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Exercise training improves blood vessel function and lowers blood pressure in individuals with high blood pressure

Submission date 17/06/2019	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 18/06/2019	**Overall study status** Completed	
Last Edited 19/07/2023	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Essential hypertension (high blood pressure) is associated with poor heart and blood vessel function, and an increase in nerve activity. It is thought that in this condition the muscle which constricts blood vessels is abnormally sensitive and contributes to high blood pressure. The current study is investigating the effect of time-efficient exercise training on the muscle activity of blood vessels in the legs and their control by locally released chemical messengers.

Who can participate?
Men aged 45 - 70 years, who do less than two hours of exercise each week.

What does the study involve?
We aimed at investigating the effect of 6 weeks of high-intensity exercise training (the 10-20-30 training principle) on leg vascular function (status of the blood vessels of the legs) in hypertensive males (high blood pressure) in comparison to matched normotensive males.

What are the possible benefits and risks of participating?
The benefits from participation is a thorough physical examination with ECG, broad blood sample screening, DXA-scan and fitness test. Furthermore subjects receive an effective and supervised training intervention with the aim at improving maximum oxygen uptake and lower blood pressure. The risks are small as all procedures have been running at the department for up to 25 years with very few minor complications such as skin numbness after muscle biopsies which is expected to be regained within 12 weeks, subcutaneous bleeding which leaves a haematoma that can be sore to pressure for up to 5 days, and headaches in some hypertensive individuals when dosing out of anti-hypertensive medication prior to experimental days. Risk for placing catheters in the femoral artery and vein, of the size that is used at the department, are not reported to have common side effects.

Where is the study run from?
University of Copenhagen, Dept. of Nutrition, Exercise and Sports, Denmark

When is the study starting and how long is it expected to run for?
March 2016 to December 2018

Who is funding the study?
1. Aase and Ejnar Danielsens Fund (Aase og Ejnar Danielsens Fond)
2. The Danish Ministry of Culture (Kulturministeriet)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Essential hypertension is associated with reduced endothelium-independent vasodilation in the lower extremity that is reversed by exercise training

Acronym

EssHypExTr

Study objectives
Exercise training improves blood vessel function which is related to a better blood pressure regulation in individuals with essential hypertension

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 01/03/2015, Ethics Committee of Copenhagen and Frederiksberg communities (: De Videnskabsetiske Komiteer, Regionsgården Kongens Vænge 2, 3400 Hillerød, Denmark; +45 3866 6395; VEK@regionh.dk), ref: H-4-2014-100

Study design
Longitudinal training intervention study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hypertension

Interventions
Both groups (hypertensive and normotensive individuals) trained in high-intensity exercise training 3x/week for 6 weeks. Groups were matched by age and no other diseases than high blood pressure was allowed.

Subjects performed exercise training adhering to the 10-20-30 training concept. Exercise training was conducted on cycle ergometers for 2x20 minutes in the first two weeks and 3x28 minutes the following 4 weeks. In short, 10-20-30 training consists of five consecutive 1 min intervals divided into 30, 20, and 10s at an intensity corresponding to ~30%, ~50% and ~100% of maximal intensity, respectively. For the first two weeks of training, subjects completed a 6 min low-intensity warm-up followed by two 5 min bouts interspersed by 3 min of recovery. From week 3, training volume was increased to three 5-min bouts per training session interspersed by 3 min of recovery. Likewise, weekly training sessions were increased from 2 (week 1-2) to 3 (week 3-6). Subjects were instructed to push maximally during the 10-s sprints. The total amount of training planned for each subject was 16 training sessions over the 6-week training intervention comprising forty-four consecutive 5-min bouts or 220 10-second all-out sprints. The participants in HYP and NORM completed 97±5 and 98±4 % of 16 training sessions planned, respectively, during the 6-week intervention period.

Intervention Type
Behavioural

Primary outcome(s)
1. Vascular function, evaluated during infusion of acetylcholine (Miochol-E, Bausch & Lomb Inc., Bridgewater, NJ) at an infusion rate of 10, 25, and 100 µg/min/kg leg mass; sodium nitroprusside

(Nitropress, Hospira Inc., Lake Forest, IL) at an infusion rate of 3, 6, and 9 µg/min/kg leg mass; and phenylephrine (Herlev apotek, Copenhagen, Denmark) at an infusion rate at 3 µg/min/kg leg mass), measured before and after the training intervention
2. Leg blood flow, ultrasound Doppler (Logic E9, GE Healthcare), measured before and after the training intervention
3. Intra-arterial and -venous blood pressure, pressure transducers (Pressure Monitoring Kit, Baxter Deerfield, IL, USA) positioned at the level of the heart, measured before and after the training intervention. Leg vascular conductance, calculated as femoral arterial blood flow divided by the difference between the mean femoral arterial and venous blood pressure, measured before and after the training intervention
4. Muscle sympathetic nervous activity (MSNA; burst frequency and incidence), microneurography i.e. direct recordings of multiunit efferent postganglionic muscle sympathetic nerve activity by use of tungsten microelectrodes with a diameter of 5µm, measured before and after the training intervention
5. 24-h ambulatory blood pressure, 24-h home measurements (TM-2430 PC2, Boso, Jungingen, Germany), measured at week -2 (screening), measured before and after the training intervention.

Key secondary outcome(s))
Before and after the six-week intervention period:
1. Body composition measured by multiple DXA scans
2. Maximum oxygen uptake measured by a GXT with online measurements of oxygen uptake (OxyCon pro, ViaSys, Healtcare)
3. Muscle protein content of endothalial NOS (eNOS) measured by the method of Westernblotting from vastus lateralis muscle biopsies.
4. Leg 6-keto PGF1α release (prostacyclin analogue) in arterial and venous blood samples taken before and during infusion of acetylcholine at 10 and 100 µg/min/kg leg mass, respectively
5. Plasma norepinephrine levels as a surrogate marker of sympathetic activity from arterial and venous blood samples obtained before and during infusions of acetylcholine (10 and 100 µg/min /kg leg mass), sodium nitroprusside (3 and 9 µg/min/kg leg mass)and phenylephrine (3 µg/min /kg leg mass), respectively

Completion date
30/11/2018

Eligibility

Key inclusion criteria
1. Age 45-70 years
2. BMI 20-35 kg·m-2
3. Ambulatory systolic/diastolic blood pressure >140/90 (hypertensive) or <140/90 (normotensive)
4. <2 h of physical activity per week
5. HbA1c <6.5% and <48 mM

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Sex
Male

Total final enrolment
18

Key exclusion criteria
1. Irregular resting ECG
2. History of cardiac symptoms during exercise
3. Chronic diseases other than essential hypertension
4. Use of medication other than anti-hypertensive drugs
5. Inability to perform physical exercise

Date of first enrolment
01/03/2016

Date of final enrolment
01/12/2018

Locations

Countries of recruitment
Denmark

Study participating centre
University of Copenhagen, Dept. of Nutrition, Exercise and Sports
Universitetsparken 13
Copenhagen
Denmark
2100

Sponsor information

Organisation
Univeristy of Copenhagen

ROR
https://ror.org/035b05819

Funder(s)

Funder type
Charity

Funder Name
Aase og Ejnar Danielsens Fond

Alternative Name(s)
Aase and Ejnar Danielsen Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Denmark

Funder Name
Kulturministeriet

Alternative Name(s)
Ministry of Culture Denmark, Danish Ministry of Culture

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Denmark

Results and Publications

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
	results				

Results article		01/06/2020	30/04/2020	Yes	No
Results article		18/08/2020	19/07/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes