

Protein synthesis rates in muscle tissue in vivo in patients with mitochondrial myopathy after high intensity interval exercise training

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To assess the effect of unilateral high intensity exercise training on in vivo protein synthesis rates of vastus lateralis muscle in patients with mitochondrial myopathy.

Ethical review	Approved WMO
Status	Pending
Health condition type	Muscle disorders
Study type	Interventional

Summary

ID

NL-OMON51490

Source

ToetsingOnline

Brief title

Psephite study

Condition

- Muscle disorders

Synonym

metabolic diseases, metabolic myopathy

Research involving

Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: MUMC+

Intervention

Keyword: Deuterium, mitochondrial myopathy, Muscle protein synthesis, single-leg training

Outcome measures

Primary outcome

Primary study parameters include mitochondrial and myofibrillar protein synthesis rates of vastus lateralis muscle, calculated from the increase in enriched deuterized alanine in muscle tissue. The trained muscle will be compared with the untrained muscle after 14 days of aerobic exercise.

Secondary outcome

Secondary study parameters are muscle tissue amino acid composition and nitrogen content. Also mitochondrial respiration of muscle tissue from the trained and untrained leg will be compared to baseline tissue using the Oroboros technique.

Study description

Background summary

Mitochondrial myopathies are caused by genetic defects in proteins essential for electron transfer chain function. The metabolic consequences of mitochondrial dysfunction results from a decrease in aerobic energy production from fat and carbohydrate oxidation, and tissues with high metabolic demand, such as heart, brain, and skeletal muscle are particularly sensitive. Exercise intolerance is a prominent symptom in patients with mitochondrial myopathy. Aerobic training increases mitochondrial volume density and expression of mitochondrial enzymes that facilitate aerobic metabolism. This will improve the capacity to oxidize fat and thereby save limited carbohydrate stores from becoming depleted. Effects on mitochondrial and myofibrillar protein syntheses after an exercise intervention could be different in mitochondrial myopathies.

Study objective

To assess the effect of unilateral high intensity exercise training on in vivo protein synthesis rates of vastus lateralis muscle in patients with mitochondrial myopathy.

Study design

Non-randomized, pre-post unilateral intervention study with intra-individual comparison.

Intervention

During a unilateral intervention period of 14 days, participants will perform high intensity dynamic knee extension training with one leg every other day (in total seven sessions). Based on leg dominance, the leg to be trained will randomly be assigned.

Training session consist of 5 minutes warming-up, three sets of 4-min high intensity training, separated by a 4-min break at very low intensity. Muscle tissue protein synthesis rates will be assessed by ingesting deuterated water ($2H_2O$) throughout the interventional period. At baseline a muscle biopsy from the vastus lateralis muscle will be performed in the control leg. After the exercise intervention a muscle biopsy will be taken in both legs.

Study burden and risks

The risks involved in participating in this study are minimal. The muscle biopsy will be obtained by a physician using the Bergström percutaneous needle biopsy method. By using the unilateral training protocol, power will greatly increase, the number of participants needed is reduced and the time needed to perform this study is shortened in comparison with a cross-over or a parallel-group design. Ingestion of deuterated water is safe and no adverse side effects are associated with the ranges of the present study. Saliva sampling for, determining body water $2H_2O$ enrichment, is risk-free and blood sampling is minimal (30mL total).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Inclusion criteria

- Age \geq 18 years
- m.3243A>G point mutation or single, large scale mtDNA deletion

Exclusion criteria

- * insufficient mastery of the Dutch language
- * pregnancy
- * severe cardiopulmonary disease (chest pain, heart failure, arrhythmia, pacemaker, cardiac surgery, severe exertional dyspnea, emphysema). If cardiac involvement is present, inclusion will be evaluated by one of the cardiologists with expertise in mitochondrial cardiomyopathy.
- * coagulopathy (anti-platelet therapy is allowed)
- * cognitive dysfunction
- * not able to perform the high intensity training protocol

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	01-08-2022
Enrollment:	16
Type:	Anticipated

Ethics review

Approved WMO	
Date:	07-12-2022
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	NL81717.091.22