Effects of Acetate on insulin Sensitivity, CNS regulation of food intake and appetite in Humans

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

Summary

ID

NL-OMON48359

Source
ToetsingOnline

Brief title
AISCHA study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes, Type 2 diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Acetate, Appetite, Gut-brain axis, Insulin sensitivity

Outcome measures

Primary outcome

The main study parameters are the differences in postprandial glucose and insulin levels upon a standardized mixed meal test (SMMT) consisting of Nutridrink after acetate infusion.

Secondary outcome

The secundary study parameters are postprandial incretins (GLP-1 and ghreline), insuline, glucose and lipid responses upon a SMM, subjective ratings of appetite in fasted state, after exposure to virtual food stimuli and upon a SMM and the CNS regulation of appetite upon virtual food stimuli and upon actual food stimuli (measured by both VAS questionnaire and functional MRI).

Study description

Background summary

Obesity is a major public health problem. Mounting evidence suggest a prominent role for the gut microbiome in pathophysiological pathways that influence the central nervous system (CNS) regulation of food intake. In this regard, the short-chain fatty acid (SCFA) acetate is one of the major metabolites produced by gut microbiota from dietary fibre. It has been established that acetate is absorbed into the blood stream and passes the blood brain barrier (BBB). In rodent studies, acetate has been shown to function as a beneficial substrate in hypothalamic brain regions to mediate both glucose metabolism and insulin secretion as central appetite regulation. However, certain other studies have shown contradicting results thus leaving the role of acetate in energy metabolism and appetite regulation controversial. Moreover, the metabolic effects of acetate in insulin resistant subjects appears to differ significantly from the physiological situation. We therefore aim to study the acute effects of intravenous (iv) infusion of the SCFA acetate on glucose

metabolism and neural regulation of food intake both in healthy lean subjects and in obese subjects with metabolic syndrome.

Study objective

The main objective of this study is to look at the effect of iv acetate infusion on postprandial glucose metabolism and whether this effect differs between healthy lean subjects and obese subjects with metabolic syndrome. The secondary objectives of this study are to study the effects of acetate infusion on postprandial incretins (GLP-1 and ghreline), insuline, glucose and lipid responses. Also both subjective ratings of appetite (VAS questionnaire) as well as fMRI for CNS regulation of appetite will be determined.

Study design

Double blind, placebo controlled crossover design.

Intervention

All participants will receive either 1700 mL of sodium acetate with a concentration of 150 mmol/L or sodium bicarbonate with a concentration of 150 mmol/L administered intravenously over a period of 180 minutes. Following a crossover design, both interventions will be done in all participants in a random order with a 1 week washout period in between.

Study burden and risks

The burden of this study is formed by the fasting from 20:30 the night before testing until 13:00 on the day of the test except for the standardized mixed meal (SMM). Also, a total of 320 ml blood will be drawn (which is lower than the 500ml of blood taken at the bloodbank). Finally, an functional magnetic resonance imaging (fMRI) scan of 1 hour will be made and this requires the participants to lay still for 60 minutes, which could cause mild discomfort.. Furthermore, the intravenous administration of acetate can be considered low risk since acetate is an endogenous molecule and the dosage that will be administered for this study will not exceed physiological concentrations for a long period of time. The fMRI scan will be preceded by a thorough screening during which all possible exclusion criteria for undergoing an fMRI scan will be ruled out and will therefore not be considered as a high risk procedure.

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

Inclusion criteria healthy lean subject group:
- Healthy Caucasian male or female
- Age 40-65
- Women must be post-menopausal
- BMI range of 19-25 kg/m²
- Subjects should be able and willing to give informed consent.

Inclusion criteria obese metabolic syndrome subject group:
- Caucasian male or female with metabolic syndrome
- Age 40-65
- Women must be post-menopausal
- BMI range of 25-40 kg/m²
- At least 3 out of 5 NCEP metabolic syndrome criteria: fasting plasma glucose * 5.6 mmol/L and/or HOMA-IR * 2.5, triglycerides * 1.6 mmol/L, waist-circumference > 102 cm, HDL cholesterol * 1.04 mmol/L, blood pressure * 130/85.
- Subjects should be able and willing to give informed consent.

Exclusion criteria

Exclusion criteria for all participants:
- Systemic medication use, except for paracetamol
- Oral or intravenous antibiotics in the past 3 months before inclusion
- Smoking
- Substance abuse
- Excessive weight loss (> 10% in past 3 monts)
- Overt diabetes mellitus type 2
- Malignancy (except for basal cell carcinoma)
- History of major heart disease
- History of major renal disease
- Pregnancy or breast feeding
- Implantable devices
- Contra-indication for MRI, such as claustrophobia or pacemaker
- Psychiatric illnesses: mood disorders, eating disorders, anxiety disorders, schizophrenia and other psychotic disorders, dissociative disorders, somatoform disorders, delirium, dementia and other cognitive disorders
- Simultaneous participation in other studies
- Inability to understand the study protocol, give informed consent or participate adequately in study protocol

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-10-2020
Enrollment:	60

Type:	Actual

Ethics review

Approved WMO Date:	17-12-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL71072.018.19