

# Liver glycogen dynamics and substrate oxidation in lean healthy volunteers (Follow-up study on study entitled \*The effect of modulating hepatic glycogen content on hepatic fat oxidation\*)

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The primary objective of this study is to examine to what extent hepatic glycogen is decreased after a prolonged overnight fast in healthy volunteers with a normal weight and low liver fat percentage.

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Hepatic and hepatobiliary disorders
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON49713

### Source

ToetsingOnline

### Brief title

Liver Glycogen Dynamics

### Condition

- Hepatic and hepatobiliary disorders
- Glucose metabolism disorders (incl diabetes mellitus)

### Synonym

Hepatic glycogen, Storage of sugar in the liver

### Research involving

Human

## Sponsors and support

**Primary sponsor:** Universiteit Maastricht

**Source(s) of monetary or material Support:** TKI

## Intervention

**Keyword:** Hepatic fat, Hepatic fat oxidation, Hepatic glycogen, Metabolic flexibility

## Outcome measures

### Primary outcome

The main study outcome is the change in hepatic glycogen in response to a 9.5hrs and a 16 hrs fast, measured with <sup>13</sup>C-magnetic resonance spectroscopy (MRS).

### Secondary outcome

Whole body fat oxidation measured using the respiratory quotient ( $VCO_2/VO_2$ ) during the night. Oxygen utilization and carbondioxide production are measured using the respiration chamber.

## Study description

### Background summary

The body switches from glucose oxidation to fat oxidation when nutrient availability is low, e.g. during a prolonged fast. This is associated with depleting hepatic glycogen stores. In a previous study, where we investigated hepatic glycogen depletion and substrate oxidation overnight in volunteers with increased liver fat (NAFL), we found that hepatic glycogen did not decrease, not even during a prolonged fast in this group of human participants. Similarly, substrate oxidation did not show the typical increase in fat oxidation during the night that is generally observed in healthy subjects. This reflects that participants with NAFL do not easily reach a truly fasted state. To link this finding to the metabolic phenotype of this subject group, we want to investigate the same parameters in healthy lean volunteers and confirm that in healthy subjects, metabolism does change during fasting. We hypothesize that a prolonged overnight fast will lead to a depletion of hepatic glycogen stores

and stimulation of whole-body fat oxidation in healthy, lean adults, while this was not the case in NAFL subjects.

## **Study objective**

The primary objective of this study is to examine to what extent hepatic glycogen is decreased after a prolonged overnight fast in healthy volunteers with a normal weight and low liver fat percentage.

## **Study design**

This is a randomized cross-over study comparing different overnight fasting times (9.5 vs. 16h fasting) that will be conducted in 13 lean (BMI: 18.5 - 25) males and postmenopausal females with a liver fat percentage <5%. The short and long overnight fast conditions will be randomized, interspersed by a minimal 2-week wash-out period. In the study liver glycogen content(MRS), liverfat oxidation (plasma beta-hydroxybutyrate), other plasma metabolites related to energy metabolism and body composition(BodPod) will be measured in both conditions.

## **Intervention**

Short overnight fasting protocol

Subjects will receive a standardized snack at 16.30. At 23.00 subjects will receive their standardized dinner, where after subjects stay fasted for 9.5 hours.

Long overnightfasting protocol

Subjects will receive their standardized dinner together with a snack at 16.30. Hereafter, subjects stay fasted for 16 hours.

## **Study burden and risks**

The burden for the participant consists of time investment, fasting for a prolonged period and blood draws. Participants are financially compensated for their burden. Participation to this study only has minor risks for the participants. Blood drawing could cause bruising and because participants with contraindications for MRI scan are excluded for participation the risk of the MRI scan is very low.

## **Contacts**

### **Public**

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Elderly (65 years and older)

### Inclusion criteria

- Participants are able to provide signed and dated written informed consent prior to any study specific procedures
- Caucasian (people will be excluded when having a \*50% racial African/Asian background)
- Participants should have suitable veins for cannulation or repeated venipuncture
- Women are post-menopausal (defined as at least 1 year post cessation of menses)
- Men and women aged \* 45 and \* 75 years at the start of the study
- Body mass index (BMI) 18.5 \* 25 kg/m<sup>2</sup>
- Stable dietary habits (no weight loss or gain >3kg in the past 3 months)
- Sedentary lifestyle (not more than 3 hours of vigorous sports per week)
- Liver fat content <5%

### Exclusion criteria

- Type 2 Diabetes Mellitus

- Active diseases (cardiovascular, diabetes, liver, kidney, cancer or other)
- Any contraindication for MRI scanning
- Alcohol consumption of >2 servings per day
- Regular smoking
- No use of medication interfering with investigated study parameters (as determined by responsible physician)
- Participants who do not want to be informed about unexpected medical findings, or do not wish that their physician

## Study design

### Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

### Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	11-09-2020
Enrollment:	22
Type:	Actual

## Ethics review

Approved WMO	
Date:	03-06-2020
Application type:	First submission
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	NL72118.068.20