regarding the effects of vibration. Although there have been varied experimental regimens used in vibration research, some consistency in findings is starting to emerge. For example, a second study has demonstrated that WBV at 90 Hz stimulates trabecular bone cellular activity, accelerates cortical bone growth, and increases bone mineral density in mice.⁵² The WBV of 90 Hz is consistent with our established RFR for mice.^{15(p1963)} Previous studies have been conducted without regard to the RFR of the animal and thus, the results may have been different if a frequency within the RFR had been used. Therefore, when designing vibration studies in animals careful consideration should be given to the frequency used as well as the magnitude.

There are also species considerations in animal study design. For example, techniques to study the effects of vibration at the molecular level are more available in mice than non-rodent species. Rats, however, may be a more appropriate rodent model for some studies, such as the study of vibration effects on the tail blood vessels and nerves, since they are larger in size. Rats share the same advantage as mice in that larger numbers can generally be used due to lower cost, reduced space requirements, rapid generation time, and increased availability.

6 | USE OF VIBRATION IN ANIMAL MODELS

The effects of vibration in animals is varied and can be either destructive or beneficial, likely depending on magnitude, duration, whole-body or localized, and presumably the sensitivity to the vibration for the species. The use of the mouse as a model to study human conditions has the advantage that transgenic, knock-out and knock-in strains are available to delineate the function of various genes in contributing to the harmful or beneficial effects of vibration in humans.

Vibration-induced effects in people include hand-arm vibration syndrome (Raynaud's phenomenon) consisting of vasospasm in hands and fingers,⁵³ lower back pain,⁵⁴ motion sickness, bone damage, varicose veins/heart conditions, stomach and digestive conditions, respiratory effects, endocrine and metabolic changes, impairment of vision/balance, and reproductive organ damage.⁵⁵ In mice, vibration-induced effects have been demonstrated in bone, muscle, hormones, metabolism, and reproduction as well as altering cardiovascular parameters, causing weight loss and increasing stress.^{44,56} The mouse, therefore, is a valuable model to study many of the adverse conditions caused by vibration in humans.

In both humans and animals, diminishment of skeletal strength and muscle atrophy can lead to decreased mobility and function.

However, the musculoskeletal system responds to dynamic load in an anabolic manner and vibration therapy may serve to augment pharmacological therapy to strengthen bone and muscle.⁵⁶ The musculoskeletal system is able to tolerate a high level of vibration without damage due to its inherent elasticity and plasticity of the system, including the natural shock absorbers of the articulating joints. As previously noted, vibration has shown positive effects on both muscle and bone in mice, and therefore, the mouse model would be useful in the study of muscle and bone health.

Osteoporosis or bone fracture repair is another area where vibration may be beneficial and rodents may serve as a translational model. However, in humans, both osteoblastic and chondroblastic osseous repair occurs, while endochondral bone formation predominates in rodents. Fracture repair of the long bones in animal models has been well described, but vibration was not assessed as an adjunct to traditional intervention.⁴⁴ Considerable variation in bone morphology and healing processes exist among animal species; thus, characterization of each model is critical to appropriately correlate experimental outcomes to a skeletal condition in human. The bones in larger species (eg, canine, caprine, ovine swine, and nonhuman primates) do not undergo the continuous growth or modeling observed in rodents, while fracture fixation methods and biomechanics of fractures in these larger species mimic those used in humans.⁵⁶ Thus, preclinical research is commonly performed in these larger species instead of rodents. Despite this difference in bone healing, 53% of animals used in fracture studies over a 10-year period were either rats or mice and the large percentage of rodents used correlates to their applicability to molecular biology techniques, the ability to use a larger number of animals, and faster healing rates.⁵⁶

Experimentally induced vibration has been used commonly in various behavioral, physiological, and psychological research models for decades as a source of stress.⁵⁷⁻⁵⁹ In these studies, stress is defined as a physical, chemical, or emotional factor that causes physical or mental tension.⁵⁸ Often stress is a chronic condition and animal studies utilizing vibration are an important part of modeling the pathological effects of stress. Depending on the model, use of vibration or shaker stress often may prove advantageous over other models of induced stress such as physical restraint, foot shocks, or forced-swim testing in rodents. Use of shaker stress in animal studies provides a mild form of stress that has been used reliably to induce a form of stress that results in changes in blood pressure, heart rate, and stress hormones. Since shaker stress can be delivered remotely to an animal's home cage, it reduces the potential for artificial enhancement of the stress response from factors such as handling, restraint, noise, or pain.

Some of the most common models that utilize shaker stress are those used to study conditions such as depression and post-traumatic stress disorder (PTSD).^{58,59(p320)} PTSD affects nearly 10% of Americans, but finding appropriate animal models is difficult due to the co-morbidities PTSD shares with other conditions such as anxiety and depressive disorders.⁵⁹ It is important for animal models to exhibit similar underlying characteristics or components of the

corresponding disorder being studied. This allows for adequate study of the various factors that may contribute to disease processes, such as genetic or environmental factors. It also ensures that more reliable predictions are made about treatment effects. A study of rats exposed to intermittent shaker stress as part of a chronic stress schedule assessed the effects of the chronic unpredictable stress on anxiety-like behavior and cognitive deficits.^{59(p320)} In conditions such as depression, human patients can also display cognitive changes.^{60,61} Rats exposed to chronic unpredictable stress displayed cognitive deficits and increased anxiety similar to effects seen in the human condition. Rats also showed improvement in cognitive deficits when common treatments were tested, such as selective serotonin reuptake inhibitors and other drugs, indicating the appropriateness of the model.^{59(p320)} Because shaker stress has also been shown to cause stress in mice and induce behavioral changes,¹⁹ vibration in mice may also provide an appropriate stressor for the study of anxiety and depression.

The availability and current use of many genetically altered strains of mice offer a wide array of potential mouse models of human disease. For example, shaker stress has been used to study how early development factors affect the stress response in later life. In one study, progeny from NOS-3 knock-out mice were exposed to shaker stress to determine how the intrauterine environment affects the cardiovascular response to stress. NOS-3 is an enzyme responsible for the generation of nitric oxide in endothelial cells. Nitric oxide is a smooth muscle relaxant that plays a vital role in maintaining uteroplacental perfusion via vasodilation. NOS-3 deficient knock-out mice are susceptible to hypertension and reduced fetal growth during gestation. In the study, mature mice born to NOS-3 knock-out dams had greater changes in blood pressure in response to intermittent two-minute shaker sessions that were repeated over 24 hours relative to wild type mice.⁶² Other studies have used shaker stress to study the interplay between circadian patterns and cardiovascular responses to stress.^{63(p768)} All of these animal models are valuable tools in advancing the knowledge of the numerous factors that determine how stress affects various disease processes in humans.

Mice may also serve as a good model to study the potential of vibration as a therapy for wound treatment. Because local vibration has been shown increase blood flow in the skin of humans, it has been proposed as a treatment for pressure ulcers or other skin wounds.⁶⁴ Pressure wounds and other skin injuries may be more prevalent or of concern in diabetics. Because wound healing time in diabetic mice decreases when vibration exposure occurs,⁴⁸ the mouse model needs to be explored further with regard to wound healing.

There is evidence that vibration therapy may be beneficial in many age-related conditions.^{65(p319)} WBV has been suggested to attenuate muscle atrophy resulting from bed rest, and may increase postural balance and gait. Similarly, exercise supplemented with WBV increases muscle strength and speed in older women following 24 weeks of treatment. Mice could play a very valuable role in studying the effects of vibration to prevent or treat conditions related to age.

7 | SUMMARY

Vibration experienced by animals can elicit stress-mediated effects and increased emphasis is being placed on vibration with regard to the welfare of animals and as a research variable. To understand the threshold for these effects, the sensitivity of a species to vibration is crucial to determine the utility of the animal as a translational model that is predictive in humans for a therapeutic effect. The mouse is a commonly used model in biomedical research, particularly when investigating molecular and cellular effects. This species, through genetic engineering and humanization, is appropriate for investigating the effects of vibration in a number of therapeutic modalities. There are numerous effects of vibration on the mouse, both those considered adverse as well as those with the potential to be used as a translational model for human therapeutics. Continued characterization of the effects of vibration in the mouse model will facilitate its use as a translational model for various therapeutic endeavors.

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