Athlete*s paradox update: Lipid Deposition in Diabetes and Athletes

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- to investigate the difference in diacylglycerol species and subcellular localisation in athletes, sedentary insulin sensitive subjects and sedentary insulin resistant subjects. - to investigate the potential effect of alternative DAG localization...

Ethical review	Approved WMO
Status	Completed
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON48980

Source
ToetsingOnline

Brief title
LIDDIA

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
noninsulin dependant diabetes, Type 2 diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Athlete's paradox, Diacylglycerol, Insulin resistance, Skeletal muscle

Outcome measures

Primary outcome

- Skeletal muscle content of DAG species and subcellular partitioning in athletes, sedentary insulin sensitive subjects and sedentary insulin resistant subjects (measured in muscle biopsies).

- Activation and isotype form of protein kinase C in athletes, sedentary insulin sensitive subjects and sedentary insulin resistant subjects (measured in muscle biopsies at baseline and after insulin stimulation).

Secondary outcome

- IMCL by 1H-Magnetic Resonance Spectroscopy

- Insulin sensitivity by implementing a 1-step hyperinsulinemic-euglycemic clamp.

- Metabolites in blood before and during insulin stimulation (i.e. glucose, free fatty acids, triglycerides, cholesterol, insulin)

Study description

Background summary

Fat accumulation in skeletal muscle is associated with the development of type 2 diabetes mellitus. Indeed, type 2 diabetes patients (T2DM) have increased levels of intramyocellular lipids (IMCL). Paradoxically, however, endurance trained athletes are also characterized by elevated levels of IMCL, while being highly insulin sensitivity. This paradox has been called the athletes paradox, and has so far not been explained. Here, we aim to investigate the levels and localization of diacylglycerol - a fatty acid intermediate that is able to impair insulin signaling - in sedentary insulin resistant subjects and

endurance trained athletes, with similar IMCL content, and compare them to a group of sedentary but insulin sensitive subjects.

Study objective

- to investigate the difference in diacylglycerol species and subcellular localisation in athletes, sedentary insulin sensitive subjects and sedentary insulin resistant subjects.
- to investigate the potential effect of alternative DAG localization on insulin signaling in the three groups by investigating activation and isotype form of protein kinase C in athletes, sedentary insulin sensitive subjects and sedentary insulin resistant subjects.

Study design

The current study is an international multicenter, exploratory, cross-sectional study without intervention.

Study burden and risks

Subjects will first visit the University once for screening purposes during which length, body weight and blood pressure will be measured. An ECG will be performed, blood will be drawn, and subjects will fill in 2 questionnaires. An oral glucose tolerance test will be performed, to determine whether the subjects are insulin sensitive or insulin resistant, by calculating OGIS values. The second screening day will contain a maximal cycling test, after approval of the dependent physician (based on the outcomes of screening day 1). If screening was successfully completed and a subject fulfils the inclusion criteria, the subject can participate in the study. The subjects will be divided into one of the three study groups (based on the results of the maximal cycling test and OGTT) and be invited for the first test day. The first test day at the university will be in the morning (fasted) for a DEXA scan (body composition measurement) and a non-invasive measurement of intramyocellular lipid content using magnetic resonance spectroscopy (MRS). On the second test day, subjects will come to the university after an overnight fast and a muscle biopsy will be taken and resting energy expenditure will be measured. Subsequently, subjects will undergo a 1-step hyperinsulinemic-euglycemic clamp. Furthermore, during the clamp, a second muscle biopsy will be obtained. For all visits, subjects have to report to the university in the morning in the fasted state, except for the second screening day. The evenings prior to the last test day, subjects have to eat a standardized meal. Muscle biopsies can cause mild discomfort and there is a risk of hematoma. During the hyperinsulinemic-euglycemic clamp, a risk of hypoglycaemia exists. In total, we will draw approximately 206 ml blood during the entire study period.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

General inclusion criteria:
- Caucasian
- Male and female
- Ages 18 - 70 years
- Generally healthy
- Stable dietary habits (no weight loss/gain > 5 kg in the last 3 months),
Group 1 and 2, normal weight to overweight/obese healthy control participants:
- BMI > 18 and BMI < 35 kg/m2
- No medication use that interferes with our research parameters.
- Sedentary lifestyle
- VO2max < 30 for women and VO2max < 40ml/kg/min for men, Group 3, endurance trained athletes:

- BMI < 25 kg/m2
- No family history of diabetes
- No medication use that interferes with our research parameters.
- VO2max > 60ml/kg/min for males and VO2max > 45ml/kg/min for females
- Active in endurance-exercise activities, 3 times a week for at least 2 years
- Stable level of training for at least 3 months

Exclusion criteria

- Regular smoking (in the last year)
- Previously diagnosed with type 2 diabetes
- Alcohol consumption (men> 30g/d; women > 20g/d)
- Medication use known to interfere with study parameters
- Use of anti-coagulants (not thrombocyte-aggregation inhibitors) or other medication known to hamper blood coagulation.
- Weight gain/loss > 5 kg in the last 3 months
- Contraindications for MRI scans
- Participation in other studies within 1 month before the start of this study.
- Participants, who do not want to be informed about unexpected medical findings, or do not wish that their physician be informed, cannot participate in the study.
- Any condition, disease or abnormal laboratory test result that, in the opinion of the investigator and the dependent physician, would interfere with the study outcome, affect trial participation or put the subject at undue risk.
- Medication will be looked into per individual participant whether it interferes with the study outcome, affect trial participation or put the subject at undue risk, with special attention to the following medication:
o Selective serotonin re-uptake inhibitors
o Antipsychotics
o Anticonvulsants
o Thiazide diuretics
o Beta-blockers
o Corticosteroids
o Levotyroxine
o GnRH agonists
o Nicotinic acid
o Protease inhibitor
o Fibrates
o NSIADs
o Anticoagulants

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-01-2018
Enrollment:	33
Type:	Actual

Ethics review

Approved WMO Date:	15-09-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	18-04-2018
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
CCMO	NL61390.068.17

Study results

Date completed: 09-08-2019

Results posted: 15-12-2020

First publication
30-09-2020