

Impact of aging and fitness on ischaemic preconditioning in humans

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To examine the impact of age and physical fitness on the ability of ischaemic preconditioning to protect endothelial damage in response to ischaemia reperfusion injury in healthy humans. A secondary objective is to explore the role of Toll-like...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Observational non invasive

Summary

ID

NL-OMON36213

Source

ToetsingOnline

Brief title

AGE-FIT-IPC

Condition

- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym

cardiovascular disease

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: aging, cardiovascular disease, ischaemic preconditioning, physical fitness

Outcome measures

Primary outcome

Change in endothelial function (measured with flow mediated dilation) after ischaemia reperfusion injury (induced by 20 minutes ischemia) with and without precedence of ischaemic preconditioning (by 3 cycles of 5-minutes of ischaemia).

Secondary outcome

Activation of PBMCs by plasma as measured in an ex-vivo assay.

Study description

Background summary

Ischaemic preconditioning (IP) refers to the reduction of ischemia-reperfusion injury induced by a brief preceding period of ischemia. Also the arterial endothelium can be protected by IP. Several studies performed in animals and humans have demonstrated that the protective effects of IP are attenuated with aging. However, no previous study directly examined the underlying mechanisms of this observation. Possibly, the reduced protective effect of IP with aging relates to a direct effect on the endothelium, consequently leading to an attenuated ability of IP to prevent endothelial dysfunction after ischaemia reperfusion injury.

Several previous studies failed to demonstrate the ability of pharmacological stimuli to mimic the beneficial effects of IP in aged vessels. Restoration of the age-related reduction in effectiveness of IP may be possible through exercise training. In aged animals, physical training restores the efficacy of ischemic preconditioning. Indirect evidence indicates that physical activity, independent of other cardiovascular risk factors, protects against a occurrence as well as the severity of a myocardial infarction in humans. Although this suggests that physical activity may beneficially influence the age-related reduction in IP, no previous study provided direct evidence for this hypothesis.

Study objective

To examine the impact of age and physical fitness on the ability of ischaemic preconditioning to protect endothelial damage in response to ischaemia reperfusion injury in healthy humans. A secondary objective is to explore the role of Toll-like receptor (TLR) signalling in the induction of IP in young and old subjects.

Study design

cross-sectional observation

Study burden and risks

Non-invasive cuff occlusion is used to examine endothelial function (5-minute ischaemia), apply ischaemic preconditioning (3 cycles of 5-minute ischaemia) and produce the stimulus that induces ischaemia-reperfusion injury (20-minute ischaemia). This repeated cuff inflation is non-invasive and not associated with a health risk for the subject. Blood will be drawn three times for ex-vivo analysis of TLR signalling. The volunteers will not benefit directly from participating in this study.

Contacts

Public

Universitair Medisch Centrum Sint Radboud

Geert Grooteplein-noord 21
6525 EZ Nijmegen
NL

Scientific

Universitair Medisch Centrum Sint Radboud

Geert Grooteplein-noord 21
6525 EZ Nijmegen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

- Healthy young volunteers : age 18-30
- Healthy sedentary older volunteers: age >55 years + sedentary (<1 h exercise per week)
- Healthy trained older volunteers: age >55 years + trained (>5 h exercise per week)
- All subjects: written informed consent

Exclusion criteria

- Smoking
- History of any cardiovascular disease
- Hypertension (in supine position: systole >140 mmHg, diastole >90 mmHg)
- Diabetes Mellitus (fasting glucose >7.0 mmol/L or random glucose >11.0 mmol/L)
- Hyperlipidaemia (fasting total cholesterol >6.5 mmol/L)
- Chronic use of medication known to interfere with the cardiovascular system
- Professional athletes

Study design

Design

Study type: Observational non invasive

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-04-2011
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO	
Date:	15-04-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL35881.091.11