Time course and nature of nutrient sensing during fasting in humans

Published: 15-10-2010
Last updated: 03-05-2024

1. To determine the nature and time course of the energy sensing machinery during starvation in humans.2. To correlate systemic adaptations with changes at the cellular level.

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

Summary

ID

NL-OMON34127

Source
ToetsingOnline

Brief title
Time course nutrient sensing during fasting

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Metabolism disorders NEC

Synonym
n.a.

Research involving
Human

Sponsors and support

Primary sponsor: Endocrinologie
Source(s) of monetary or material Support: CMSB,(industrieel) geld uit ander(e) project(en)

Intervention

Keyword: AMPK, Fasting, Nutrient-sensing

Outcome measures

Primary outcome

• Plasma parameters: cortisol, IGF-1, free thyroxine, triiodothyronine, testosterone, oestradiol, SHBG, prolactin, TSH, GH, LH, FSH, ACTH, insulin, glucose, ketones, adiponectin, leptin, ghrelin.

• Biochemical measures in skeletal muscle (m. vastus lateralis biopsy): phosphorylation state, enzyme activity and gene expression of AMPK, mTOR, SIRT1/2, FOXO1/3 and various up- and downstream targets of these enzymes and transcription factors.

• Fuel oxidation (indirect calorimetry)

Secondary outcome

n.a.

Study description

Background summary

Supply of fuel is of critical importance for survival. Evolution therefore provided highly conserved, sensitive cell autonomous and systemic *energy gauges* to safeguard adequate availability of fuel. Energy deprivation engages a plethora of endocrine and metabolic mechanisms to reduce energy expenditure and increase energy production from endogenous sources. Pituitary, gastrointestinal and adipose hormones are components of the systemic response to fasting. At the cellular level, AMP activated protein kinase (AMPK) plays a pivotal role. It is activated by nutrient deprivation via a reduced intracellular ADP/AMP ratio and a variety of endocrine cues (including insulin and leptin) and controls energy balance by shutting off energy consuming processes while activating the machinery to produce ATP (1). The sirtuins are a family of highly conserved nicotinamide adenosine dinucleotide (NAD)+ dependent

deacetylases that play similar roles by histone modification of genes encoding proteins involved in energy metabolism (2). Importantly, calorie restriction extends lifespan in all species examined (including non-human primates) and prevents chronic disease in mammals, most likely via mechanistic routes that involve this energy sensing machinery.

Several studies have begun to determine the time course of events sensing energy availability in rodents. In contrast, there is not a single study that has examined this in humans to date. A better understanding of this energy sensing machinery in humans is of utmost importance to give us new insights for the development of new therapies for common diseases such as obesity, diabetes mellitus, cardiovascular diseases and cancer. This are diseases in which disturbances of the energy-sensing machinery might play a role.
To determine the time course of energy sensing events in humans, we will measure the concentration of various hormones in plasma, and biochemical changes in skeletal muscle at sequential time points during starvation. We choose to study the molecular machinery in muscle, since muscle is very sensitive to fuel deprivation.

Study objective

1. To determine the nature and time course of the energy sensing machinery during starvation in humans.
2. To correlate systemic adaptations with changes at the cellular level.

Study design

Observational intervention study.

All participants will be screened prior to this intervention study. We will include 12 healthy young, lean, Caucasian men.
All participants will be admitted to the clinical research unit of the department of internal medicine for a 24 hour fast. After arrival anthropometric measurements and a bioelectrical impedance analysis (BIA) will be performed, after which volunteers will be given a standardized breakfast. We will take muscle biopsies, preceded by indirect calorimetry and a blood sample, at different time points: 1 * hours of fasting, 4 hours of fasting, 10 hours of fasting and 24 hours of fasting.

Study burden and risks

A muscle biopsy will be taken from the musculus vastus lateralis. Some, but not all, patients experience some pain at the moment the biopsy is taken. Sometimes a small haematoma will develop. Furthermore the patient might experience a heavy feeling in the involved muscle during 24 to 48 hours after the biopsy. After the muscle biopsy a pressure bandage will be applied to the leg which has

to remain for 24 hours. In the previous years during which we have performed muscle biopsies, a bleeding or other complication has never occured.

Contacts

Public
Selecteer

Albinusdreef 2
2333 ZA Leiden
NL
Scientific
Selecteer

Albinusdreef 2
2333 ZA Leiden
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy males
Age 19-29 yrs
BMI 19-25 kg/m2
Stable weight for the last 3 months
Caucasian
FPG < 6 mmol/L
Well-controlled blood pressure (< 150/95 mmHg)
Creatinine <100 umol/l

Hb > 7.5 mmol/l
Negative family history (first degree) of DM2

Exclusion criteria

Use of medication known to affect glucose metabolism (for example prednisone) or lipid metabolism
Significant (chronic) disease
Smoking (current)
Alcohol consumption of more than 14 units per week at present or in the past
Difficult accessible veins for insertion of an intravenous catheter
Recent blood donation (within the last 3 months)
Recent participation in other research projects (within the last 3 months), participation in 2 or more projects in one year
Rigorous exercise/sports 5 or more days a week

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-01-2011
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO

Date:	15-10-2010
Application type:	First submission

Review commission: METC Leids Universitair Medisch Centrum (Leiden)

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	NL33757.058.10