

Examining Cerebrovascular Changes after Aerobic Exercises by Analyzing Magnetic Resonance Angiography Images

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Aerobic exercise is effective for preventing cerebrovascular diseases. In that, this study focuses on investigating cerebrovascular changes with MRA (Magnetic Resonance Angiography) images by comparing before and after the aerobic activity. As a result, acquired MRA images indicate that signal intensity is increased in case of ECA (External Carotid Artery), STA (Superficial Temporal Artery) with relation to comparing before-after aerobic activities. However, ICA (Internal Carotid Artery), VA (Vertebral Artery), BA (Vertebral Artery) decreased. The comparison of vessel thickness before-after exercising aerobics results in the rise of ECA, STA, while ICA, and VA, BA decreased. Cerebrovascular transformation during aerobic exercises is analyzed with MRA image. Such data show the changes of both blood flow volume and vessel thickness after aerobic activities. As the study demonstrates, aerobic exercises increase cerebral blood flow and vessel thickness. Therefore, aerobic exercises are expected to help preventing cerebrovascular diseases.

Keywords : MRA, Aerobic exercise, signal intensity, Vessel thickness

1. Introduction

According to the “2013 cause of death statistics report” released by the National Statistical Office (NSO), cancer, cerebrovascular disease, and heart disease accounted for 47.4 % of all deaths. While cancer is an overwhelming cause of death in Korea, it is followed closely by vascular diseases, such as cerebrovascular disease and heart disease. The mortality rate of cerebrovascular disease in Korea is 71.6 per 100,000 people, which is higher than the average mortality rate (65.7 persons) in Organization for Economic Co-operation and Development (OECD) countries [1].

According to the “2014 cause of death statistics”, the incidence of cerebrovascular disease was the highest (48.2 %) among the circulatory system diseases in individuals in their 20s [2]. In a recent study, Mc-Farlane *et al.* reported that metabolic imbalances, including hyperlipidemia, hyperinsulinemia, and arteriosclerosis with obesity, were associated with decreased physical activity,

which lead to increased mortality from vascular diseases, such as cerebrovascular disease and cardiovascular disease [3]. Treatment for cerebrovascular disease is costly and time-consuming and even when treated, it is likely to persist. In addition, because of its high risk of recurrence, the importance of early diagnosis and prevention is being realized [4]. The National Institutes of Health (NIH) reports that the recommended duration (> 30 minutes) of daily exercise and walking prevents cerebrovascular disease [5]. In recent years, as society develops, the complex division of labor increases the proportion of sedentary jobs, traffic and communication have become more convenient due to advancements in science and technology, and the majority of people living in urban areas lack exercise [6]. Presently, the rate of ischemic diseases, in which the blood viscosity is increased and the blood vessels are blocked, has increased due to the decline in physical activity [7]. This differs from the past when there were many hemorrhagic diseases. While periodic exercise is necessary for prevention, leisurely exercise is insufficient [8]. Therefore, there is a growing need for exercise regimens that affect the cerebral blood vessels as well as studies on the effective amount and intensity of exercise

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[9]. Magnetic resonance angiography (MRA), which is one of the indispensable diagnostic methods for suspected cerebrovascular disease, can measure not only the shape of the cerebral vessels but also the cerebral blood flow (CBF) rate and velocity [10]. The time of flight (TOF) and phase contrast (PC) techniques are typical examples [11]. The TOF technique is widely used in clinical practice since it is less time-consuming and an angiogram is easily obtained. In addition, because of their superior signal to noise ratio (SNR), small voxel size, and short reverberation time, 3D techniques are more widely used than 2D techniques [12]. The CBF can be accurately measured during conventional MRA imaging, thus making it a very practical technique that circumvents previous inconveniences [13]. However, few studies have observed the changes in CBF using these techniques [14]. Thus, the purpose of this study was to use MRA for the investigation of the degree of vascular to aerobic exercise and to establish an exercise regimen for the prevention of disease.

2. Materials and Methods

2.1. Experimental material

We used a 3-Tesla magnetic resonance imaging scanner (3T MRI; Siemens, Verio, Erlangen, Germany; Fig. 1) with a 12-channel head coil, manufacturer, which was used to acquire the measurements for the comparative analysis of changes in blood pressure in healthy adults (mean age: 22.74 ± 1.58 , 8 men and 7 women) before and after using a treadmill. [Horizon Fitness ID100; running area: 15×48 inches, manual speed: 0.8-13 km/h, user weight: 100 kg, Dimensions (cm); Fig. 2].

2.2. Research Methods

This study was conducted with the approval of the Institutional Review Board (IRB). The experiment was

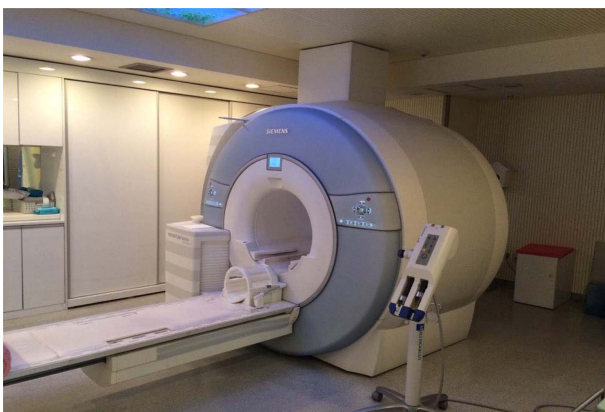


Fig. 1. (Color online) 3T Magnetic Resonance Image (Siemens, Verio, Erlangen, Germany).



Fig. 2. (Color online) Treadmill machine (Horizon ID100).

conducted after thoroughly explaining the purpose and procedure of the study to the subjects, who all provided individual consent. Subjects were asked to sleep adequately, refrain from drinking, smoking, and excessive physical activity 24 hours prior to taking the measurements. On the day the measurements were taken, they were asked to refrain from drinking coffee and eating food, and were only allowed to drink water prior to arriving at the laboratory. On arrival to the laboratory, the purpose of the measurement, the items to be measured, the order of measurement, and precautions for measurement were fully explained to the subjects. Subjects completed questionnaires, based on factors affecting blood vessels, as a preliminary assessment of their lifestyle habits. Markers were positioned on the face for the magnetic resonance angiography (MRA) scan to maintain the same position before and after exercising on the treadmill. The time-of-flight (TOF) technique was used for angiography, which was approximately a 10-minute process. After the first MRA image was obtained as the baseline cerebral angiogram prior to the use of the treadmill, the second cerebral angiogram was taken after 10 minutes of treadmill use at a speed of 7 km/h (Fig. 3). Based on the two images, we attempted to divide the blood vessel image signal in order to measure the degree of cerebral blood vessel change by stimulation. We selected the boundary value of the video signal to remove the tissue or external noise signal, and determined the proportion of

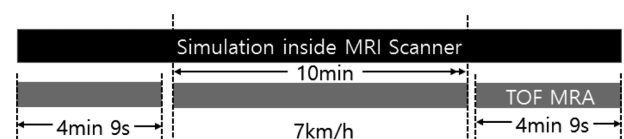


Fig. 3. Experimental protocols of aerobic-exercise and MRA imaging.

Table 1. Magnetic Resonance Artery Parameters.

Parameters	TOF magnetic resonance artery
TR / TE (ms)	20 / 3.3
Flip angle (°)	20
FOV (mm)	200 × 200
Number of slabs	5
Number of partitions	44
Matrix size	320 × 320
Voxel size (mm)	0.63 × 0.63 × 0.63
Elliptical scanning	Yes
TONE pulse	Slow
Partial Fourier	6/8
Overlap between slabs (%)	16
Pixel bandwidth (Hz)	100
TA (m:s)	4:09

blood vessels by setting the region of interest (ROI) to be compared. We compared the vascular changes before and after treadmill use and verified differences in blood vessel changes with the paired t-test, The p-value < 0.05 was considered to indicate a significant difference when p statistically significant < 0.05 (Table 1). Statistical analysis was performed with SPSS software, version 23.0.

2.3. Analysis Method

We set the ROI by dividing the intracranial and extracranial blood vessels seen in the angiograms obtained by the TOF technique using a 3-T MRI scanner (Siemens, Verio, Erlangen, Germany) before and after treadmill use. Intracranial blood vessels included the internal carotid artery (ICA), vertebral artery (VA), basilar artery (BA) and their small blood vessels, Extracranial blood vessels included the external carotid artery (ECA), superficial temporal artery (STA), and their small blood vessels (Fig. 4).

The mean signal intensities and diameters of the blood vessels were calculated for each of the 15 subjects whose

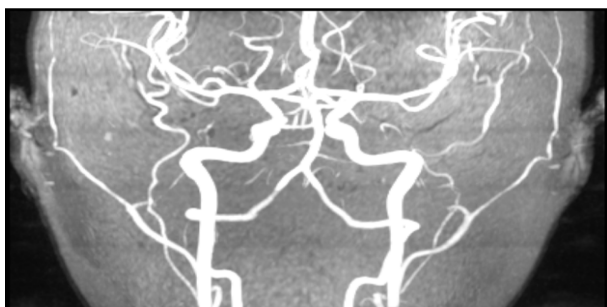


Fig. 4. MRA Image.

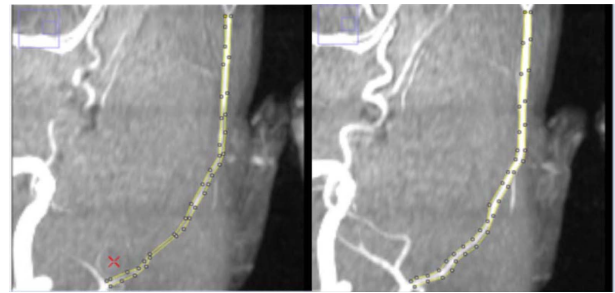


Fig. 5. (Color online) Measurement in signal intensity of arteries before and after aerobics-exercise.

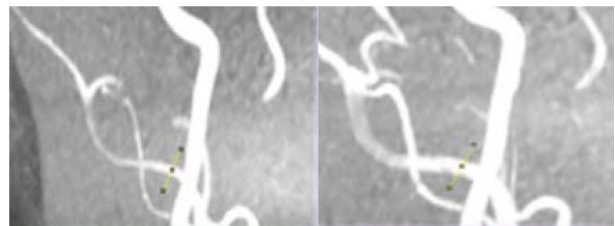


Fig. 6. (Color online) Measurement in Diameter of arteries before and after aerobics-exercise.

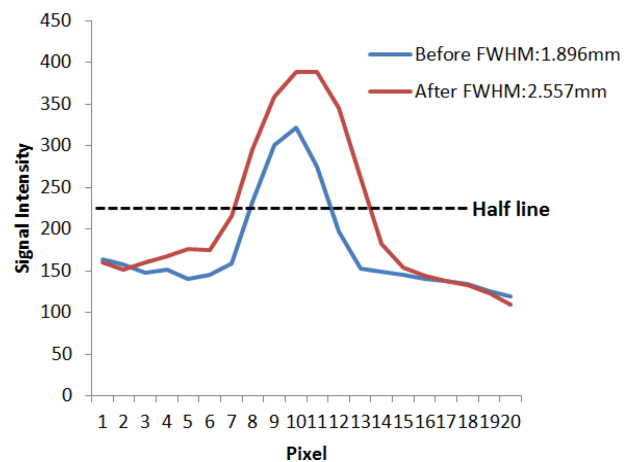


Fig. 7. (Color online) Measurement in Diameter of arteries before and after aerobics-exercise.

ROIs were set using a medical image processing program (ImageJ, National Institutes of Health, USA).

The ROI was set for each vessel to be measured, and signal intensities were measured before and after exercise to reduce the error, basing the measurement on the mean values obtained by five researchers (Fig. 5).

For the diameter, We obtained the diameter by measuring the full width at half maximum (FWHM) value of the blood vessels and the average measurements from the 5 researchers was calculated for each patient (Fig. 6, 7).

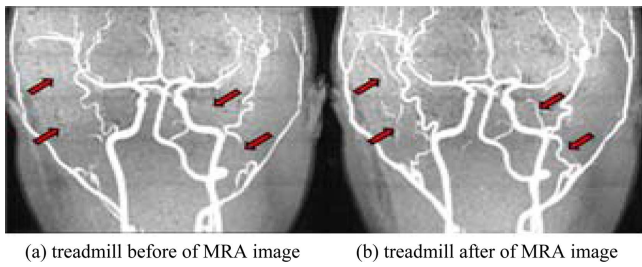


Fig. 8. (Color online) The changes of capillaries as aerobic-exercise.

3. Results

The results of the visual examination showed that small blood vessels, which were not seen in the MRA image before aerobic exercise, appeared in the MRA image after aerobic exercise (Fig. 8).

We compared the TOF signal intensities and blood vessel diameters before and after aerobic exercise in the 15 subjects. The results showed that before and after exercise, the signal intensities of the ICA changed by -2.789% ($p = 0.000$) from 450.911 to 438.336, respectively, VA changed by -2.031% ($p = 0.091$) from 307.682 to 301.431, and BA changed by -0.853% ($p = 0.240$) from -471.770 to 467.748. The changes in VA and BA were not statistically significant. STA significantly increased by 12.961% ($p = 0.000$) from 301.773 to 340.885 and ECA by 2.033% ($p = 0.007$) from 325.589 to 332.210 (Table 2).

The measurements of the diameters before and after exercise showed that the ICA changed by -5.750% ($p = 0.000$) from 3.368 to 3.573, respectively, while BA changed by -5.500% ($p = 0.000$) from 2.124 to 2.007, and VA changed by -2.251% ($p = 0.541$) from 1.942 to 1.898. The change in VA was not statistically significant.

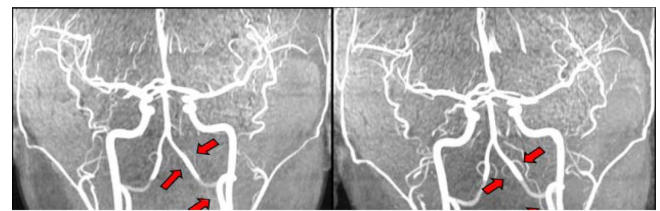
Table 2. The change in Signal intensity of Cerebral artery

Artery	Average	N	Change (%)	P value
ICA_before	450.911 ± 22.315	15		
ICA_after	438.336 ± 28.546	15	-2.789	.000
VA_before	307.682 ± 43.788	15		
VA_after	301.431 ± 34.587	15	-2.031	.091
BA_before	471.770 ± 45.021	15		
BA_after	467.748 ± 59.301	15	-0.853	.240
ECA_before	325.589 ± 23.359	15		
ECA_after	332.210 ± 28.415	15	2.033	.007
STA_before	301.773 ± 31.358	15		
STA_after	340.885 ± 42.692	15	12.961	.000

Data presented as mean ± SD

Table 3. The change in Diameter of Cerebral artery

Artery	mean	N	Change (%)	P value
ICA_before	3.573 ± 0.392	15		
ICA_after	3.368 ± 0.546	15	-5.750	.000
VA_before	1.942 ± 0.353	15		
VA_after	1.898 ± 0.482	15	-2.251	.541
BA_before	2.124 ± 0.278	15		
BA_after	2.007 ± 0.399	15	-5.500	.000
ECA_before	1.866 ± 0.295	15		
ECA_after	2.138 ± 0.557	15	14.570	.000
STA_before	1.271 ± 0.244	15		
STA_after	2.107 ± 0.436	15	65.717	.000



(a) Before aerobic exercise (b) After aerobic exercise

Fig. 9. (Color online) The results of visual inspection for Internal vessel as capillary changes.

STA changed by 65.717% ($p = 0.000$) from 1.271 to 2.107, and ECA by 14.570% ($p = 0.000$) from 1.866 to 2.138 (Table 3).

When the cerebral angiograms were visually evaluated in the study, it was confirmed that the capillaries surrounding the ICA, VA, and BA were enlarged and observed clearly. Although there was no significant difference in the blood flow of the intracranial blood vessels, the significant increase in the blood flow of the capillary vessels of the medial cerebral blood vessels was thought to be a positive effect of aerobic exercise on the intracranial blood vessels (Fig. 9).

4. Discussion

Recent studies have shown that regular aerobic exercise removes foreign substances from the blood vessels, reduces and suppresses abnormal hypertrophy of vascular endothelial cells, and increases the diameter of the vessels [15]. In addition, exercise directly increases blood flow, which can improve vascular endothelial cell function by increasing nitric oxide (NO) secretion in the endothelial cells, up regulation of endothelial constitutive nitric oxide synthase (eNOS) expression, and NO bioavailability [16]. Vascular endothelial cells produce vasoactive substances, such as endothelin-1 and NO, which play an important

role in the regulation of vascular activity [17].

Endothelin-1 is produced in the vascular endothelial cells and is involved in vasoconstriction [18]. Increased concentrations of endothelin-1 in the blood induces cardiovascular disease [19]. It has been reported that aerobic exercise reduces blood endothelin-1 concentration [20]. On the other hand, aerobic exercise increases the concentration of NO [21], which is involved in blood vessel relaxation and vascular growth [22]. The American College of Sports Medicine (1995) reports that moderate-intensity aerobic exercise improves blood pressure and vascular elasticity [23]. The dilation of blood vessels is caused by vascular smooth muscle relaxation induced by prostaglandin and endothelium-derived relaxing factor (EDRF), these are produced in vascular endothelial cells in response to events such as changes in blood flow and oxygen concentration. NO is a typical EDRF [24]. In NO, constitutive nitric oxide synthetase (NOS) acts on platelets, activating guanylate cyclase and increasing the amount of cyclic GMP (cGMP), thereby inhibiting adhesion and aggregation of vascular endothelial cells or platelets [25]. Prostaglandin, which is produced by the arachidonic acid released from the cell membrane, activates the cyclooxygenase, inhibits aggregation of platelets, and increases the cardiac output and blood flow to each organ [26]. In the present study, the signal intensities and diameters of ECA and STA, which are extracranial blood vessels, were significantly increased. However, the signal intensities and diameters of ICA, VA and BA, which are intracranial blood vessels, were marginally decreased or almost unchanged. This appears to be due to the control mechanism of CBF. Total CBF is constantly maintained at about 50 mL/100 gm of brain/min, and local CBF increases at the site where brain cells are activated. In the normal state, the whole blood flow and blood volume of the brain are regulated to a certain level irrespective of various physiological changes outside the brain. These CBF regulating mechanisms include metabolic control, neurogenic control, blood gas control, and autoregulation. First, the metabolic control mechanism is the reason local CBF increases at the site of increased local brain cell activity. It is presumed that it works when either the products of brain metabolism (i.e., Lactic acid) affect the peripheral cerebral blood vessels or nerve cells are connected directly or indirectly. The accumulation of either carbon dioxide or lactic during activities such as aerobic exercise is known to dilate blood vessels and increase blood flow [27]. Second, regulation of CBF is also based on neurogenic control of the cerebral blood vessels. Although the mechanism by which nerves contribute to the regulation of CBF has not been explained yet, it has been suggested

that it is attributed to the phenomenon that facilitates the balance between the sympathetic nerve, which comes from the superior cervical ganglion to reduce blood vessels by secreting norepinephrine and neuropeptide-Y, and parasympathetic nerve, which comes out from Sphenopalatine ganglion to expand the blood vessels by secreting acetylcholine and vasoactive intestinal peptide (VIP). The vasomotor nerve that controls the vascular smooth muscle is an efferent nerve that causes vasoconstriction and expansion depending on the stimulus. It is composed of the vasodilator nerves belonging to the sympathetic nervous system and the vasodilating nerves belonging to the parasympathetic nervous system and has been reported to regulate the blood pressure or the local blood flow by the antagonism between the nerves [28]. Third, regulation of CBF is based on the blood gas regulation mechanism in which a sensitive response of the cerebral artery occurs as PaCO₂ changes. The decrease in pH dilates the cerebral blood vessels and changes in the CO₂ tension affect the change in cerebral blood vessel diameter. In addition, vascular endothelial cells detect increases in PaCO₂ and secrete EDRF (Endothelium-derived relaxing factor, NO) to expand the blood vessels. Fourth, it is based on the autoregulatory mechanism that keeps CBF constant even when the cerebral perfusion pressure (CPP) changes. Increased transluminal pressure causes reflexive contraction of internal vascular muscle cells, resulting in vascular endothelial cells responding to changes in cerebral perfusion pressure, controlling EDRF secretion, and dilating and constricting cerebral blood vessels to maintain a constant CBF [29]. In other words, the combination of these four regulatory mechanisms results in a local increase in the extracranial blood vessels of the head based on the changes in vascular endothelial cells. In particular, no significant changes in the intracranial blood vessels were observed which is thought to be due to the CBF regulation reaction by neurogenic regulation and autoregulation.

Hellstrom *et al.* reported that the velocity of the middle cerebral artery and the left internal carotid artery tended to decrease slightly in high intensity exercise (VO_{2max} 80-90 %), but that the left common carotid artery was continuously increased [30]. These results are consistent with our results. This large change in the extracranial blood vessels indicates that aerobic exercise dilates the blood vessels locally to increase the blood flow [31] and at the same time causes vasodilation in the vascular motor nerve [32]. This eventually promotes metabolism, the removal of waste products [33], and plays a role in facilitating blood circulation in the cerebral blood vessels [34].

The blood flow rate (Q) and the blood flow velocity (V) per unit time have a functional relationship ($V = Q/A$)

with the cross-sectional area (A) of the blood vessel [35]. As a result of the experiment, the increase in blood vessel wall thickness and blood flow velocity means that the blood flow increased more than expected [36]. In other words, aerobic exercise has the effect of improving blood flow and blood vessels. 3D TOF MRA, uses very short radio pulses as the segment selection frequency. It is based on the principle that stationary tissue has a decreased signal intensity, but when it reaches more than a certain speed, a high signal intensity is produced [37]. Therefore, it is possible to capture images in a relatively short period of time with a high level of spatial resolution [38]. In addition, since it better visualizes the physiology and function of the blood flow, it is also broadly applied in clinical practice [39]. MRA is known to be an effective imaging technique for the evaluation of internal carotid artery disease, cerebrovascular aneurysm, and large vessel obstruction disease [40]. Masaryk *et al.* reported that MRA was more accurate, with 83 % to 94 % accuracy, than conventional angiography (CA) [41] when determining the degree of internal carotid artery occlusion [42]. Although computed tomography (CT) angiography has a higher spatial resolution than MRA [43], and digital subtraction angiography (DSA) is known to be the most accurate method for evaluating the stenosis or occlusion of intracranial cerebral vessels, MRA is noninvasive, non-irradiating, and its [44]. This was the basis of this study. Important lifestyle-related factors that affect blood vessel changes include drinking, smoking, caffeine intake, and normal exercise [45]. However, in this study, only the blood vessels were compared before and after exercise and lifestyle-related factors were not considered. This study had limitations, We did not control for psychological factors, such as stress, tension, and the environment, that may have altered the blood vessels. In addition, when MRA is used to measure the velocity of CBF, it can be measured using the PC (phase contrast) technique in addition to the TOF technique; however, we could not perform both in this study. It was difficult to utilize the captured PC image because the ROI of the image was narrow and deviated from the pre-exercise position in the second post-exercise MRA. Therefore, we expect more accurate research results if complementary studies are carried out in the future. According to the assessment and treatment of hypertension from the 7th report of the United Nations Commission on Diagnosis (JNC7, 2003), regular aerobic exercise reduces the risk factors for cardiovascular disease. It is reported that exercising for 30 minutes or more, three times a week, with a 40-60 % strength of VO_{2max} reduces systolic blood pressure by 4-9 mmHg [46]. Changes in blood vessels after regular ex-

ercise are known to be influenced by various factors, such as the decrease in sympathetic nervous system activity [47], increase in factor that promote relaxation from vascular endothelial cells [48], decrease in contractility of contraction material [49], and increase in aortic elasticity [50]. Therefore, additional studies that observe the changes in intracranial blood vessels (ICA, VA, BA) through regular and continuous exercise for long periods of time are needed.

5. Conclusion

By using MRA, we could observe the changes in CBF before and after aerobic exercise. Specifically, we were able to measure the degree of increase in blood flow and vasodilation of ECA and STA. The signal intensity of the ECA and STA increased by 2 % and 12 %, respectively, after aerobic exercise. In addition, the post-exercise image showed a remarkable increase (65 %) in the diameter of the STA. Thus, these results showed that aerobic exercise resulted in the dilation of the extracranial (ECA, STA) blood vessels. Although there was no statistically significant difference in the intracranial blood vessels (ICA, BA, VA) pre-and post-exercise, the finding that the fine blood vessels were not visible in the baseline image, but were clearly and distinctly increased in the post-exercise image, suggests that aerobic exercise also has a positive effect on intracranial blood vessels. This study will contribute to improving vascular health by systematic study of exercise patterns for vascular health.

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