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# Whole-Body Periodic Acceleration Enhances Brachial Endothelial Function

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**Background** Periodic acceleration in the direction of the spinal axis through repetitive movement increases the shear stress on the vascular endothelium. In the present study it was assessed whether whole-body periodic acceleration with a new device would enhance endothelial function in sedentary adult volunteers.

**Methods and Results** Twenty-six sedentary subjects (44±3 years) were randomly assigned to remain sedentary or perform exercise training for 4 weeks, followed by crossover. Periodic acceleration was applied with a horizontal motion platform at 2–3 Hz and approximately ±2.2 m/s$^2$ for 45 min. Increases in the brachial artery diameter were examined at rest, during reactive hyperemia (flow-mediated dilatation: %FMD) and after sublingual administration of 0.3 mg nitroglycerin (%NTG) using high-resolution ultrasound. All subjects completed the study with no adverse side-effects. There were no significant changes in the resting heart rate or arterial pressure, body weight, or lipid profiles during the study. Although %FMD did not change during the non-training period with periodic acceleration, it significantly increased from 7.3±0.4% at baseline to 8.4±0.4% after the training period ($p<0.05$), while %NTG remained unchanged.

**Conclusions** Whole-body periodic acceleration with a horizontal motion platform improved vascular endothelial function in sedentary adults. This device might offer an alternative to active exercise for patients whose medical condition limits physical activity. (*Circ J* 2008; **72:** 139 – 143)

**Key Words:** Endothelial function; Exercise; Life-style

Habitual physical activity may reduce the risk of cardiovascular disease,[1] but the prevalence of physical inactivity is increasing. This life-style change is of interest because physical inactivity has been proposed as an independent cardiovascular risk factor. Studies of endurance exercise training support the notion that it is effective for preventing cardiovascular events.

Endothelium-dependent coronary or peripheral vasomotor dysfunction has been reported as an independent predictor of cardiovascular disease events.[2–4] Aerobic exercise training improves endothelial vasomotor function in both healthy subjects and patients with coronary artery disease,[5] and this effect has been attributed to local repetitive increases in the shear stress on the endothelium.

On the other hand, there have been few studies on the effects of passive exercise on endothelial function. This type of exercise may be useful in sedentary subjects. It has been shown that periodic acceleration in the direction of the spinal axis through repetitive movement also increases the shear stress to the endothelium.[6,7] A passive exercise device using whole-body periodic acceleration might gain credibility as a therapeutic modality if it can be shown to improve vascular endothelial function in humans.

The analysis of coronary endothelial function is suitable for the prediction of cardiovascular events,[8] although this method is limited by the risk and expense of cardiac catheterization. At present, the most commonly used method for evaluating vascular endothelial function is flow-mediated vasodilation of the brachial arteries.[9,10] Therefore, in the present study we assessed whether whole-body periodic acceleration by means of a new passive exercise device could improve brachial artery flow-mediated vasodilation in a population of adults with no history of regular exercise.

## Methods

*Study Patients*

We studied 26 adult volunteers (44±3 (SE) years; 14 women, 12 men) who were not taking any medication. None of the subjects had a habit of regular exercise and all maintained a sedentary lifestyle. The study protocols were approved by the institution's Ethical Committee on Human Research and written informed consent was given by all patients. All subjects fasted for at least 8–12 h, and did not ingest substances that might affect vasoreactivity, such as caffeine or vitamin C, for 4–6 h before the study. Smokers included subjects with a current history of tobacco use for more than 1 year. Subjects were considered to have hypertension if they had a blood pressure level ≥140/90 mmHg or were being treated. Patients with secondary hypertension were excluded. Subjects were considered to have diabetes mellitus if they had a fasting blood glucose level ≥126 mg/dl

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Fig 1. The AT101 motion platform.

**Table 1 Baseline Characteristics of All Subjects**

| | |
|---|---|
| *Age (years)* | *44±3 (range 28–59)* |
| *Gender (M/F)* | *12/14* |
| *BMI (kg/m²)* | *24.8±0.4* |
| *Hypertension (%)* | *7 (27%)* |
| *Hypercholesterolemia (%)* | *7 (27%)* |
| *Current smoker (%)* | *9 (35%)* |
| *Diabetes mellitus (%)* | *3 (12%)* |
| *Total cholesterol (mg/dl)* | *193±3* |
| *LDL-cholesterol (mg/dl)* | *120±3* |
| *HDL-cholesterol (mg/dl)* | *47±3* |
| *Triglycerides (mg/dl)* | *140±10* |
| *Mean arterial pressure (mmHg)* | *99±4* |
| *Resting heart rate (beats/min)* | *69±6* |

*BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein.*

**Table 2 Parameters Before and After Non-Training and Training**

| | *Non-training* | | *Training* | |
|---|---|---|---|---|
| | *Before* | *After* | *Before* | *After* |
| *BMI (kg/m²)* | *24.1±0.4* | *24.1±0.4* | *24.1±0.4* | *24.0±0.4* |
| *Total cholesterol (mg/dl)* | *192±3* | *191±3* | *194±3* | *193±3* |
| *LDL-cholesterol (mg/dl)* | *120±3* | *118±3* | *122±3* | *120±3* |
| *HDL-cholesterol (mg/dl)* | *47±2* | *46±2* | *47±2* | *47±2* |
| *Triglycerides (mg/dl)* | *139±10* | *142±7* | *137±9* | *137±7* |
| *FBG (mg/dl)* | *92±1* | *91±1* | *92±1* | *91±1* |
| *Aldosterone (pg/ml)* | *73±8* | *77±10* | *75±9* | *76±11* |
| *Norepinephrine (pg/ml)* | *243±38* | *250±52* | *238±42* | *247±41* |
| *hsCRP (mg/L)* | *1.6±0.4* | *1.5±0.4* | *1.7±0.4* | *1.6±0.4* |
| *Resting MAP (mmHg)* | *99±5* | *97±6* | *102±3* | *98±5* |
| *Resting HR (beats/min)* | *69±5* | *66±3* | *72±5* | *66±4* |
| *Resting blood flow (ml/min)* | *175±24* | *184±35* | *182±29* | *178±32* |

*FBG, fasting blood glucose; hsCRP, high-sensitivity C-reactive protein; MAP, mean arterial pressure; HR, heart rate. Other abbreviations see in Table 1.*

**Table 3 Ultrasound Measurements of Brachial Artery at the First Assessment**

| | |
|---|---|
| *Brachial artery diameter (mm)* | |
| *Baseline* | *4.1±0.1 (range 3.0–5.1)* |
| *After hyperemia* | *4.4±0.1 (range 3.3–5.5)* |
| *After nitroglycerin* | *4.8±0.1 (range 3.5–6.1)* |
| *Flow-mediated dilation (%)* | *7.6±0.2 (range 3.8–12)* |
| *Nitroglycerin-induced dilation (%)* | *14.2±0.4 (range 8.0–22.1)* |

*Data are presented as the mean value±SEM.*

or were already being treated. Body mass index (BMI) was calculated (kg/m²). Subjects were instructed not to eat or drink on the morning of each visit and, if applicable, not to smoke for at least 24 h prior. All vasoactive medications were withheld for 24 h before the evaluation.

*Protocol*

Whole-body periodic acceleration was achieved with a gurney-like motion platform device driven by a 2-flywheel motor assembly (Acceleration Therapeutics AT101; Non-Invasive Monitoring Systems; North Bay Village, FL, USA; Fig 1)[6,7] The device is 222 cm long, 77.5 cm wide, and weighs 211 kg. A foot board, 112 cm high, for strapping the subject's feet enclosed in shoes, is used to couple the body to the motion platform during periodic acceleration. The supine subject lies on a mattress placed on the motion platform for repetitive head-to-foot movements delivered at approximately 140 cycles/min and approximately ±2.2 m/s² The device also has a stop switch for the patient. A hand-held controller allows the operator to start and stop the device, and to adjust the speed and acceleration of the device. The motion platform is capable of moving subjects with a body weight of up to 150 kg at between 60 cycles and 200 cycles/min and up to ±3.9 m/s².

All subjects had 4 weeks of sedentary activity and then 4 weeks of passive training in a randomized and crossover design. Vital signs were recorded, a fasting blood sample was obtained, and vascular function was studied at baseline and 4, 8 and 12 weeks.

Periodic acceleration was applied with the AT101 at a frequency of 2–3 Hz and approximately ±2.2 m/s² for 45 min. The exercise procedure was repeated 20 times over 4 weeks.

*Ultrasound of the Brachial Artery*

All individuals underwent an ultrasound examination according to the guidelines of the International Brachial Artery Reactivity Task Force[9] The diameter of the right brachial artery (20 mm proximal to the antecubital fossa) was assessed using a high-resolution machine (SONOS 5500; Philips Medical Systems, Bothell, WA, USA) with a broadband (7–15 MHz) linear array transducer. To secure the ultrasound image and measurement position throughout the study, we used a stereotactic probe-holding device (MIST-100; Saraya Co Ltd, Osaka, Japan) while the subject's arm was positioned on a foam cast (MIST-100) to inhibit movement. Ultrasound images were recorded on S-VHS videotape and analyzed by blinded investigators.

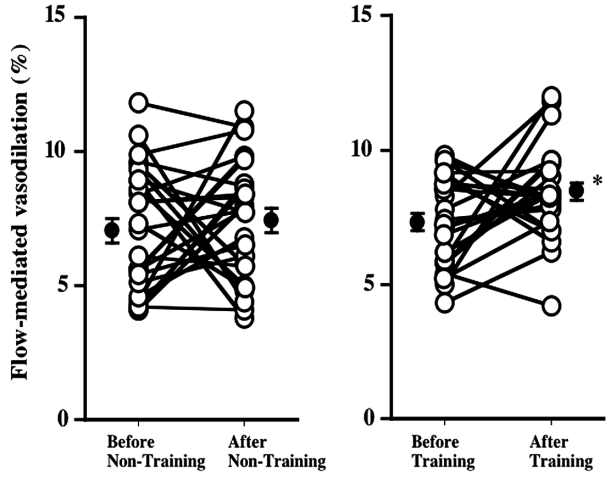


Fig 2. Flow-mediated vasodilatation of the brachial artery. Data from individual subjects and mean values (±SE) are plotted for results following 4-week non-training (Left panel) and training (Right panel) periods. *p<0.05 vs before training.

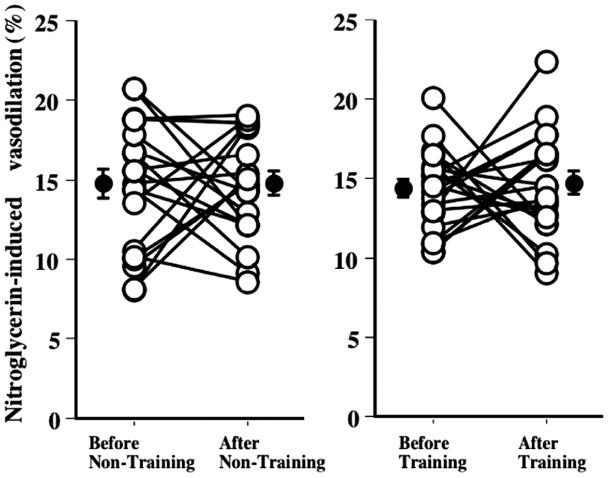


Fig 3. Nitroglycerin-induced vasodilatation of the brachial artery. Data from individual subjects and mean values (±SE) are plotted for results following 4-week non-training (Left panel) and training (Right panel) periods.

The mean values of 3 measurements were averaged for each datum. A pressure cuff, placed on the forearm, was inflated and kept constant at 50 mmHg above the systolic pressure to induce forearm ischemia. Blood flow was calculated by multiplying the velocity–time integral of the Doppler flow signal and the vessel cross-sectional area. After 5 min, the cuff was released, and the increase in blood flow caused increased shear stress, which served as the stimulus for flow-mediated dilatation (FMD). FMD occurred maximally approximately 60 s after release of the occlusive cuff, and the maximum brachial artery diameter was measured. Brachial artery FMD was expressed as the change in the post-stimulus arterial diameter divided by the baseline diameter. Next, 20 subjects were given a 15-min rest to return to the baseline condition and baseline diameter was re-measured. A single tablet of nitroglycerin (NTG) at a dose of 0.3 mg (Nihonkayaku Co, Tokyo, Japan) was then administered sublingually. After 5 min, the brachial artery diameter was determined again. NTG-induced brachial artery vasodilation was expressed in the same way as a percentage of the baseline diameter.

Reproducibility was assessed in 10 individuals (5 men) who were examined twice at a 2-week interval. The intra-observer intersession coefficients of variation were 2.8% for diameter, 2.5% for brachial artery FMD, and 1.6% for NTG-induced brachial artery vasodilation (the latter 2 values are expressed as the absolute diameter change).

*Measurements of Biochemical Markers*

Blood for the measurement of plasma levels of aldosterone and norepinephrine was collected in tubes containing EDTA (1 mg/ml). Plasma aldosterone levels were measured using commercial radioimmunoassay kits. Plasma norepinephrine concentrations were measured by high-performance liquid chromatography. Serum high-sensitivity C-reactive protein (hsCRP) was measured by a sensitive nephelometric assay (Behring Diagnostics, Marburg, Germany).

*Statistical Analysis*

Data are expressed as the mean value ± SEM. To compare differences between groups, Student's paired t-test was used (StatView version 5.0, Abacus Concepts Inc, Calabasus, CA, USA). A value of $p<0.05$ was considered statistically significant.

## Results

*Clinical Characteristics*

The baseline characteristics of the study group are listed in Table 1. The study population had a combination of risk factors. None of the women were postmenopausal. All subjects completed the study without any adverse side-effects.

*Exercise Training Effects*

There were no significant changes in BMI, plasma levels of total, high or low-density lipoprotein-cholesterol, triglycerides, fasting blood glucose, aldosterone, norepinephrine, serum hsCRP, resting heart rate or arterial pressure following training or non-training (Table 2).

*Brachial Artery Responses*

Baseline brachial artery diameter and vascular responses are shown in the table 3.

Four weeks of the exercise regimen significantly increased the %FMD value from 7.3±0.4% at baseline to 8.4±0.4% at 4 weeks ($p<0.05$) (Fig 2). The %FMD value at baseline was comparable to that at 4 weeks of non-training (7.1±0.5% to 7.6±0.5%) (Fig 2). In the 13 subjects who trained first, the %FMD value at baseline after crossover (7.2±0.6%) returned to the first baseline value before training (7.3±0.7%).

No significant differences were observed in the vasodilator responses to NTG before and after 4 weeks of training or non-training (Fig 3).

## Discussion

Whole-body periodic acceleration for 4 weeks, by means of a new passive exercise device, improved vascular endothelial function in sedentary adults. These benefits disappeared after 4 weeks of non-training. Constant passive exercise training with this new device may be beneficial for preventing cardiovascular disease, as an alternative to

active exercise for patients whose medical condition limits physical activity.

Vascular endothelial function is essential for maintaining the health of the vessel wall and for vasomotor control in both conduit and resistance vessels. Physical inactivity, the so-called sedentary lifestyle, increases cardiovascular risk in healthy individuals by inducing endothelial dysfunction. An early study reported that 4 weeks of regular exercise improved coronary endothelial function in subjects who were exposed to a high-intensity inpatient exercise program.[5] Furthermore, whole-body exercise training improved endothelial function as measured by brachial artery FMD in normal subjects.[11]

We previously reported that periodic acceleration with a motion platform increased plasma nitrite and nitrate levels in healthy adults.[12] Exercise training increased the basal production of plasma nitrite and nitrate.[13,14] Periodic acceleration applied to the whole body in the direction of the spinal axis adds pulses to the circulation, because fluid shifts occur within the body as the motion platform accelerates and decelerates, thereby increasing the shear stress on the vascular endothelium. The benefits of this exercise in individuals with cardiovascular risk or established disease may be related to nitric oxide (NO) released into the circulation through the activation of endothelial NO synthase because of the increased shear stress to the endothelium. In the present study, exercise training did not change the vasorelaxant responses to NTG, an endothelium-independent NO donor. These findings suggest that the beneficial effect may be caused by a change in the function of endothelial cells, but not smooth muscle itself.

It has been shown that enhanced external counterpulsation (EECP) may improve endothelial function, promote coronary collateral supply, and enhance ventricular function.[15,16] EECP may also contribute to a decrease in oxidative stress, which is associated with various cardiovascular risk factors. The effects of EECP on endothelial function have been attributed to enhanced endothelial shear stress in the large arteries of the trunk as a consequence of rhythmic compression of the legs. This mechanism may be similar to that proposed for whole-body periodic acceleration. The chronic intermittent enhancement of shear stress, as caused by exercise training with the use of the AT101, may lead to endothelial NO release via the activation of endothelial NO synthase.

Cardiovascular risk factors, including hypercholesterolemia, diabetes mellitus, hypertension, and smoking, are associated with endothelial dysfunction.[17,18] The present data showed that the benefits of exercise training go beyond the recognized benefits of lipids or glycemic control, blood pressure reduction, and smoking avoidance. In men with polymetabolic syndrome, 3 months of cycle training produced an increase in brachial artery flow-mediated dilation without changing the BMI, blood pressure, or lipids, and thus suggested a direct beneficial effect on arterial function.[19] In the present study, none of the data for the vasoactive factors significantly changed throughout the study (Table 2). Further studies that address the effect of whole-body periodic acceleration on well-established parameters of endothelial function are needed.

The %FMD returned to baseline levels after non-training. Exercise training improves endothelium-dependent vasodilation in post-AMI patients, and these beneficial effects disappear after 1 month of non-training.[20] With non-training, most of the exercise-gained aerobic fitness acquired over 2–3 months is lost within 2–4 weeks.[21] A reversal of the improvement in FMD of the brachial artery has been observed 6 weeks after the cessation of forearm hand-grip exercise in patients with heart failure.[22] Therefore, an appropriate exercise program is necessary to maintain the vascular benefits of exercise.

*Study Limitations*

The present study lacked sufficient power to address the influence of coronary risk factors because of its modest sample size. Our study was carried out in volunteers with a combination of risk factors. Therefore, it is difficult to assess the effect of any individual risk factor on endothelial function. Many risk factors are not simply present or absent, but rather are present to a greater or lesser extent in each individual.

Endothelium-dependent vasodilatation varies during the menstrual cycle. Endogenous estradiol may be involved in this menstrual cycle-related vasodilatation. However, we did not estimate the phase of the menstrual cycle or check the women's body temperature every morning.

## Conclusion

Whole-body periodic acceleration enhances vascular endothelial function in adults with low fitness levels. Therefore, the device used in the present study might substitute for or complement active exercise in patients whose medical condition limits physical activity.

### *Disclosure*

*We have not any commercial associations that might pose a conflict of interest in connection with this article.*

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