HHS Public Access

Author manuscript

J Occup Environ Med. Author manuscript; available in PMC 2019 May 23.

Published in final edited form as:

J Occup Environ Med. 2019 February ; 61(2): 162–167. doi:10.1097/JOM.0000000000001509.

Can Blood Flow be Used to Monitor Changes in Peripheral Vascular Function That Occur in Response to Segmental Vibration Exposure?

Kristine Krajnak, PhD, **Stacey Waugh, MS**, and **Khachatur Sarkisian, MS**

Engineering Controls and Technology Branch (Dr Krajnak, Ms Waugh); Biostatistics and Epidemiology Branch (Mr Sarkisian), National Institute for Occupational Safety and Health, Morgantown, West Virginia.

Abstract

Objectives: Laser Doppler blood flow measurements have been used for diagnosis or detection of peripheral vascular dysfunction. This study used a rat tail model of vibration-induced vascular injury to determine how laser Doppler measurements were affected by acute and repeated exposures to vibration, and to identify changes in the Doppler signal that were associated with the exposure.

Methods: Blood flow was measured immediately after a single exposure to vibration, or before vibration exposure on days 1, 5, 10, 15, and 20 of a 20 days exposure.

Results: After a single exposure to vibration, average tail blood flow was reduced. With 20 days of exposure, there was a reduction in the amplitude of the arterial pulse on days 10 to 20 in vibrated rats and days 15 to 20 in control rats.

Conclusions: More detailed statistical analyses of laser Doppler data may be needed to identify early changes in peripheral circulation after exposure to vibration.

Keywords

fast Fourier transform; hand-transmitted vibration; laser Doppler; vascular dysfunction

Workers who are regularly exposed to hand-transmitted vibration through the use of power or pneumatic hand tools, may develop disorders of the sensorineural and peripheral vascular systems commonly referred to as hand-arm vibration syndrome (HAVS).[1,2] Workers with HAVS can experience cold-induced vasospasms, and blanching of the fingers and hands.[1,3] These symptoms are commonly referred to as vibration white finger (VWF)[1,2,4]; although the use of anti-vibration gloves and tool-handle wraps,[5–8] along with job rotation[9,10] can reduce transmission of vibration to the body, at present, there are still many workers that are exposed to significant levels of hand-transmitted vibration (HTV) at work every day. In

Address correspondence to: Kristine Krajnak, PhD, Engineering Controls and Technology Branch, MS 2027, National Institute for Occupational Safety and Health, Morgantown, WV 26505 (kmk1@cdc.gov).

The authors have no conflict of interest.

order to assess the health of the peripheral vascular system in workers exposed to vibration, and improve the diagnosis of HAVS, various methods for measuring peripheral vascular function are being assessed to determine which tests can be used to monitor changes in the vascular system that may lead to alterations in blood flow in workers. By identifying consistent changes blood flow in response to occupational vibration exposure, appropriate interventions can be implemented to prevent the development of VWF in workers.

A number of recent studies have used laser Doppler to measure vibration-induced changes in peripheral blood flow.[3,11–13] Laser Doppler is a non-invasive, fairly inexpensive procedure that can be used to measure changes in blood flow that are a result of normal aging,[14] various diseases such as diabetes,[15–17] or induced by occupational vibration exposure.[12,18] For example, studies have shown that workers diagnosed with VWF display a lower baseline blood flow when at rest, and a reduced recovery of blood flow in response to a temporary occlusion.[12,18] Other studies have shown that workers with HAVS also display a reduced recovery of blood flow after exposure to cold.[3,12,13] Finally, studies on subjects that have never been exposed to hand-transmitted vibration have demonstrated that acute exposures to vibration induce transient reductions in finger blood pressure.[19,20] Together, the results of these studies support the idea that measuring peripheral blood flow by laser Doppler can be used for the diagnosis of VWF.

Although laser Doppler can measure changes in blood flow associated with various disease states such as VWF (secondary Raynaud), primary Raynaud, and diabetes,[12] when the vascular system is challenged, it’s unclear if changes in resting blood flow can be used as an early indicator of peripheral vascular disease or dysfunction. Measuring blood flow by laser Doppler does not require implantation of any device or extensive patient preparation to perform. This measure also can be performed repeatedly at regular intervals to track changes in a subject’s, worker’s, or patient’s blood flow over time. Therefore, the goal of the current study was to use a well characterized rat-tail model of vibration-induced vascular and sensorineural dysfunction to determine if changes in peripheral blood flow could be detected using laser Doppler. The rat-tail serves as a good model for estimating the effects of vibration on the human fingers because the resonant frequency of the rat tail is in the same range as the resonant frequency of the human finger, and thus, the physical response of the tail and fingers to vibration are similar.[21] The biological and physiological responses of the peripheral vascular and nervous systems to repetitive vibration exposure are also similar in humans[22,23] and animals.[24,25] Because of these similarities in the responsiveness to vibration, the rat tail model was used to examine both the acute, and longer-term effects of vibration on blood flow. The first experiment examined the direct, acute effects of vibration exposure on tail blood flow to determine if they were similar to those seen in humans. The second experiment used a repeated exposure to vibration to determine if there were changes in basal blood flow that could be used as a potential physiological marker for the development of peripheral vascular dysfunction.

METHODS

Animals

Male Sprague Dawley rats (6 weeks age, from Hilltop Breeders, PA) were used for all experiments. Rats were housed on a 12:12 LD cycle (lights on 06:00 hour), with food and water available ad libitum, in an AAALAC International accredited animal facility. All procedures performed in the experiments were approved by the Animal Care and Use Committee at the National Institute for Occupational Safety and Health (NIOSH) prior to the beginning of the experiment. The temperature range of the animal housing and experimental room was 21.1 to 22.2°C during both experiments. Rats were acclimated to the facility for 1 week prior to being included in an experiment. In Experiment 1, rats (n = 4/group) were acclimated to restraint by placing them into Broome style restrainers every day for a week. After acclimation, rats were assigned to one of three groups, a cage control (no exposure or restraint), restraint control (restrained and placed into vibration exposure chambers), or vibration-exposed group (restrained, placed into the exposure chamber, and their tail exposed to vibration). Animals were exposed to a single, 4 hours bout of tail vibration or restraint and blood flow was measured immediately following the exposure. In Experiment 2, rats (n = 6/group) were acclimated to restraint and then assigned to one of two groups; a restraint control or vibrated group. Because there were no significant differences between the cage and restraint control groups in Experiment 1, a cage control group was not used in Experiment 2. In Experiment 2, rats were exposed to vibration or restraint control conditions for 4 h/d, 5 days a week (M-F) for 20 days.

Exposure

Vibrated and restraint control rats were placed into Broome style restrainers prior to each exposure. Vibrated rats had their tails secured to a platform attached to a shaker as previously described.[21] The tails were secured with four, 1 cm wide elastic straps. These straps kept the tail in contact with the platform without applying too much pressure. Restraint control rats also had their tail secured to a platform in an identical manner, but the platform was secured to isolation blocks so the animals did not receive a vibration exposure. In Experiment 1, rats were exposed to a single 4 hours bout of cage control, restraint control, or vibration (frequency: 125 Hz, acceleration 49 m/s^2, root mean squared). In Experiment 2, rats were exposed to restraint or vibration for 4 h/d, 5 days (M-F) per week for 20 days using an exposure with the same vibration frequency and acceleration as that used in Experiment 1. This frequency was chosen for these experiments because it is within the resonant frequency range of the tail,[21] and exposures at this frequency induce changes in peripheral vascular function and morphology.[25–27]

Laser Doppler Blood Flow and Skin Temperature Measurements

Laser Doppler measurements were made using a Peri-flux system 5000 and PF 450 thermostatic small angle probe (Primed, Stockholm, Sweden). Prior to each reading the machine was calibrated by placing the probe into the calibration solution supplied by the manufacturer. Once calibrated, the probe was secured in a ring stand and positioned below the opening of a stainless steel, rectangular holder used to support the tail stable during recording. Measurements of blood flow were collectedat 30 Hz, inan isolationchamber to

prevent external noise or stimuli from affecting the measurements. In Experiment 1, blood flow (perfusionunits) and tail temperature (°C) were collected for 5 minutes immediately before and immediately following the exposure. A 5-minute collection period was chosen because studies in humans have demonstrated that blood flow returns to pre-exposure levels fairly quickly after an acute exposure to vibration.[20,28] To collect the blood flow measurement, each animal was placed into an isolation chamber, and their tail was placed into a specialized holder with the laser Doppler probe attached. PF 450 thermostatic small angle probe measured blood flow in a 1 cm area between the 15th and 16th vertebrate of the tail. The temperature sensor surrounding the laser simultaneously measured the temperature of the tail. After the blood flow measurement was completed, animals were returned to their home cage. In Experiment 2, rats were restrained, placed into the isolation chamber, and blood flow and tail temperature were collected for 15 minutes prior to vibration exposure on day 1 (pre-exposure), 5, 10, 15, and 20 of the exposure. Measurements were made prior to the exposure to determine if there were any effects of vibration on blood flow that were maintained and may be indicative of a longer term problem in the functioning of the peripheral vascular system. Laser Doppler data were collected for 15 minutes because the goal of the study was to determine if there were vibration-induced changes in basal or resting blood flow. Collecting measurements for an extended period of time, provided more data that could be used to identify changes smaller changes that are associated with the exposure.[13,14,17] Immediately following the blood flow measurements, rats were exposed to vibration or restraint conditions.

Statistical Analyses

To determine if vibration exposure had a significant effect on blood flow in Experiment 1, the average tail temperature and blood flow were calculated over the 5 minutes before and after the exposure and data were analyzed using 2-way mixed model analysis of variances (ANOVAs) (treatment [2] × pre vs post [2]) where animal served as a random factor. In Experiment 2, average blood flow was calculated for the 15 minutes collection period. Some animals moved during blood flow measurement, resulting in either very high readings of blood flow, or the inability to measure blood flow. The time over which these disruptions occurred was usually brief (usually less than 10 seconds), but the fluctuations in blood flow measurements during these periods greatly affected the average blood flow calculation. To reduce variability in the mean due to motion, limits were set (blood flow less than 2 or greater than 100 perfusion units) based on previous data collected in the laboratory, and these regions of the data were normalized by calculating running means. To calculate a running means the 20 measures prior to and the 20 measures following motion or loss of the blood flow reading were averaged, and this average (ie, the running mean) was used to replace data lost to movement during the measurement. Data were analyzed using a 2 (treatment) × 5 (days) mixed model ANOVA where animal served as a random variable. In addition, the average blood flow over each 3-minute interval was calculated and analyzed using the mixed model ANOVAs to determine if there were differences in blood flow over the testing interval. Multiple pairwise comparisons were made using Tukey-HSD tests. Fast Fourier transform (FFT) analyses were also performed to identify peaks in the Doppler signal. To perform these analyses, the data were divided into 25 sampling boxes for analyses. Therefore, the window length for Experiment 1 was 12 s/box and the window

length for Experiment 2 was 36 s/box. Studies have shown that the higher frequency peak is representative of blood flow, and the lower frequency peak is usually indicative of the arterial pulsatile movement.[13,17,29] Changes in the area of the curves obtained by FFT were analyzed using one way-ANOVAS to determine if these parameters changed as a result of vibration exposure. Statistical analyses were performed using Jmp 13.0.0 (SAS Institute, 2016). Differences with $P < 0.05$ were considered statistically significant.

RESULTS

Experiment 1

Prior to the exposure, there were no significant differences in tail temperature between the three groups (Table 1). However, after the exposure tail temperature was significantly lower than pre-exposure temperature in all three groups of animals. When post-exposure tail temperature was compared, temperature in restraint controls and vibrated rats were significantly lower than the tail temperature in cage control rats (Table 1). Tail blood flow data are presented in Fig. 1. Prior to exposure, there were no significant differences in blood flow between the different groups of animals. However, there was a pre-post exposure difference in blood flow in vibrated rats, with blood flow being lower post- than pre-exposure (A: $^{*}P < 0.05$). In addition, when just the post-exposure data were analyzed, blood flow was significantly lower in vibrated than cage control rats (A: $^{\#}P < 0.05$). Restraint control rats did not display significant changes in blood flow as compared with the cage control animals. FFT analyses were also performed on the raw data from each animal, and these analyses identified two specific peaks in the data; one peak with a frequency of approximately 1 Hz and another with a peak frequency of approximately 0.4 Hz. There were no significant group or pre-post exposure differences in the peak height at either the 1 or 0.4 Hz peaks (Fig. 1B and C).

Experiment 2

Tail temperature collected prior to restraint control or vibration exposure (during the pre-test [day 1], and on days 5, 10, 15, and 20 of the experiment) did not differ over the duration of the experiment, or between groups (Table 2). There also were no significant effects of restraint or vibration on average blood flow (perfusion units) on over the course of the experiment (Fig. 2). Averages calculated every 3 minutes during the recording period were also analyzed and there were no significant group differences in blood flow over any of these intervals. FFT analyses were also performed on the raw data from each animal. Analysis of the first peak (ie, 1 Hz) revealed that there was a significant reduction in the height of this peak in the control animals on day 5 (Fig. 3A $^{*}P < 0.05$). Figure 3B and C shows the average peak heights of the lower frequency peak (0.4 Hz) over the exposure period. In restraint control rats, the amplitude of this peak was lower on days 15 and 20 of the experiment than it was pre-exposure (Fig. 3B). In the vibration exposed rats, there was a reduction in the amplitude of lower frequency peak on days 10 and 15 of the experiment as compared with the pre- and 5-day exposure measurements. Although the measure was also slightly reduced on day 20, this difference was not statistically significant (Fig. 3C: $P < 0.07$).

DISCUSSION

The goal of this study was determine if laser Doppler measurements could be used to identify changes in basal blood flow that could be used as a maker of vibration-induced vascular dysfunction. Previous studies from a number of laboratories have shown that the rat-tail model is a good surrogate for studying the effects of vibration on the human fingers.[8,21,24,25,30,31] In Experiment 1, the acute effect of vibration on blood flow was measured. Blood flow was reduced immediately following a single 4 hours exposure to vibration. These data are consistent with the results of other studies showing that an acute exposure to vibration results in a reduction in blood flow in a rat-tail model,[32] and in human fingers.[33–35] However, based on the analyses of the laser Doppler measurements collected after repeated exposure to vibration in Experiment 2, a more detailed analyses of blood flow data might needed detect early changes, and monitor the progression of peripheral vascular dysfunction.

In the first experiment tail temperatures were lower in all animals after exposure than prior to exposure. These pre-post exposure changes in temperature are most likely the result of the time of day that the measurements were taken. The pre-exposure measure was collected at approximately 08:30 and the post-exposure measure was collected at approximately 13:00 hours. In animals housed on a 12:12 LD cycle, the daily nadir in body temperature occurs approximately 6 hours after the lights on in the colony room.[36] Thus, it is likely that pre-post exposure decrease in temperature seen in all the animals was the result of the circadian fluctuation in temperature. Analyses of tail temperature post-exposure found that temperature was significantly lower in restraint control and vibrated rats than in cage control rats. In restraint-control rats, this reduction in tail temperature may have been the result of inactivity, the fact that the tail was held in a static posture for 4 hours, or a combination of restraint and inactivity. The reduction in tail temperature was associated with a slight reduction in blood flow in restraint control rats. Tail temperature was also lower in vibration-exposed than cage control rats following the exposure. This reduction in tail temperature was associated with a significant reduction in blood flow in vibration exposed rats. These results suggest that although restraint may have a small effect on blood flow and tail temperature, vibration exacerbates the effects of restraint, and further reduces blood flow to the exposed appendage. These data are consistent with ex vivo data showing that a single exposure to vibration, but not restraint, results in an increased sensitivity to vasoconstriction induced by a α2C- adrenoreceptor agonist, and a reduced sensitivity to acetylcholine-induced vasodilation.[10,26,37]

In the second experiment, blood flow was measured prior to beginning the experiment (pre-exposure or day 1) and on days 5, 10, 15, and 20 of exposure. Because the results of Experiment 1 demonstrated that the responses of animals and humans to vibration are similar, in that there are acute effects of vibration on blood flow, the goal of the second experiment was to determine whether there were changes in blood flow that developed and were maintained over repeated exposures. Prior to the beginning of the experiment, blood flow wasn't different in restraint control (control) and vibration exposed rats. Average blood flow was not significantly affected by vibration or restraint over the course of the experiment, although there was a trend for it to be lower in vibrated rats on day 20 of the

exposure. These data suggest that it may be possible to detect a change in average basal blood flow with a longer exposure to vibration. There is some indication that basal laser Doppler measurements can be used to detect age and disease-related changes in peripheral blood flow.[12,14,38] However, there are also studies showing that vibration- or disease-induced changes in peripheral blood flow are only apparent after some type of vascular challenge, such as a cold exposure.[11,13,17,18,39] In fact the International Standards Organization-recommended method for assessing vibration-induced vascular dysfunction uses cold exposure to induce a vasoconstriction and perform finger thermography or plethysmography to assess both the response to and recovery from the cold exposure.[40] However, exposure to cold can induce stress and is painful for workers or patients with peripheral vascular disorders.[41–43] Therefore, the ability to detect alterations in blood flow without making a worker or patient uncomfortable would be preferable if a reliable change in either blood flow, or the pattern of the laser Doppler signal can be detected.

Recent studies using laser Doppler to assess changes in blood flow have performed time-series analyses using a number of methods, including FFT's to analyze changes in the frequency spectrum that may indicate early changes in blood flow.[17,29,38] We performed a FFT on each data set (every recording from each animal) and identified two prominent peaks (1.0 Hz and between 0.4 Hz). The higher frequency peak (1 Hz) is an estimate of blood flow.[17,29] Blood flow was reduced on day 5 in restraint control animals, however, the reduction was only significant in control rats. It is unclear why there was a reduction in blood flow on this day. However, it's possible that the animals were still adjusting to the exposure environment. Although animals were acclimated to restraint prior to the beginning of the experiment, once, the study begins, both restraint control and vibration-exposed animals are exposed to the noise generated by the shaker during the experiment. This noise produced by the shaker at 125 Hz is between 75 and 80 dB, and therefore may initially induce some stress in the animals. The peak of the 1 Hz signal seemed to go back to pre-exposure levels for the rest of the experiment, although there was a trend for a decrease in the peak of the 1 Hz signal in vibration exposed rats ($P < 0.06$ from same day restraint control). It is possible that with longer exposures, this estimate of blood flow would show a significant decrease. In the current study, longer exposures were not performed because previous data suggested that morphological and biological changes indicative of vascular dysfunction are apparent after 10 days of exposure.[27] However, morphological and cellular changes seen after 10 days of exposure, may not be directly related to, or indicative of blood flow.

Analyses of the lower frequency peak (0.4 Hz) in the laser Doppler recording, which is indicative of arterial pulsation or motility,[17,29] showed changes in response to both restraint control and vibration exposure. In restraint control rats, peak amplitudes were significantly reduced on days 15 and 20 of the experiment, where as in vibration-exposed rats, peak amplitudes were significantly reduced on days 10 and 15, and marginally reduced on day 20 of the exposure ($P < 0.07$). Because both groups displayed changes in the amplitude of this peak, it is likely that restraint of the animal and the tail contributed to a reduction in the vascular pulse. Studies in both humans and animals have shown that maintaining a static position over a period of time can induce a thickening of the smooth muscle walls of larger arteries and a reduction in blood flow to the immobile area of the body.[44–46] These data also are consistent with the findings of anatomical studies in both animals and humans showing

that there is a remodeling of the arterial wall with exposure to vibration[22,27] and in people or animals with certain diseases such as diabetes.[39,47,48] The arterial wall becomes thicker, and the internal wall of the blood vessel is reduced.[27,31] These changes make the artery less pliable and could affect the measure or arterial pulsativity.[25,27] Because the reduction in the amplitude of this peak occurred earlier in vibration-exposed than restraint-control rats, it is likely that vibration exposure exacerbates the effects of restraint. In fact, the histological and biological changes that occur as a result of repetitive vibration exposure show that exposure to vibration at the resonant frequency results in changes morphology, and the expression of reactive oxygen species, inflammatory factors and factors involved in remodeling, and these changes may result in a reduction in blood flow (because the lumen of the artery is narrowed) and an increase in vascular stiffness.[27] However, longer exposures could be performed to determine if the reductions in these peaks is maintained and if these markers can be used to as a monitoring tool, to identify individuals at risk for developing vibration-induced vascular disorders.

Laser Doppler is a fairly simple and non-invasive technology that could potentially be used to assess vascular health in workers regularly exposed to HTV. The results of this study suggest that average blood flow measurements can be used to detect changes immediately following an exposure to vibration. However, if basal blood flow is to be used to assess the more chronic effects of vibration exposure on the peripheral vascular system, more complex analysis methods that not only assess blood flow, but also the composition of the laser Doppler signal may be more sensitive, and better early indicators of changes in vascular health than average blood flow.

Funding:

This work was funded and performed as part of the official duties of the authors.

REFERENCES

1. Bovenzi M, Griffin MJ, Hagberg M. New understanding of the diagnosis of injuries caused by hand-transmitted vibration. Int Arch Occup Environ Health. 2008;81:505. [PubMed: 17955257]
2. Griffin MJ. Handbook of Human Vibration. San Diego: Academic Press; 1996.
3. Mahbub M, Harada N. Review of different quantification methods for the diagnosis of digital vascular abnormalities in hand-arm vibration syndrome. J Occup Health. 2011;53:241–249. [PubMed: 21597234]
4. Griffin MJ. Negligent exposures to hand-transmitted vibration. Int Arch Occup Environ Health. 2008;81:645–659. [PubMed: 17901977]
5. Dong RG, Welcome DE, Peterson DR, et al. Tool-specific performance of vibration-reducing gloves for attenuating palm-transmitted vibrations in three orthogonal directions. Int J Ind Ergon. 2014;44:827–839. [PubMed: 26726275]
6. Krajnak K, Waugh S, Johnson C, et al. Antivibration gloves: effects on vascular and sensorineural function, an animal model. J Toxicol Environ Health A. 2015;78:571–582. [PubMed: 25965192]
7. Welcome DE, Dong RG, Xu XS, Warren C, McDowell TW. Tool-specific performance of vibration-reducing gloves for attenuating fingers-transmitted vibration. Occup Ergon. 2016;13:23–44. [PubMed: 27867313]
8. Xu XS, Riley DA, Persson M, et al. Evaluation of anti-vibration effectiveness of glove materials using an animal model. Biomed Mater Eng. 2011;21:193–211. [PubMed: 22182788]

9. Cherniack M, Morse TF, Brammer AJ, et al. Vibration exposure and disease in a shipyard: a 13-year revisit. Am J Ind Med. 2004;45:500–512. [PubMed: 15164394]
10. Krajnak K, Waugh S, Miller GR, Johnson C. Recovery of vascular function after exposure to a single bout of segmental vibration. J Toxicol Environ Health A. 2014;77:1061–1069. [PubMed: 25072825]
11. Miyai N, Terada K, Sakaguchi S, et al. Preliminary study on the assessment of peripheral vascular response to cold provocation in workers exposed to hand-arm vibration using laser Doppler perfusion imager. Ind Health. 2005;43:548–555. [PubMed: 16100932]
12. Stoyneva ZB, Dermendjiev SM, Medjidieva DG, Vodenicharov VE. Micro-vascular reactivity during sympathetic stimulations in Raynaud's phenomenon. Int Angiol. 2016;35:593–598. [PubMed: 27015234]
13. Terada K, Miyai N, Maejima Y, et al. Laser Doppler imaging of skin blood flow for assessing peripheral vascular impairment in hand-arm vibration syndrome. Ind Health. 2007;45:309–317. [PubMed: 17485876]
14. Sorelli M, Perrella A, Bocchi L. Detecting vascular age using the analysis of peripheral pulse. IEEE Trans Biomed Eng. 2018;65:2742–2750. [PubMed: 29993447]
15. Ministrini S, Fattori C, Ricci MA, et al. Microcirculatory improvement induced by laparoscopic sleeve gastrectomy is related to insulin sensitivity retrieval. Obes Surg. 2018;28:3151–3158. [PubMed: 29752665]
16. Kulikov D, Glazkov A, Dreval A, et al. Approaches to improve the predictive value of laser Doppler flowmetry in detection of microcirculation disorders in diabetes mellitus. Clin Hemorheol Microcirc. 2018;70:173–179. [PubMed: 29710677]
17. Mizeva I, Zharkikh E, Dremin V, et al. Spectral analysis of the blood flow in the foot microvascular bed during thermal testing in patients with diabetes mellitus. Microvasc Res. 2018;120:13–20. [PubMed: 29802880]
18. Stoyneva Z Postocclusive reactive hyperemia in hand-arm vibration syndrome. Int J Occup Med Environ Health. 2016;29:659–666. [PubMed: 27443761]
19. Bovenzi M Finger systolic pressure during local cooling in normal subjects aged 20 to 60 years: reference values for the assessment of digital vasospasm in Raynaud's phenomenon of occupational origin. Int Arch Occup Environ Health. 1988;61:179–181. [PubMed: 3220589]
20. Bovenzi M, Griffin MJ, Ruffell CM. Acute effects of vibration on digital circulatory function in healthy men. Occup Environ Med. 1995;52:834–841. [PubMed: 8563848]
21. Welcome DE, Krajnak K, Kashon ML, Dong RG. An investigation on the biodynamic foundation of a rat tail vibration model. Proc Inst Mech Eng H. 2008;222:1127–1141. [PubMed: 19024160]
22. Takeuchi T, Futatsuka M, Imanishi H, Yamada S. Pathological changes observed in the finger biopsy of patients with vibration-induced white finger. Scand J Work Environ Health. 1986;12:280–283. [PubMed: 3775312]
23. Takeuchi T, Takeya M, Imanishi H. Ultrastructural changes in peripheral nerves of the fingers of three vibration-exposed persons with Raynaud's phenomenon. Scand J Work Environ Health. 1988;14:31–35.
24. Govindaraju SR, Curry BD, Bain JL, Riley DA. Comparison of continuous and intermittent vibration effects on rat-tail artery and nerve. Muscle Nerve. 2006;34:197–204. [PubMed: 16691604]
25. Krajnak K, Riley DA, Wu J, et al. Frequency-dependent effects of vibration on physiological systems: experiments with animals and other human surrogates. Ind Health. 2012;50:343–353. [PubMed: 23060248]
26. Krajnak K, Dong RG, Flavahan S, Welcome D, Flavahan NA. Acute vibration increases alpha2C-adrenergic smooth muscle constriction and alters thermosensitivity of cutaneous arteries. J Appl Physiol (1985). 2006;100:1230–1237. [PubMed: 16339346]
27. Krajnak K, Miller GR, Waugh S, Johnson C, Li S, Kashon ML. Characterization of frequency-dependent responses of the vascular system to repetitive vibration. J Occup Environ Med. 2010;52:584–594. [PubMed: 20523237]
28. Bovenzi M, Lindsell CJ, Griffin MJ. Acute vascular responses to the frequency of vibration transmitted to the hand. Occup Environ Med. 2000;57:422–430. [PubMed: 10810133]

29. Qi W. Fourier and Wavelet Analysis of Skin Laser Doppler Flowmetry Signals. School of Engineering Sciences, University of Southamptom; 2011
30. Thompson AM, House R, Krajnak K, Eger T. Vibration-white foot: a case report. Occup Med (Lond). 2010;60:572–574. [PubMed: 20682742]
31. Curry BD, Govindaraju SR, Bain JL, et al. Evidence for frequency-dependent arterial damage in vibrated rat tails. Anat Rec A Discov Mol Cell Evol Biol. 2005;284:511–521. [PubMed: 15791580]
32. Curry BD, Bain JL, Yan JG, et al. Vibration injury damages arterial endothelial cells. Muscle Nerve. 2002;25:527–534. [PubMed: 11932970]
33. Bovenzi M, Welsh AJ, Griffin MJ. Acute effects of continuous and intermittent vibration on finger circulation. Int Arch Occup Environ Health. 2004;77:255–263. [PubMed: 15034718]
34. Griffin MJ, Welsh AJ, Bovenzi M. Acute response of finger circulation to force and vibration applied to the palm of the hand. Scand J Work Environ Health. 2006;32:383–391. [PubMed: 17091206]
35. Bovenzi M, Welsh AJ, Della Vedova A, Griffin MJ. Acute effects of force and vibration on finger blood flow. Occup Environ Med. 2006;63:84–91. [PubMed: 16421385]
36. Goh GH, Mark PJ, Maloney SK. Altered energy intake and the amplitude of the body temperature rhythm are associated with changes in phase, but not amplitude, of clock gene expression in the rat suprachiasmatic nucleus in vivo. Chronobiol Int. 2016;33:85–97. [PubMed: 26745660]
37. Krajnak K, Waugh S, Johnson C, Miller R, Kiedrowski M. Vibration disrupts vascular function in a model of metabolic syndrome. Ind Health. 2009;47:533–542. [PubMed: 19834263]
38. Straface G, Landini L, Barrella M, Bevilacqua M, Evangelisti A, Bocchi L. Analysis of the microcirculatory pulse wave: age-related alterations. Conf Proc IEEE Eng Med Biol Sci. 2015;2015:7362–7365.
39. Heidarianpour A, Hajizadeh S, Khoshbaten A, Niaki AG, Bigdili MR, Pourkhalili K. Effects of chronic exercise on endothelial dysfunction and insulin signaling of cutaneous microvascular in streptozotocin-induced diabetic rats. Eur J Cardiovasc Prev Rehabil. 2007;14:746–752. [PubMed: 18043294]
40. Organization IS. ISO 14835–1-Mechanical vibation and shock-cold provocation tests for the assessment of periphral vascular function In: Part 1: Measurement and Evaluation of Finger Skin Temperature. Geneva, Switzerland: ISO; 2005.
41. House R, Krajnak K, Jiang D. Factors affecting finger and hand pain in workers with HAVS. Occup Med (Lond). 2016;66:292–295. [PubMed: 26928857]
42. Bovenzi M Cardiovascular responses of vibration-exposed workers to a cold provocation test. Scand J Work Environ Health. 1986;12:378–381. [PubMed: 3775327]
43. Bovenzi M, Alessandrini B, Mancini R, Cannava MG, Centi L. A prospective study of the cold response of digital vessels in forestry workers exposed to saw vibration. Int Arch Occup Environ Health. 1998;71:493–498. [PubMed: 9826083]
44. Antle DM, Cormier L, Findlay M, Miller LL, Cote JN. Lower limb blood flow and mean arterial pressure during standing and seated work: Implications for workplace posture recommendations. Prev Med Rep. 2018;10:117–122. [PubMed: 29850397]
45. Stewart JM, Taneja I, Medow MS. Reduced central blood volume and cardiac output and increased vascular resistance during static handgrip exercise in postural tachycardia syndrome. Am J Physiol Heart Circ Physiol. 2007;293:H1908–H1917. [PubMed: 17616747]
46. Tachi M, Kouzaki M, Kanehisa H, Fukunaga T. The influence of circulatory difference on muscle oxygenation and fatigue during intermittent static dorsiflexion. Eur J Appl Physiol. 2004;91:682–688. [PubMed: 14704798]
47. Krajnak KM. Potential contribution of work-related psychosocial stress to the development of cardiovascular disease and Type II diabetes: a brief review. Environ Health Insights. 2014;8:41–45. [PubMed: 25525370]
48. McCormick KG, Scorletti E, Bhatia L, et al. Impact of high dose n-3 polyunsaturated fatty acid treatment on measures of microvascular function and vibration perception in non-alcoholic fatty liver disease: results from the randomised WELCOME trial. Diabetologia. 2015;58:1916–1925. [PubMed: 26021488]

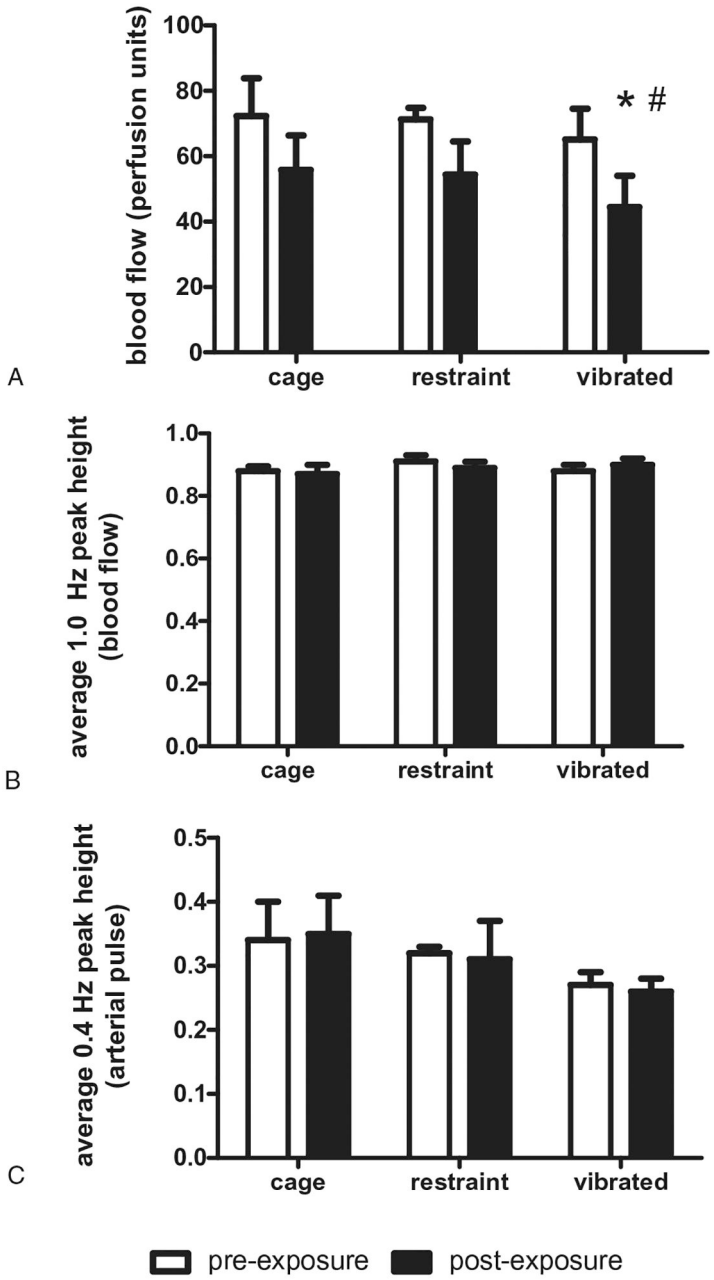

FIGURE 1.

Average blood flow over a 5-minute period was collected in cage control, restraint control, and vibrated rats before (pre) and after (post) exposure. Average blood flow was lower post-exposure than pre-exposure in vibration exposed rats (A: $^{*}P < 0.05$). Post-exposure blood flow in vibration exposed rats was also lower than blood flow in cage or restraint control rats (A: $^{\#}P < 0.05$). FFT analyses of the data revealed two prominent peaks in the laser Doppler signal, a 1 Hz peak indicative of blood flow and a 0.4 Hz peak that is associated with vascular pulsativity. A single exposure to vibration did not affect the peak amplitude of either 1.0 or 0.4 Hz peaks (B and C, respectively). FFT, Fast Fourier transform.

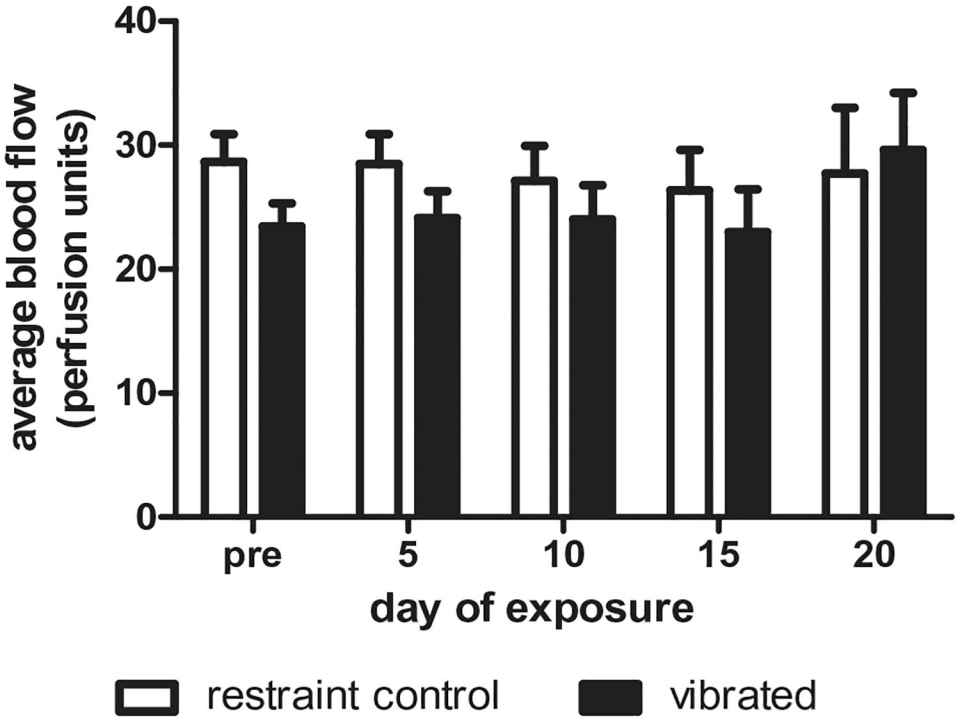

FIGURE 2.

Average blood flow on days 1 (pre-exposure), 5, 10, 15, and 20 during a 20 days exposure. Vibration exposure did not significantly alter average blood flow in the tail. The data represent total average blood flow during 15 minutes measurement.

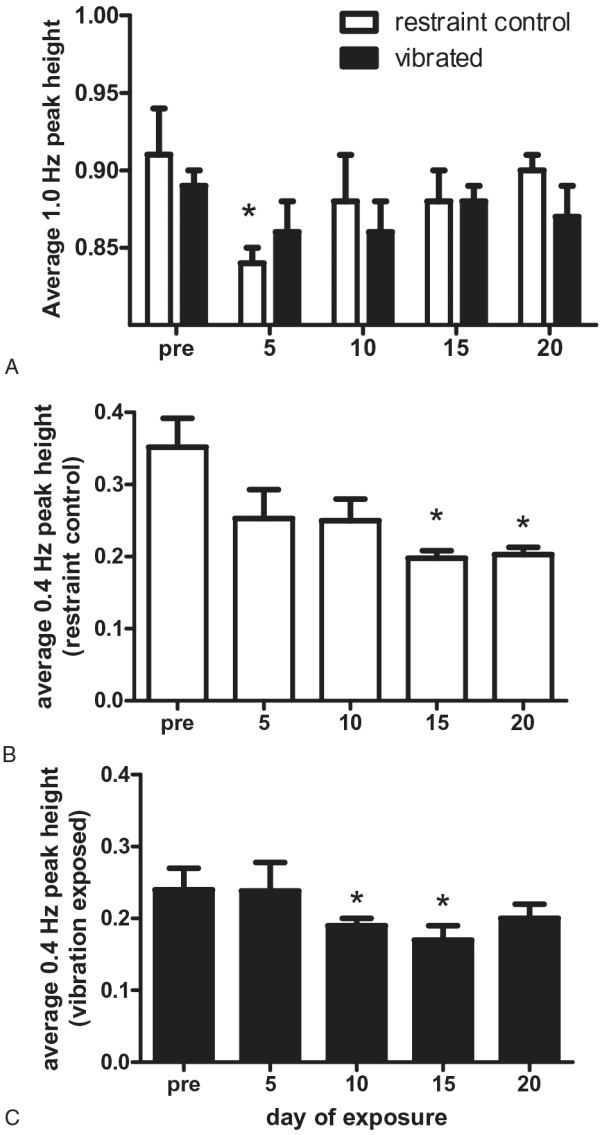

FIGURE 3.

Two peak frequencies in the measured blood flow were identified. The first peak (1.0 Hz) represents blood flow (A), and the other peak (0.4 Hz) represents arterial pulse (B: control, C: vibrated). The amplitude of the 1.0 Hz peak was reduced on day 5 of the experiment, but the difference was only significant in control rats (*$P < 0.05$, different than pre-exposure). There was also a marginal reduction in the 1 Hz peak in vibrated rats on day 20 of the exposure ($P < 0.06$). The amplitude of the 0.4 Hz peak was significantly lower on days 15 and 20 of the exposure than pre-exposure in restraint control rats (B). In vibrated rats (C), the amplitude of the 0.4 Hz peak was lower on days 10 and 15 (*$P < 0.05$ as compared with pre-exposure). On day 20 the peak amplitude in the vibrated animals was also lower but this reduction was not significant ($P < 0.07$).

TABLE 1.

These Data are the Mean (±SEM) Tail Temperatures (°C) Pre- and Post-Exposure in Rats Exposed to Cage Control, Restraint Control, or Tail Vibration

	Cage Control	Restraint Control	Vibrated
Pre-exposure	33.942 ± 0.005	33.952 ± 0.003	33.048 ± 0.003
Post-exposure	24.190 ± 0.25*	22.511 ± 0.110*#	22.462 ± 0.05*#

The post-exposure tail temperature in all groups of rats was lower than pre-exposure temperature (*$P < 0.05$). However, analyzing only post-exposure temperature revealed that tail temperature was lower in restrain control and vibrated rats than in cage-control rats (#$P < 0.05$).

TABLE 2.

These Data are the Mean (±SEM) Tail Temperatures (°C) Before Exposure to Vibration or Restraint on Days 1, 5, 10, 15, and 20 of the Second Experiment

	Day 1	Day 5	Day 10	Day 15	Day 20
Restraint control	33.952 (0.001)	33.941 (0.002)	33.385 (0.502)	33.946 (0.001)	33.947 (0.001)
Vibrated	33.949 (0.004)	33.940 (0.002)	33.047 (0.003)	33.947 (0.003)	33.945 (0.001)

There were no significant changes in tail temperature in either group over the different tails of the experiment.