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Impact of a physical activity program on cerebral vasoreactivity in sedentary elderly people

D. VICENTE-CAMPOS [1], J. MORA [2], J. CASTRO-PIÑERO [2]
J. L. GONZÁLEZ-MONTESINOS [2], J. CONDE-CAVEDA [2], J. L. CHICHARRO [3]

[1]School of Physiotherapy, Francisco de Vitoria University, Madrid, Spain
[2]Department of Physical Education, School of Education University of Cadiz, Puerto Real, Cádiz, Spain
[3]Department of Infirmary, School of Infirmary, Physiotherapy and Podology Complutense University, Madrid, Spain

***Aim*. The aim of the present study was to determine the effect of a physical activity program on the hemodynamic response of the brain (vasoreactivity) in elderly people.**
***Methods*: Eighteen men and 25 women (aged 62-67 years) were randomly assigned to an experimental (EXP, N.=22, 12 women) and a control (CON, N.=21, 13 women) group. Subjects in EXP group were required to complete a 7-month program based on aerobic training (3-4 sessions/weekd, 50 min/session, 3-4 sessions/week, at 70% maximum heart rate). Transcranial Doppler ultrasound was used to examine the cerebral blood flow response to hypercapnic and hypocapnic stimuli. We also determined blood pressure, total serum cholesterol, HDL and LDL cholesterol, and triglycerides, and conducted an aerobic capacity test (the 2.4-Km walking test).**
***Results*. Brain vasomotor reactivity improved in the EXP group, reflected by a higher blood flow velocity in the middle cerebral artery (MCA) in both cerebral hemispheres in response to hypercapnia (induced by breath holding) (P<0.05). Subjects in EXP group also improved the cardiovascular profile aerobic physical condition (P<0.001) in terms of reduced arterial pressure, total cholesterol and triglyceride levels.**
***Conclusion*. Our findings indicate that cerebral vasoreactivity in elderly may be improved by undertaking an aerobic exercise program.**

KEY WORDS: Motor activity - Cerebral circulation - Aging.

Age-related changes produced in the blood system [1] and prevalent risk factors for atherosclerosis in the elderly (such as hypertension or diabetes mellitus) could diminish the distensibility of the cerebral vessels leading to a reduced hemodynamic response during focal brain activation due to increased metabolic activity in the brain.[2, 3] The capacity of the cerebral arteries to modify their diameter and thus the blood supply to the brain is known as cerebral vasomotor reactivity or vasoreactivity. Several studies [4-6] have reported that this property of blood vessels is impaired in subjects with a high risk of cerebrovascular disease. During resting conditions, age-related decreases in cerebral blood flow (CBF), cerebral blood volume,[7] and cerebral blood flow velocity in the basal intracerebral arteries [8] have been reported.

Transcranial Doppler ultrasound (TCD) assesses changes in blood flow produced in the cerebral arteries, mainly the middle cerebral artery (MCA), in response to vasodilatory stimuli such as the intravenous administration of acetazolamide or inhaled carbon dioxide. The vasodilation induced in arterioles by these stimuli increases regional blood flow (Q) and diminishes the pressure gradient between arteries and arterioles. Assuming no changes in the caliber of the MCA, the vasodilatory stimulus on the arteriole will determine its increased flow according to the equation $Q=V \times pR^2$, where V is the velocity of flow and R is the vessel radius. This increase manifests as an increased mean blood flow velocity and a drop in the pulsatility index. The main shortcoming

Corresponding author: D. Vicente Campos, School of Physiotherapy, Francisco de Vitoria University, Ctra. Pozuelo-Majadahonda km.1800, 28223 Pozuelo de Alarcón, Madrid, Spain.
E-mail: d.vicente.prof@ufv.es

of both methods is that these substances have to be exogenously administered.

In 1990, Ratnatunga and Adiseshiah [9] introduced a non-invasive method in which the vasodilatory stimulus was hypercapnia induced by breath-holding. When the subject holds his or her breath, this produces an increase in the partial pressure of arterial CO_2 that is able to induce vasodilation in the cerebral arteries provided these find themselves in a normal physiological state. Hence, by determining the relative change in flow sustained by these arteries, this will give a measure of the vasoreactivity and thus the capacity of the cerebral arteries to adapt to any change, and of the likelihood that the brain tissue will or not undergo ischemic damage.

This procedure was subsequently modified by Markus and Harrison [10] who calculated the breath holding index (BHI) by dividing the percentage blood flow increase recorded in the MCA during breath holding by the number of seconds of voluntary apnea.

Regular physical exercise has been associated with improved systemic function of the arterial endothelium reducing the rigidity of the arteries thereby diminishing the risk of arterial atherosclerotic disease in middle aged and older individuals.[11-13] The results of several studies [14-16] have shown that regular endurance training and vigorous physical activity might also reduce the age-related increase in arterial stiffness observed among men. Mayhan *et al.* [17] examined the effects of exercise on the nitric oxide synthase dependent reactivity of cerebral blood vessels and concluded that exercise-induced activation of the nitric oxide biosynthetic pathway could be an important factor for preventing diabetes-induced cerebrovascular abnormalities, possibly including stroke. Findings from a meta-analysis also establish the clear benefits of physical activity in terms of both reducing the incidence of stroke, and the mortality rate when stroke occurred.[18]

The effects of the adaptations that regular physical activity provokes on cerebral vasoreactivity capacity in healthy elderly prople are poorly understood. The present study was designed to assess the impact of a 7-month physical activity intervention program on the hemodynamic cerebral response in elderly people.

Materials and methods

Subjects

The study population was selected from 82 men and women between the ages of 60 and 75 years. For this first selection stage, subjects were required to: have a sedentary lifestyle, have no contraindications for conducting physical activity, not have participated in any physical activity program in the past year, not have high blood pressure, not be under treatment with any drug with cardiovascular effects, not have or have had a cerebrovascular disease, not have diabetes, nor consume alcohol (>0.5 litters per day of alcohol) nor smoke.

A total of 55 subjects fulfilled these inclusion criteria, and were randomly assigned to an experimental (EXP; N.=28) or a control (CON; N.=27) group. Of these, 43 subjects completed the study leaving a final study population of 22 subjects (12 women, 10 men) in EXP group and 21 subjects (13 women and 8 men) in CON group (Table I).

The study was conducted according to the principles expressed in the Declaration of Helsinki. The study was approved by the Review Committee for Research Involving Human Subjects at the University of Cádiz, Spain. The study was carried out with written informed consent of the participants.

Measures

The examination protocols described below were conducted before and after the 7-month period of study. All variables were determined 20-24 hours after the last exercise training session to avoid the immediate (acute) effects of exercise.

TABLE I.—*Subject characteristics (mean ± SD).*

Variable	Experimental group (N.=22)	Control group (N.=21)
Age (years)	64±4	64±5
Height (cm)	161.67±7.59	163.35±6.76
Weight (kg)	75.00±7.97	73.99±5.48
BMI ($kg \cdot m^{-2}$)	29.00±2.76	27.89±1.56

Cerebral hemodynamic reserve

Subjects arrived at the laboratory following a 20-24 h period free of exercise and alcohol intake and without having consumed a large meal or caffeine in the last 4 hours.

TCD was performed using a Multi-Dop P/TCD device (DWL Elektronische Systeme, Sipplingen, Germany) with a 2 MHz probe according to the procedure described by Aaslid *et al.*[19] The examination was undertaken in a quiet room with the subject in a supine decubitus position breathing ambient air. The technique was first explained to each subject to ensure an adequate level of relaxation. The same clinician conducted all exams at the same time of day.

In each subject, the right cerebral hemisphere was examined and after a 4-minute rest period, the protocol was repeated in the left hemisphere. On the side of insonation, hemodynamic assessment was made of the supraaortic trunks to rule out any hemodynamically significant stenosis. The MCA was identified through the transtemporal window and the most appropriate insonation depth selected for the entire hemodynamic study.

First, we determined baseline mean blood flow velocity in the MCA (Vmca) after several minutes of normal respiration. At least 10 cardiac cycles were selected to obtain an average value. Next, the subject was instructed to take a deep breath and then hold his/her breath for as long as possible. The variables recorded were the time it took for the maximum increase in peak MCA velocity to occur (TV-max), peak velocity during breath holding (Vmca BH) and the pulsatility of flow during breath holding (Pulsat BH).

The percentage increase in mean velocity in response to hypercapnia (TAP1) was calculated using the equation: TAP1= Vmca BH - Vmca rest / Vmca rest x 100. The breath holding index was obtained [10] by dividing the percentage increase in Vmca by the time in seconds over which the subject was able to hold his/her breath (BHI=TAP1/seconds of BH).
When the velocity of the MCA returned to baseline, the subject was asked to hyperventilate for 20 seconds (THV) and the time elapsed until the lowest mean velocity during hypocapnia (T Vmin), the value of this velocity under hypocapnia (V THV) and the pulsatility (Pulsat THV) recorded.

The percentage decline in mean MCA blood flow in response to this hypocapnia (hyperventilation) (THVPO) was calculated as: THVPO=Vmca normocapnia - Vmca hypocapnia / Vmca normocapnia x 100.

The hyperventilation index (THVBHI) was calculated by dividing the percentage MCA flow velocity decrease (THVPO) by the time in seconds that the subject was hyperventilating.

Arterial blood pressure

Arterial blood pressure was measured using a manual sphygmomanometer (OMRON M6 Confort, Amsterdam, Netherlands) at rest immediately after getting up in the morning (between 08.00 a.m. and 10.00 a.m.) on each of the 4 days preceding the first day of the exam protocol, and the mean of all the measurements recorded.

Biochemical tests

On the day before the exam protocol, blood samples collected into a Vacutainer containing EDTA-2Na and Trasylol were mixed with 1 ml of distilled water and centrifuged for 15 min at 4,000 rpm. Fasting (at least 12 hours) serum concentrations of cholesterol (total, HDL and LDL) and triglycerides were determined using standard enzymatic techniques with intra and inter-assay coefficients of variance of <5.0%.

2.4-Km walking test

One day before the start and two days after the end of the physical activity program, the subjects after a short warm up period were instructed to complete 6 laps of a 400 m track walking as quickly as possible (2.4-Km track walk).

During the test, all the subjects wore a pulsometer (Polar RS800sd, Kempele, Findland) indicating the number of laps remaining. The variables mean velocity (m/min) and mean heart rate for the last 2 minutes were recorded.

Physical activity program

The 7-month physical activity program was conducted in three stages (I, II, III). Over the first 5 weeks (stage I or adaptation stage), the intensity and duration of exercise sessions was stepped up from two weekly 15-min sessions to three weekly 60-min

sessions. Heart rate was used to control the intensity of aerobic exercise during this period, starting at 50% the maximum heart rate and ending at 60%.

Stage II comprised 24 sessions, three per week, during 8 weeks. Sessions commenced with a 12-15 min warm up (pacing, moving joints and muscle stretching). During a further 50 min, circuits including aerobic work, muscle strengthening exercises and coordination exercises were completed. The intensity increased gradually from 60% to 70%.

During the 15 weeks of stage III, weekly exercise sessions increased from three to four, and one of these sessions was entirely devoted to aerobic work. This involved 50 min of sustained walking at a constant intensity of 70% maximum heart rate. The remaining sessions were as in stage II, though intensity was revised.

Statistical analysis

Statistical tests were performed using Statistical Package for Social Sciences (SPSS) 17.0 software (SPSS Inc., Chicago, IL, USA). Mean values of all the variables at baseline were compared between the two groups using unpaired t-tests. Paired t-tests were used to compare pre- and post-intervention variables in the two groups. To assess the combined effect of group and time, independent t-tests were used to compare changes in scores (post-intervention minus pre-intervention) in the experimental and control groups for all variables measured. For all variables, results are expressed as mean (SD). The size of a change and its precision were provided by reporting the change in mean values and the 95% confidence intervals (95% CI) for the change, respectively. The level of significance was set at 0.05.

Results

MCA blood flow velocity (Vmca)

Table II (pre- and postintervention values for variables measured in the left hemisphere determined in the experimental (N.=22) and control (N.=21) groups and 3) and III (Pre- and post-intervention values for the variables measured in the right hemisphere determined in the experimental (N.=22) and control (N.=21) groups) provide the mean values of Vmca obtained at rest. No significant differences were detected between pre and post-intervention values in the CON and EXP groups for either the right or left hemisphere.

Time of maximum increase in peak MCA velocity (T Vmax)

No significant differences were detected in response to the training intervention for the right or left hemisphere in terms of the time taken for the

TABLE II.—*Pre- and postintervention values for variables measured in the left hemisphere determined in the experimental (N.=22) and control (N.=21) groups (mean ± SD).*

Variable	Experimental group pre-test	Experimental group post-test	Control group pre-test	Control group post-test	Overall change in means[a]	95%CI for overall change in means
Vmca	59.19±6.49	58.97±7.22	55.29±8.92	55.76±10.14	-0.58 (P=0.61)	-2.94 to 1.76
T Vmax	8.86±3.52	8.68±2.74	8.66±2.61	9.04±1.90	-0.56 (P=0.51)	-2.2 to 1.15
Vmca BH	74.04±9.59	78.18±10.08	71.52±10.64	72.00±11.01	3.66* (P=0.02)	0.62 to 6.7
Pulsat BH	0.88±0.19	0.92±0.24	0.89±0.11	0.92±0.10	0.12 (P=0.77)	-0.07 to 0.10
TAP1	25.18±6.38	32.71±6.54	29.63±6.24	27.85±7.95	9.30* (P=0.000)	5.82 to 12.78
BHI	0.85±0.19	1.09±0.21	0.93±0.18	0.95±0.17	0.22* (P=0.000)	0.14 to 0.30
T Vmin	9.68±2.95	9.81±2.57	9.80±2.13	9.85±2.32	0.08 (P=0.88)	-1.1 to 1.34
V THV	47.77±5.07	46.86±5.75	44.66±7.37	44.61±7.96	-0.86 (P=0.41)	-2.9 to 1.27
Pulsat THV	1.29±0.35	1.26±0.26	1.30±0.30	1.29±0.23	-0.02 (P=0.75)	-0.19 to 0.14
THVPO	19.06±3.76	20.50±2.81	19.16±4.23	19.87±4.46	0.72 (P=0.51)	-1.5 to 2.96
THVBHI	0.95±0.18	1.02±0.14	0.95±0.21	0.99±0.22	0.03 (P=0.58)	-0.08 to 0.14

Vmca: middle cerebral artery blood flow velocity; T Vmax: time of maximum increase in peak middle cerebral artery; Vmca BH: middle cerebral artery blood flow velocity during breath holding; Pulsat BH: pulsatility of flow during breath holding; TAP1: percentage increase in mean velocity in response to hypercapnia; BHI: breath holding index; T Vmin: time elapsed until the lowest mean velocity during hypocapnia; V THV: velocity under hypocapnia; Pulsat THV: pulsatility of velocity under hypocapnia; THVPO: percentage decline in mean blood flow in hypocapnia; THVBHI: hyperventilation index. (a) Overall change in means: the change (post-intervention minus pre-intervention means) for the training group minus the change (post minus pre means) for the control group.

maximum increase in peak MCA velocity to occur (Tables II, III)

MCA velocity during breath holding (Vmca BH)

The velocity of flow in the MCA on breath holding (Tables II, III) failed to differ in CON group, while this variable showed a significant increase both for the right hemisphere (71.04±9.62 *vs.*. 77.22±10.68, P<0.05) and left hemisphere (74.04±9.59 *vs.* 78.18±10.08, P<0.05) in response to the training intervention.

BHI and % increase in mean velocity in response to hypercapnia (TAP1)

Tables II and III provide the values of TAP1 and BHI obtained, indicating significant improvements in the reactivity times shown by the EXP group, both in the left hemisphere (25.18±6.38 *vs.* 32.71±6.54; P<0.001 and 0.85±0.19 *vs.* 1.09±0.21; P<0.001, respectively) and right hemisphere 23.98±6.31 *vs.* 33.90±8.45; P<0.001, and 0.81±0.20 *vs.* 1.13±0.28; P<0.001, respectively). The CON group showed no significant differences in these variables in neither of the brain hemispheres.

Pulsatility index and hyperventilation test

No significant differences in these variables were observed in either group (Tables II, III).

2.4-Km walking test

Table IV (Pre- and postintervention values for variables determined in the experimental [N.=22] and control [N.=21] groups) provides the results of the cardiorespiratory resistance test, revealing significant increases in mean velocity in the EXP group (89.67±7.45 *vs.* 95.32±8.90; P<0.001) but not the CON group. Not significant differences were observed in the heart rate measures, except in the resting heart measure in the EXP group (71.36±3.146 *vs.* 69.41±2,462; P=0.003).

Biochemical variables

The results in Table IV indicate significant reductions in total cholesterol (217.18 ±19.61 *vs.* 205.72 ±18.52; P<0.001) and triglycerides (170.09±17.82 *vs.* 164.59±12.41; P<0.05) and an increase in HDL (40.31±4.13 *vs.* 47.95±4.90; P<0.001) in EXP group but not in CON group.

Blood pressure

Table IV provides the resting arterial blood pressure data, revealing a significant drop both in the systolic (135.16±4.44 *vs.* 132.55±5.15; P<0.001) and diastolic (81.09±6.84 *vs.* 78.96±5.95; P<0.05) pressure in EXP group but not in CON group.

TABLE III.—*Pre- and postintervention values for the variables measured in the right hemisphere determined in the experimental (N.=22) and control (N.=21) groups (mean ± SD).*

Variable	Experimental group pre-test	Experimental group post-test	Control group pre-test	Control group post-test	Overall change in means[a]	95%CI for overall change in means
Vmca	57.23±8.34	57.80±8.19	55.63±8.06	56.42±10.11	-0.22 (P=0.89)	-3.6 to 3.2
T Vmax	9.45±3.66	7.45±2.17	7.38±2.41	8.28±1.58	-2.8* (P=0.02)	-5.17 to -0.45
Vmca BH	71.04±9.62	77.22±10.68	71.90±10.06	72.71±11.41	5.3* (P=0.02)	0.62 to 10.12
Pulsat BH	0.94±0.32	0.92±0.26	0.90±0.11	0.95±0.23	0.07 (P=0.40)	-0.25 to 0.10
TAP1	23.98±6.31	33.90±8.45	27.46±3.65	28.64±5.07	8.74* (P=0.00)	5.79 to 11.69
BHI	0.81±0.20	1.13±0.28	0.87±0.14	0.96±0.20	0.23* (P=0.00)	0.11 to 0.34
T Vmin	9.81±2.23	10.09±2.48	10.09±2.84	10.71±3.33	-0.34 (P=0.70)	-2.19 to 1.49
V THV	46.63±6.72	46.68±7.14	44.85±7.61	45.19±8.29	-0.28 (P=0.83)	-3.02 to 2.45
Pulsat THV	1.47±0.56	1.59±0.46	1.39±0.36	1.49±0.42	0.02 (P=0.91)	-0.34 to 0.38
THVPO	18.39±3.79	19.42±3.07	18.62±2.68	19.87±3.77	-0.20 (P=0.85)	-2.49 to 2.07
THVBHI	0.92±0.18	0.97±0.15	0.94±0.14	0.99±0.18	-0.00 (P=0.97)	-0.11 to 0.11

Vmca: middle cerebral artery blood flow velocity; T Vmax: time of maximum increase in peak middle cerebral artery; Vmca BH: middle cerebral artery blood flow velocity during breath holding; Pulsat BH: pulsatility of flow during breath holding; TAP1: percentage increase in mean velocity in response to hypercapnia; BHI: breath holding index; T Vmin: time elapsed until the lowest mean velocity during hypocapnia; V THV: velocity under hypocapnia; Pulsat THV: pulsatility of velocity under hypocapnia; THVPO: percentage decline in mean blood flow in hypocapnia; THVBHI: hyperventilation index. (a) Overall change in means: the change (post-intervention minus pre-intervention means) for the training group minus the change (post minus pre means) for the control group.

TABLE IV.—*Pre- and postintervention values for variables determined in the experimental (N.=22) and control (N.=21) groups (mean ± SD).*

Variable	Experimental group pre-test	Experimental group post-test	Control group pre-test	Control group post-test	Overall change in means[a]	95%CI for overall change in means
Resting heart rate (beats/min)	71.36±3.146	69.41±2.462	71.19±4.297	70.48±1.887	-1.240 (P=0.229)	-3.293 to 0.813
Exercise heart rate (beats/min)	122.68±13.418	122.64±9.016	125.57±7.884	126.19±8.530	-0.665 (P=0.807)	-6.111 to 4.782
Systolic arterial pressure (mmHg)	135.16±4.44	132.55±5.15	135.72±5.54	135.63±6.70	-2.52 (P=0.00)	-4.39 to -0.65
Diastolic arterial pressure (mmHg)	81.09±6.84	78.96±5.95	81.20±4.15	82.14±5.08	-3.07 (P=0.01)	-5.35 to -0.78
Walking velocity (m/s)	89.67±7.45	95.32±8.90	91.88±3.73	92.66±4.75	4.87 (P=0.00)	3.51 to 6.24
Cholesterol (mg/dL)	217.18±19.61	205.72±18.52	213.23±13.03	215.71±16.00	-13.93 (P=0.00)	-21.27 to -6.58
HDL-C (mg/dL)	40.31±4.13	47.95±4.90	39.09±2.40	38.85±2.35	7.87 (P=0.00)	6.39 to 6.37
LDL-C (mg/dL)	132.59±10.07	128.31±9.84	134.28±8.60	135.66±7.78	-5.65 (P=0.06)	-11.69 to 0.38
Triglycerides (mg/dL)	170.09±17.82	164.59±12.41	166.33±13.19	170.19±13.99	-9.35 (P=0.00)	-16.22 to -2.49

(a) Overall change in means: the change (postintervention minus preintervention means) for the training group minus the change (post minus pre means) for the control group.

Discussion

To the best of our knowledge, this is the first study to show that long-term physical exercise improves the responsiveness of cerebral hemodynamics in elderly subjects. The most significant finding supporting such improved cerebral vasomotor reactivity was an increased blood flow velocity in the MCA in both cerebral hemispheres produced in response to a hypercapnic stimulus (breath-holding).

Physical training has several beneficial effects on many cardiovascular risk factors such as dyslipemia, arterial hypertension, diabetes and cardiovascular events.[11] The present findings confirm the efficacy of a 7-month physical activity program in improving the cardiorespiratory capacity of this study population, increasing the velocity in the 2.4-Km walking test (P<0.001). The walking velocity values obtained both in the control and experimental groups were in the range quoted by Centeno *et al.*[20]

In addition, we observed an improved biochemical profile in response to regular exercise such that total cholesterol and triglyceride levels declined, while HDL concentrations increased. These changes, along with a significant drop in resting arterial blood pressure, have been linked to a reduced incidence of stroke, particularly ischemic stroke in elderly persons. Several studies [21, 22] have shown, that physically active older subjects have higher levels of the protecting factor, high-density lipoprotein, than their non-active counterparts. This is important, because high HDL cholesterol and low LDL cholesterol levels have been attributed a role in maintaining health in elderly persons. In contrast, studies such as those of Fonnong *et al.*[23] and Nieman *et al.*[24] failed to detect any changes in serum lipoprotein levels in response to an exercise program. Shintani *et al.*[25] reported significantly lower HDL levels in patients who had suffered large vessel and lacunar cerebral infarctions, but also failed to detect differences in total and LDL cholesterol levels between their patients and controls.

Several studies [26-28] observed that the Vmca decreases with age. We detected no modification in the Vmca measured in resting conditions, attributable to our physical training intervention. Similar Doppler velocimetry variables for the MCA were reported by Egido *et al.*[29] and Jimenez-Caballero and Segura [30] in subjects over the age of 65 years. However, our training program had some effect on Vmca during breath holding recorded in both cerebral hemispheres and on the indices TAP1 and BHI, suggesting improved cerebral vasoreactivity. Ainslie *et al.*[28] observed an elevated Vmca in response to aerobic training in eld-

erly individuals, though it should be highlighted that their trained subjects undertook vigorous aerobic-endurance exercise more than 4 times per week and competed in local road running or cycling races, and were therefore much more endurance trained than our subjects. We should also mention that our TAP1 response times were slightly lower than those obtained by Widder *et al.*,[21] both in control and trained subjects.

The mechanisms underlying the reduced endothelial-dependent vasodilatory capacity of older subjects have not been well established and it remains unclear whether the vasodilatory dysfunction associated with age is related to an agonist-specific defect or to a more general endothelial vasomotor deficiency.[31] The effect of physical training observed could be related to endothelial function in conducting arteries [12] or the peripheral microcirculation.[32, 33] Hence, regular physical exercise seems to be linked to increased endothelium-dependent vasodilation.[13] In this context, DeSouza *et al.*[12] showed that regular aerobic exercise can prevent the age-associated loss in endothelium-dependent vasodilation and restore levels in previously sedentary middle aged and older healthy men. They suggest that impaired endothelium-dependent vasodilation may not be an inevitable consequence of biological aging. Rather, this dysfunction may be due, at least in part, to age-related reductions in physical activity/aerobic fitness and associated increases in body fat. Moreover, they suggest that regular aerobic exercise may be an effective lifestyle intervention strategy for improving endothelial vasodilatory function. Specifically, 3 months of regular aerobic exercise (primarily walking) resulted in a 30% increase in endothelium-dependent vasodilation in sedentary middle aged and older men.

Other studies [34-36] have observed a relationship between endothelial function and cerebrovascular function, suggesting a common pathway for these responses. Whether this is true or not, the results of our study point to the idea that physical activity could serve as a preventive measure for stroke.

When we assessed the cerebral hemodynamic response by instructing the subjects to hyperventilate to induce a stimulus of hypocapnia, no effects on THVPO or THVBHI were observed in neither the right or left hemispheres. Arjona *et al.*[37] suggest that the cerebrovascular reactivity response could be depleted despite mean arterial flow velocity returning to baseline values. This could explain the lack of changes detected following hyperventilation.

Considering that many of the cardiovascular complications associated with sedentary aging such as hypertension, coronary artery disease, and thrombosis are pathogenetically linked to endothelial dysfunction, the present results may have important implications regarding both primary and secondary prevention of cardiovascular disease. Thus, an improved hemodynamic response could translate to a somewhat reduced risk of suffering cardiovascular disease, especially in older persons in whom the cerebral hemodynamic response is less efficient, by acting as a protective factor against possible ischemic brain damage.

Conclusions

Our findings indicate that a 7-month physical activity program was able to improve indicators of cerebral vasoreactivity in both brain hemispheres in elderly people. This improvement translates to an improved capacity of the arterioles in the brain to dilate when confronted with an adverse stimulus in an effort to maintain a constant flow of cerebral perfusion. The novel idea that physical activity could be viewed as a treatment strategy to improve cerebral blood flow and thus reduce the risk of ischemic damage to the brain warrants further investigation.

Based of these findings, and from a practical point of view, a regular physical activity in sedentary ederly people might exert a protective effect on cerebrovascular health, improving cerebral blood flow and thus reduce the risk of ischemic damage.

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