Acute vibration increases $\alpha_{2C}$-adrenergic smooth muscle constriction and alters thermosensitivity of cutaneous arteries

K. Krajnak, R. G. Dong, S. Flavahan, D. Welcome, and N. A. Flavahan. Acute vibration increases $\alpha_{2C}$-adrenergic smooth muscle constriction and alters thermosensitivity of cutaneous arteries. J Appl Physiol 100: 1230–1237, 2006. First published December 8, 2005; doi:10.1152/japplphysiol.00761.2005.—The vascular symptoms of hand-arm vibration syndrome, including cold-induced vasospasms, are in part mediated by increased sensitivity of cutaneous arteries to sympathetic stimulation. The goal of the present study was to use a rat tail model to analyze the effects of vibration on vascular function and $\alpha$-adrenoceptor (AR) responsiveness. Rats were exposed to a single period of vibration (4 h, 125 Hz, constant acceleration 49 m/s$^2$ root mean square). The physical or biodynamic response of the tail demonstrated increased transmissibility or resonance at this frequency, similar to that observed during vibration of human fingers. Morphological analysis demonstrated that vibration did not appear to cause structural injury to vascular cells. In vitro analysis of vascular function demonstrated that constriction to the $\alpha_1$-AR agonist phenylephrine was similar in vibrated and control arteries. In contrast, constriction to the $\alpha_2$-AR agonist UK14304 was increased in vibrated compared with control arteries, both in endothelium-containing or endothelium-denuded arteries. The $\alpha_{2C}$-AR antagonist MK912 ($3 \times 10^{-10}$ M) inhibited constriction to UK14304 in vibrated but not control arteries, reversing the vibration-induced increase in $\alpha_2$-AR activity. Moderate cooling (to 28°C) increased constriction to the $\alpha_2$-AR agonist in control and vibrated arteries, but the magnitude of the amplification was less in vibrated compared with control arteries. Endothelium-dependent relaxation to acetylcholine was similar in control and vibrated arteries. Based on these results, we conclude that a single exposure to vibration caused a persistent increase in $\alpha_{2C}$-AR-mediated vasoconstriction, which may contribute to the pathogenesis of vibration-induced vascular disease.

Hand-arm vibration syndrome; Raynaud’s phenomenon; rat tail artery; cold
been questioned because it is unclear whether the physical response (i.e., the biodynamic response) is similar in rat and human tissues. Therefore, before the effects of vibration on vascular function were analyzed, the response of the tail to different vibration frequencies was measured. These data were used to determine whether the frequency-dependent biodynamic response of the tail was similar to the fingers and which frequency to use for the functional studies.

**METHODS**

**Animals.** Male Sprague-Dawley rats (6 wk of age; Hilltop Lab Animals, Scottsdale, PA) were used for all exposures. All rats were maintained on a 12:12-h light-dark cycle with food and water available ad libitum at the NIOSH facilities in WV, which are accredited by the Association for Assessment and Accreditation of Laboratory Animal Care. All procedures were approved by the NIOSH Animal Care and Use Committee and were in compliance with Centers for Disease Control guidelines for the care and use of laboratory animals.

**Vibration apparatus.** Vibration was generated by V408 electromagnetic shakers and PA100E amplifiers (both from Ling Dynamic Systems, Royston, Herts, UK) and controlled via a closed-loop feedback system. Vibration levels were monitored with 353B15 accelerometers and 482A20 signal conditioners (both from PCB Piezotronics, Depew, NY). Data acquisition and vibration control were performed through PCI-MIO-16XE-10 data-acquisition boards, PCI-6713 analog output boards, and custom LabView 5.0 programming (all from National Instruments, Austin, TX). The exposure components were enclosed in fan-ventilated, sound-attenuating cubicles (Med Associates, St. Albens, VT). Constant white noise (~70 dB) generated through a speaker inside the cubicles masked extraneous noises.

The shaker platforms were aluminum, 50 × 25 mm (major and minor radii) elliptical platforms, which were 12.7 mm thick, tapered down to 6.35 mm at the ends, and had 14-mm-wide extensions that lengthen the entire platform from the middle ellipse to 170 mm. Each platform was mounted onto a shaker and centered directly below the animal. The platform was fastened to the shaker, which oscillated the platform in a vertical direction.

**Vibration exposure.** Before vibration exposure, rats were placed in Broome-style restrainers 4 h/day for 5 days to acclimatize them to restraint and reduce the physiological effects of restraint stress (48). Rats were allowed to walk into the restrainers, head first, and their tail was gently threaded through a hole in the removable hatch. The hole in the hatch had been enlarged so that the rats’ tails were not held in an awkward position in relationship to their bodies.

On the day of the exposure, each rat’s tail was gently placed on top of the platform and four elastic straps (6.35 mm wide) were pulled over the tail and fastened over screws secured into the side of the platform. Care was taken to make sure that the tail was secured to the platform without compressing the tissue. To assess the biodynamic responses of the tail to different vibration frequencies, the rats’ tail and the shaker platform were positioned under the scanning laser vibrometer (Polytec PSV-300-H), and the vibration amplitude was measured at eight chosen points along the length of the tail (including points next to and between the strap restraints; see diagram in Fig. IA) along with a number of reference points on the platform using Polytec PSV software. The amplitude of the tail vibration was measured at 31.5, 63, 125, 160, and 250 Hz with a constant acceleration of 49 m/s² root mean squared.

To analyze the physiological effects of vibration on the ventral tail artery, rats were exposed to a single 4-h period of vibration at 125 Hz and with a constant acceleration of 49 m/s² root mean square (based on the results of the biodynamic study). Rats were acclimated to restraint as described above. On the day of the experiment, all rats were restrained and placed in sound-attenuated isolation chambers. The animals’ tails were strapped to a platform attached to a shaker (vibration-exposed group) or to a control platform that was mounted on isolation blocks (restraint control group). Immediately following the exposure, rats were euthanized with an overdose of pentobarbital sodium (100 mg/kg). The tails from some animals were fixed over night in 4% paraformaldehyde for histological analysis. The tails from remaining animals were placed in cold DMEM (with glucose; Invitrogen, Carlsbad, CA) and transported from NIOSH to The Ohio State University where the physiological analysis was performed the following day. Preliminary experiments (n = 4) demonstrated that overnight cold storage did not alter the responsiveness of rat tail arteries at 37 or 28°C.

**Histology.** The ventral tail artery was dissected from the region around the C10 vertebrae (point 4 in Fig. IA) of the tail and cryoprotected in 20% sucrose. The tissue was then embedded in OTC compound (VWR International, Bridgeport, NJ), and frozen sections (20-μm thickness) were cut on a cryostat and thaw-mounted onto SuperPlus slides (Fisher Scientific, Pittsburgh, PA). Tail segments from some animals were kept intact, processed as above, and thaw-mounted onto clean glass slides. Sections were viewed in a Leitz DMRB microscope to determine whether there were morphological changes in the vascular smooth muscle or endothelial cells that would be consistent with tissue damage. Images of sections were captured using a Sony Progress 3 charge-coupled device color video camera.

**Blood vessel chamber.** Tail arteries from restraint control and vibrated rats were analyzed simultaneously. Segments of artery from the mid-tail section (point 4 in Fig. IA) were removed and placed in cold Krebs-Ringer bicarbonate solution (in mM): NaCl 118.3, KCl 1.2, MgSO4 1.2, KH2PO4 2.5, CaCl2 2.5, NaHCO3 25.0, NaH2PO4 1.1 (glucose control solution). The small arteries were cannulated at both ends with glass micropipettes, secured using 12-0 nylon monofilament suture and placed in a microvascular chamber (Living Systems, Burlington, VT). The arteries were maintained at a constant transmural pressure of 60 mmHg in the absence of flow (2, 16). The chamber, which was superfused with control solution maintained at 37°C, pH 7.4 (passed with 16% O2-5% CO2-balance N2), was placed on the stage of an inverted microscope (×20, Nikon, Japan) connected to a video camera (Panasonic, CCTV camera, Japan). The vessel image was projected onto a video monitor, and the internal diameter was continuously determined by a video dimension analyzer (Living Systems Instrumentation, Burlington, VT) (2, 16) and monitored using a BIOCAP (Santa Barbara, CA) data-acquisition system.

**Physiological analyses.** Small arteries were allowed to equilibrate for 30–40 min at a transmural pressure of 60 mmHg before commencing experiments (2, 16). Concentration-effect curves for the selective α1-AR agonist, phenylephrine, or the selective α2-AR agonist, UK14304, were generated by increasing the concentration of the agonist in half-log increments once the constriction to the previous concentration had stabilized. Following completion of the concentration-effect curve, the influence of the agonists was terminated by repeatedly exchanging the buffer solution and allowing the artery to return to its stable baseline level. In some experiments, concentration-effect curves for UK14304 were determined under control conditions and in the presence of the selective α2-AR antagonist MK912 (3 × 10−9 M) (2, 16). When required, the preparations were incubated for 30 min with MK912 before and during exposure of the arteries for UK14304. A paired artery that was not treated with MK912 served as a time control to confirm that responses to the agonist did not change over time. When analyzing the influence of cold on α2-AR responsiveness, the temperature of the superfusate was decreased to 28°C for 30 min before commencing a concentration effect curve to UK14304. This provides sufficient time for the effect of cold on adrenergic reactivity to stabilize (26, 28). Endothelial function was assessed by analyzing relaxation to the endothelium-dependent dilator, acetylcho-
line in arteries constricted with the α₁-AR agonist phenylephrine (10⁻⁶ M). In some arteries, the endothelial cells were denuded mechanically before cannulation (2). This procedure was confirmed functionally by the absence of relaxation to acetylcholine (3 × 10⁻⁷ M) during constriction to ~60% of baseline diameter using UK14304 or phenylephrine.

Reagents. Acetylcholine, phenylephrine, and UK14304 were from Sigma (St. Louis, MO). MK912 was a gift from Merck (West Point, PA). Stock solutions of drugs were prepared fresh each day and stored at 4°C during the experiment. Drugs were dissolved in distilled water, with the exception of UK14304, which was dissolved in DMSO (highest chamber concentration of 0.001%). At this concentration, DMSO did not alter reactivity of tail arteries. All drug concentrations are expressed as final molar concentration in the chamber superfusate.

Data analyses. The transmissibility of the vibration from the platform to the tail was calculated by dividing the amplitude of the tail vibration by the amplitude of the platform vibration. Transmissibility was calculated for each frequency and at each location on the tail and was analyzed using a two-way ANOVA (frequency × location, with location nested within animal). The average internal and external circumferences of artery sections were analyzed with Student’s t-tests using JMP 5.0.1 software (SAS, Cary, NC).

Vasomotor responses were expressed as a percentage change in internal diameter before administering the agent. Data are expressed as means ± SE for n number of experiments, where n equals the number of animals from which blood vessels were studied. When parameters (e.g., internal diameter) were available for more than one artery from each animal, the average of the individual measurements was used for the analyses. Concentration-effect curves were analyzed by determining the concentration of constrictor agonist that evoked 15% constriction (CC₁₅), the concentration of dilator agonist that reduced constriction to 15% of baseline diameter (CR₁₅), or the maximal response (25). Statistical evaluation of the data was performed by Student’s t-test for either paired or unpaired observations. When more than two means were compared, a Bonferroni adjustment was performed.

RESULTS

Biodynamic analyses. Transmissibility of vibration to the tail was frequency-dependent. Analyses of the transmissibility data revealed significant main effects of frequency [F(4,40) = 140.38, P < 0.0001] and measurement location [F(7,40) = 65.57, P < 0.0001], along with a significant frequency by location-interaction [F(28,40) = 17.40, P < 0.0001]. Further analyses demonstrated that transmissibility was generally higher at 125, 165, and 250 Hz than at 31.5 or 63 Hz (P <
0.001; see Fig. 1, B–F). However, the greater transmissibility seen at these higher frequencies was location dependent. Examining the effects of location at each frequency demonstrated that transmissibility at all locations on the tail was similar at 31.5 and 63 Hz. In contrast, at 125 and 165 Hz, transmissibility was significantly increased in the midportion of the tail (location 4, Fig. 1, D, E, and G). At 165 and 250 Hz, transmissibility was increased at the tip of the tail. The tails of both animals showed very similar responses to the different vibration frequencies. Because these results demonstrate that transmissibility is increased at 125 Hz and because epidemiological and experimental data in humans have shown that the risk of developing HAVS is increased in workers using tools with a dominant frequency ~125 Hz (12), this frequency was used for the physiology analyses.

**Ventral artery histology.** Hematoxylin and eosin-stained sections (20 μm thick from the C10 region of the tail artery or control; n = 7) and vibrated rats (n = 6) were examined at a total magnification of ×200 using a Leitz DMRB microscope. There were no obvious signs of trauma to the vascular smooth muscle or the endothelial cell layer in arteries collected from either group of animals (Fig. 2A). However, the internal elastic membrane appeared to be constricted and endothelial cells compressed in the arteries of vibrated but not restraint control rats (Fig. 2, B and C).

**In vitro physiological analyses.** At a transmural pressure of 60 mmHg, the baseline diameters of control and vibrated tail arteries were similar: 472.1 ± 13.0 and 445.0 ± 8.9 μm, respectively (n = 13; P = not significant). In the absence of stimulation, these small arteries did not display significant basal constriction.

The selective α1-AR agonist phenylephrine (10⁻⁸ to 10⁻⁶ M) caused constriction that was similar in control and vibrated arteries (log CC₁₅ values of −6.57 ± 0.05 and −6.53 ± 0.06, respectively; n = 9, P = not significant) (Fig. 3).

The selective α₂-AR agonist UK14304 (10⁻⁹ to 10⁻⁶ M) caused concentration-dependent constriction that was significantly increased in vibrated compared with control arteries (log CC₁₅ values of −7.86 ± 0.13 and −7.22 ± 0.10, respectively; n = 12, P < 0.001; Fig. 3). Although α₂-ARs may be present on endothelial cells and initiate endothelium-dependent relaxation (27), differences in endothelial function did not contribute to the increased constriction of vibrated arteries. When the analysis was restricted to arteries without endothelium, constriction to UK14304 (10⁻⁹ to 10⁻⁶ M) was still significantly increased in vibrated compared with control arteries (log CC₁₅ values of −7.83 ± 0.16 and −7.17 ± 0.13, respectively; n = 7, P < 0.01). To determine whether the increased α₂-AR constriction was mediated by α₂C-ARs, responses to UK14304 were assessed in endothelium-denuded arteries in the absence and presence of the selective α₂C-AR antagonist MK912 (3 × 10⁻¹⁰ M) (2, 16). MK912 (3 × 10⁻¹⁰ M) significantly inhibited constriction evoked by UK14304 in vibrated arteries [log rightward shift at the CC₁₅ level of constriction of 0.48 ± 0.04 (3-fold); n = 4, P < 0.01] but not control arteries [log leftward shift at the CC₁₅ level of constriction of 0.15 ± 0.02; n = 4]. Indeed, although vibration was associated with increased constriction to UK14304 in untreated arteries (log CC₁₅ values of −6.96 ± 0.05 and −7.81 ± 0.11 for control and vibrated arteries, respectively; n = 4, P < 0.05), after MK912 there was no longer any significant difference between control and vibrated arteries (log CC₁₅ values of −7.11 ± 0.02 and −7.33 ± 0.14 for control and vibrated arteries, respectively; n = 4, P = not significant).

Cold-induced amplification of α₂-AR constriction is mediated by a selective increase in α₂C-AR activity (2, 16). In
control arteries, cooling to 28°C caused a significant increase in response to UK14304 (log CC15 values of 7.32 ± 0.12 and 8.08 ± 0.08 for 37 and 28°C, respectively; n = 8, P < 0.001), which was reversed on rewarming (Fig. 4). Cooling to 28°C also caused a significant increase in response to the α2-AR agonist in vibrated arteries (log CC15 values of 8.00 ± 0.16 and 8.36 ± 0.08 for 37 and 28°C, respectively; n = 8, P < 0.05), which also was reversed on rewarming (Fig. 4). Interestingly, the augmentation caused by cooling was significantly less in vibrated compared with control arteries (log rightward shifts of 0.36 ± 0.10 (2.3-fold) and 0.76 ± 0.11 (5.8-fold), respectively, at the CC15 level of response; n = 8, P < 0.05) (Fig. 4). Indeed, although constriction to UK14304 at 37°C was significantly increased in vibrated compared with control arteries (P < 0.05, n = 8; Fig. 4), at 28°C responses to the agonist were not significantly different between control and vibrated arteries (P = not significant, n = 8; Fig. 4).

In arteries constricted to ~60% of baseline diameter with the α1-AR agonist phenylephrine (1 μM), acetylcholine (0.01 to 1 μM) caused concentration-dependent relaxation that was not significantly different between control and vibrated arteries (log CR15 values of −6.78 ± 0.14 and −6.67 ± 0.10, n = 6, P = not significant; and maximal responses of 98.9 ± 4.4 and 97.5 ± 2.9% of phenylephrine-induced constriction, respectively, n = 6, P = not significant) (Fig. 5).

**DISCUSSION**

Previous studies have demonstrated that the vascular response (38), and soft tissue damage (15, 39) caused by vibrating the rat tail are similar to those observed in patients with HAVS (46, 47). The vibration-induced physical responses of fingers appear to be one of the critical risk factors associated with the development of HAVS. In human fingers, vibration transmissibility is usually greater than one between 60 and 250 Hz (22). Peak mechanical impedance of the fingers is also in this frequency range (23). These observations indicate that human fingers have a resonance response in this frequency range. As shown in Fig. 1, transmissibility on rat tails was also amplified between 63 and 250 Hz. At 125 Hz, the amplification or resonance was restricted to the midportion of the tail. Finger
resonance is also location specific (44). These observations indicate that fingers gripping on a tool handle and rat tails restrained on the plate have similar biodynamic responses and support the use of the rat tail model for studying HAVS. Based on laboratory (12, 13) and epidemiological studies (6, 9), workers using tools with a dominant frequency near 125 Hz have the greatest risk for developing HAVS, which may reflect the increased stress and strain caused by an amplified biodynamic response. Physiological analyses on rat tail arteries were therefore performed using this vibration frequency and using the anatomical location displaying the amplified biodynamic response (location 4, Fig. 1).

Vasoconstriction caused by acute vibration in human volunteers is mediated by systemic (i.e., sympathetic) and local effects of the exposure (10). Therefore, after an acute vibration exposure, reductions in blood flow can be measured in both the exposed and unexposed hands of subjects. However, the reduction in blood flow is significantly greater in the exposed hand (12), suggesting that direct exposure to vibration enhances the response to systemically induced vasoconstriction. In addition, increased sensitivity to norepinephrine-induced vasoconstriction can be induced in anesthetized dogs exposed to vibration (1). Anesthesia blocks the sympathetic response to vibration, but a local increase in vascular sensitivity to norepinephrine is still apparent. Thus vasoconstriction in response to acute vibration results from increased sympathetic activity and a local vibration-induced increase in sensitivity of the vessels to sympathetic stimulation. By isolating rat tail arteries for in vitro functional analysis, they are separated from sympathetic stimulation or from circulating agents that might initiate vasoconstriction. Under these quiescent conditions, there was no change in diameter and no differences in baseline tone between arteries from control and vibrated tails. Therefore, in the absence of external stimulation, there appears to be no inherent myogenic mechanisms initiating vasoconstriction in these vibrated arteries. Sympathetic constriction of cutaneous arteries is mediated by \( \alpha_1 \)- and \( \alpha_2 \)-ARs located on vascular smooth muscle cells (16, 24). Vasoconstriction evoked by the selective \( \alpha_1 \)-AR agonist phenylephrine was similar in control and vibrated arteries, indicating that there was no change in \( \alpha_1 \)-AR reactivity. In contrast, vibration increased the responsiveness of the tail artery to the selective \( \alpha_2 \)-AR agonist UK14304. Vascular endothelial cells express \( \alpha_2 \)-ARs, which can mediate endothelium-dependent relaxation (27). Although endothelial \( \alpha_2 \)-ARs are more prominent on coronary compared with cutaneous arteries (25, 27), a vibration-induced decrease in activity of endothelial receptors could contribute to a selective increase in \( \alpha_2 \)-AR constriction. However, in arteries that had been denuded of endothelium, constriction to \( \alpha_2 \)-AR activation with UK14304 was still increased in vibrated compared with control arteries. Therefore, the vibration-induced increase in \( \alpha_2 \)-ARs is mediated by increased activity of smooth muscle rather than decreased activity of endothelial receptors. The results indicate that vibration can augment sympathetic vasoconstriction by selectively increasing \( \alpha_2 \)-AR reactivity. However, the present study cannot determine whether this was mediated by a direct effect of vibration on the arterial wall or an indirect action mediated by neurohumoral mechanisms.

\( \alpha_2 \)-ARs comprise \( \alpha_{2A} \), \( \alpha_{2B} \), and \( \alpha_{2C} \)-ARs (42). \( \alpha_{2A} \) and \( \alpha_{2B} \)-ARs were originally thought to be responsible for smooth muscle contraction, whereas \( \alpha_{2C} \)-ARs were considered silent or vestigial receptors (36, 42). Indeed, at warm temperatures, constriction of cutaneous arteries to \( \alpha_2 \)-AR activation is mediated by \( \alpha_{2A} \)-ARs, with no apparent contribution from \( \alpha_{2C} \)-ARs (16). However, after moderate cooling, \( \alpha_{2C} \)-ARs are no longer silent and mediate the cold-induced augmentation of \( \alpha_2 \)-AR reactivity and contribute to cold-induced constriction of the cutaneous circulation (16). In nonneuronal cell types, \( \alpha_{2C} \)-ARs are normally retained in the endoplasmic reticulum/Golgi complex (21, 31, 42) and cold exposure stimulates translocation of the receptors to the cell surface where they can respond to activation (2, 32). This is mediated by the cold-induced generation of reactive oxygen species from smooth muscle mitochondria, which cause activation of RhoA and Rho kinase and the subsequent mobilization of \( \alpha_{2C} \)-ARs to the plasma membrane (2, 3, 16, 32). In the present study, the selective \( \alpha_{2C} \)-AR antagonist MK912 (2, 16) did not inhibit constriction of control tail arteries to \( \alpha_2 \)-AR stimulation with UK14304, which is consistent with \( \alpha_{2C} \)-ARs normally being silent at warm temperature. In contrast, the \( \alpha_{2C} \)-AR antagonist inhibited the increased constrictor response to UK14304 in vibrated arteries, reversing the vibration-induced increase in \( \alpha_2 \)-AR reactivity. Therefore, these results suggest that the vibration-induced increase in \( \alpha_2 \)-AR activity is mediated by the \( \alpha_{2C} \)-AR subtype. Interestingly, this vibration-induced increase in \( \alpha_{2C} \)-AR activity was associated with an altered response to moderate cooling. Cold increased constriction to \( \alpha_2 \)-AR stimulation in control and vibrated arteries; however, the magnitude of the increase was less in vibrated compared with control arteries. Because of this differential sensitivity to cold, the augmentation in \( \alpha_2 \)-AR response observed in vibrated arteries at warm temperature was not present during cooling. By increasing the activity of \( \alpha_{2C} \)-ARs, vibration may have reduced the receptor pool available for translocation during cold exposure, causing a reduced cold-induced amplification of \( \alpha_2 \)-AR constriction. It is not known whether vibration mimicked the...
effect of cooling to mobilize $\alpha_{2C}$-ARs by increasing reactive oxygen species or RhoA activity within smooth muscle cells. Prolonged exposure to vibration is associated with increased sensitivity to cold, resulting in cold-induced vasospasm or Raynaud’s phenomenon. The present results demonstrating a reduction in cold-induced reactivity in vibrated arteries may therefore appear somewhat counterintuitive. However, in healthy human volunteers, acute exposure to vibration causes persistent vasoconstriction but reduces cold-induced vasoconstriction (11, 40), consistent with the results of the present study. We have previously demonstrated that prolonged exposure to vascular stress can increase $\alpha_{2C}$-AR expression in human cultured cutaneous smooth muscle cells (17, 18). Therefore, chronic exposure to vibration-induced shear and bending stress may act as vascular stressors leading to increased $\alpha_{2C}$-AR expression in vascular smooth muscle cells. By increasing the available pool of $\alpha_{2C}$-ARs for mobilization, increased expression of these receptors may contribute to increased vasoconstriction and cold sensitivity in individuals exposed to chronic vibration. Indeed, the increased cold-induced vasoconstriction occurring in HAVS is prevented by inhibition of $\alpha_2$-ARs (35). Most vascular symptoms displayed by HAVS patients are induced by exposure to cold (45). In addition, the prevalence of HAVS is much higher in cold climates (37). Thus it is possible that cold and vibration exposure work through similar or synergistic mechanisms to alter vascular function. Endothelial cell injury has been postulated to contribute to the vasculopathy of HAVS (19, 45). However, a clinical study demonstrated that endothelium-dependent dilation to acetylcholine was normal in individuals with HAVS, and circulating levels of endothelium-derived products have not demonstrated consistent changes during acute or chronic exposure to vibration (33, 34). In the present study, endothelium-dependent dilation to acetylcholine was similar in control and vibrated arteries. Likewise, histological analysis of vibrated tail arteries demonstrated no signs of endothelial cell injury. The vibration-induced compression of endothelial cells likely reflects persistent vasoconstriction after the vibration exposure. There was also no evidence of structural damage to the medial smooth muscle layer. Previous studies have demonstrated that chronic exposure to vibration (>30 days) is associated with structural lesions of rat tail arteries (39).

In conclusion, a single exposure to vibration (125 Hz) caused a persistent increased constriction to $\alpha_2$-AR but not $\alpha_1$-AR stimulation. This was not associated with endothelial dysfunction. The vibration-induced increase in smooth muscle $\alpha_2$-AR activity was selectively inhibited by blockade of $\alpha_{2C}$-ARs. $\alpha_{2C}$-ARs, which are normally silent at warm temperatures, mediate cold-induced amplification of $\alpha_2$-ARs and cold-induced constriction of cutaneous arteries. Indeed, although cold increased $\alpha_2$-AR activity in control and vibrated arteries, the magnitude of the amplification was reduced after vibration. The results suggest that vibration amplifies sympathetic vasoconstriction by increasing $\alpha_{2C}$-AR activity, perhaps by causing inappropriate functional rescue of these receptors.

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**REFERENCES**


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VIBRATION AND \(\alpha_2\)-ADRENOCEPTORS


