The effects of exercise training combined with NR supplementation on metabolic health in older individuals

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON50867

Source
ToetsingOnline

Brief title
Exercise combined with NR supplementation

Condition

- Other condition

Synonym
Ageing, overweight

Health condition

veroudering, energiemetabolisme, type 2 diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: ERC starting grant 2017

Intervention

Keyword: Exercise training, Metabolic health, NR supplementation

Outcome measures

Primary outcome

The primary study endpoints is ex vivo skeletal muscle mitochondrial function

measured via high-resolution respirometry.

Secondary outcome

The secondary study outcome is sleeping metabolic rate measured during an

overnight stay in the respiration chamber.

Explorative objectives are muscle (NAD) metabolites, energy metabolism and

physical performance.

Study description

Background summary

The number of age-related chronic diseases (like obesity, type 2 diabetes and cardiovascular diseases) is increasing rapidly worldwide, reaching pandemic proportions. These age-related chronic diseases are associated with metabolic disturbances and mitochondrial dysfunction in humans. Nicotinamide adenosine dinucleotide (NAD) levels play an important role in energy metabolism and mitochondrial functioning and indeed it has been shown that high concentrations of NAD+ as well as a high NAD+/NADH ratio are strongly associated with metabolic and mitochondrial health. In contrast, decreased NAD+ bioavailability is reported in both ageing and obese humans as well as in diabetic mice. These findings fuelled the idea of influencing NAD+ bioavailability in order to improve metabolic disturbances and mitochondrial dysfunction in humans. Supplementation with nicotinamide riboside (NR), a naturally occurring form of vitamin B3, may provide a way to boost cellular NAD+ levels. However, in

contrast to animal studies, NR supplementation in humans has so far been unsuccesful in improving skeletal muscle mitochondrial function, exercise capacity or insulin sensitivity. Recently, it has been suggested that a situation where NAD+ levels become limited, is needed for NR supplementation to exert beneficial health effects. This situation could be achieved by combining exercise and NR supplementation. However, studies combining NR and exercise are lacking, which is why we would like to perform such a study here.

Study objective

The primary objective of this study is to determine whether combined treatment of exercise and NR imposes greater improvements in skeletal muscle mitochondrial metabolism in older humans compared to exercise treatment alone. The secondary objective of this study is to determine whether combined treatment of exercise and NR imposes greater improvements in sleeping metabolic rate in older humans compared to exercise treatment alone. As explorative objectives, we will examine whether combined treatment with exercise and NR imposes greater improvements in muscle (NAD) metabolites, energy metabolism and physical performance.

Study design

The present study is a randomized, double-blinded, placebo-controlled double arm longitudinal intervention study in a pre and post design.

Intervention

Participants will be asked to take two pills of NR (250mg/pill), or placebo, twice daily (two with breakfast and two with diner, a total of 4 pills/day; 1000mg/day), for 40 days. During days 17-38 of the NR intervention, participants will perform a 3-weeks supervised exercise training program with four ~30 min exercise sessions per week (two endurance session on a bike at 70%Wmax and two high intensity interval (HIIT) sessions. Participants will be randomly assigned to the placebo + exercise or NR + exercise arm. To assess the outcomes, participants will undergo three test days before the start of the NR supplementation and repeat these three test days at the end (day 38-40) of NR supplementation.

Study burden and risks

Before starting the intervention (exercise training + placebo or exercise training + NR), participants will visit the University 4 times for the screening and pre-intervention test days (total time investment 20.5 hours, divided over 4 days). During the intervention period, subjects will visit the University 4 times per week for 3 weeks to receive supervised exercise training (total time investment 6 hours; 2 hours/week). The last exercise session

(training session 12) and post-intervention test day 1 will be combined on day 38. Post-intervention test day 2 will be performed on day 39-40. The time investment for the post-intervention test days includes 20.5 hours. The main burden of this study is the large time investment for the exercise training period (3 weeks, 4 times/week). Moreover, the pre- and post-training test days comprise several non-invasive and invasive measurements. The used techniques are safe, but the muscle biopsies can cause some discomfort and may result in a local bruise or hematoma. Likewise, blood sampling can cause a local hematoma. The risk of infection and/or prolonged bleeding is very low due to state-of-the-art techniques and sterility measures. Measurements performed during the time course of the study can potentially lead to unexpected medical findings. Subjects will be informed about such a finding and possible advised to contact a doctor about this. If a subject does not want to be informed about incidental findings, participation in this study is not possible.

Contacts

Public
Universiteit Maastricht

P. Debyelaan 25
Maastricht 6229 HX
NL
Scientific
Universiteit Maastricht

P. Debyelaan 25
Maastricht 6229 HX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Elderly (65 years and older)

Inclusion criteria

• Participants are able to provide signed and dated written informed consent prior to any study specific procedures
• Aged >= 65 and <= 80 years
• Body mass index (BMI) 25 - 35 kg/m2
• Stable dietary habits (no weight loss or gain > 5 kg in the past 3 months)
• No signs of active cardiovascular disease, liver or kidney malfunction

Exclusion criteria

• Type 2 diabetes
• Patients with congestive heart failure and and/or severe renal and or liver insufficiency
• Uncontrolled hypertension
• Any contra-indication for MRI scanning
• Alcohol consumption of >3 servings per day for man and >2 servings per day for woman
• Smoking
• Unstable body weight (weight gain or loss > 5kg in the last 3 months)
• Engagement in structured exercise activities > 2 hours a week
• Previous enrolment in a clinical study with an investigational product during the last 3 months or as judged by the Investigator which would possibly hamper our study results
• Medication use known to hamper subject*s safety during the study procedures
• Subjects who do not want to be informed about unexpected medical findings
• Subjects who intend to donate blood during the intervention or subjects who have donated blood less than three months before the start of the study
• Use of food supplements containing NR or Resveratrol (similar working mechanisms)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-08-2021
Enrollment:	72
Type:	Actual

Ethics review

Approved WMO Date:	26-07-2021
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-08-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
ClinicalTrials.gov	NCT04907110
CCMO	NL77756.068.21