Evaluating the effects of acute LPS exposure on Energy metabolism and Substrate utilization as well as markers reflecting lipid and glucose metabolism: The LES trial

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The main objective for the current project is to investigate the effect of acute systemic inflammation - induced by LPS exposure - on energy metabolism, measured as resting metabolic rate (RMR), in apparently healthy volunteers.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON54328

Source
ToetsingOnline

Brief title
LPS, energy metabolism and substrate utilization

Condition

- Other condition

Synonym
energy use, Metabolic rate

Health condition

Energieverbruik

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Energy expenditure, Inflammation, LPS, Substrate utilisation

Outcome measures

Primary outcome

The primary study parameter is energy metabolism in apparently healthy

volunteers.

Secondary outcome

Secondary outcome parameters are substrate oxidation, glucose and lipid

metabolism, hepatic, kidney and pancreatic function, vascular function,

oxidative stress and clinical and inflammatory parameters.

Study description

Background summary

Patients in the ICU are often critically ill and are sometimes being fed via enteral nutrition. In addition, these patients often have a highly variable energy expenditure which is changing in time. To maintain in energy balance, it is important to understand the effect of inflammation on energy expenditure and substrate utilization to better tailor the amount and composition of tube feeding. Intravenous injection of purified lipopolysaccharide (LPS) - a component of the outer membrane of Gram-negative bacteria - into healthy subjects is a well-characterized model of human inflammation. In this current study, we want to use LPS to measure how energy metabolism and substrate utilization is affected by inflammation.

Study objective

The main objective for the current project is to investigate the effect of acute systemic inflammation - induced by LPS exposure - on energy metabolism, measured as resting metabolic rate (RMR), in apparently healthy volunteers.

Study design

The study is a single-blind, randomized, placebo-controlled, cross-over study to evaluate the effects of acute LPS exposure on energy metabolism, substrate utilization and lipid and glucose metabolism, hepatic, kidney, pancreatic and vascular function.

Study burden and risks

During a screening visit, a physical examination takes place. Body weight and height will be determined and heart rate and blood pressure will be measured. A urine dip-stick pregnancy test will be used for women only to exclude pregnancy. Thereafter a fasted blood sample will be obtained and to assess a normal cardiac function, an electrocardiogram (ECG) will be performed.

Each participant will be studied twice and during both periods (each period has a duration of 10 hours), subjects will stay in a monitored ward at the MUMC+. Two intravenous catheters will be inserted and a feeding tube will be placed. Participants will also be asked to wear a continuous glucose monitor, an ambulatory blood pressure device, an activity tracker and wearables to assess body temperature, respiration rate and oxygen saturation. On several timepoints, participants will be asked to perform cognitive tests on an iPad, while wearing glasses that record eye tracking movement. During this stay, whole body energy expenditure and substrate metabolism will be continuously measured in the respiration chamber. At the monitored ward in the hospital, this will be done in regular 30-minutes interval, depending on the well-being of the participants. Venous blood will be collected directly before LPS injection at regular intervals thereafter. Moreover, 24h urine will be collected in batches.

After both periods, subjects will return to the university for a follow-up meeting where a postprandial test will be performed. Subjects are requested to consume a standardized mixed meal and blood samples will be collected at regular intervals. Energy expenditure and substrate metabolism will be measured by ventilated hood measurements. Between the test day and the follow-up meeting, 48h glucose profiles, 48h blood pressure profiles and 48h activity monitoring will be measured.

Venepuncture and insertion of a cannula can cause discomfort and possibly a local haematoma or bruise. Indirect calorimetry might evoke claustrophobic reactions, but there are no physical risks involved. Total time investment will be approximately 31 hours and 361.5 mL blood will drawn during a period of 6

weeks. Time invested is excluding travel time.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Provision of signed and dated informed consent prior to any study specific procedures
• Willingness to comply with study protocol
• Apparently healthy men and women as judged by the study physician
• Non-smoking
• Aged between 18 and 35 years
• BMI >=20 and <=25 kg/m2
• Agreeing to be informed about medically relevant personal test-results by a physician

Exclusion criteria

• Having a medical condition or use of medication which might lead to an intensified response towards LPS exposure to be judged by the study physician
• Having a medical condition or history which might impact study measurements to be judged by the study physician (e.g. myocardial infarction, angina, thrombosis, stroke, cancer, liver or bowel disease or diabetes)
• Use of over-the-counter and prescribed medication, which may interfere with study measurements (to be judged by the principal investigator and physician)
• Use of oral antibiotics (with the exception of topical antibiotics) in 40 days or less prior to the start of the study
• Current use of antihypertensive, antidiabetic or lipid lowering medication
• Females who are pregnant, breast feeding or may wish to become pregnant during the study
• Abnormal ECG result
• Fasting glucose >7.0 mmol/L
• Total cholesterol >8.0 mmol/L
• Clinically significant out of range values of serum levels of liver, kidney and pancreatic enzymes, to be judged by the study physician
• Anaemia, Hb-level <7.8 mmol/L (female) and <8.3 mmol/L (male)
• Body mass index < 20 kg/m2 or > 25 kg/m2
• Reported alcohol consumption > 14 units/week (female) or > 21 units/week (male)
• History of illicit drug use
• Reported weight loss or gain of 3 kg or more during a period of 2 months prior to screening
• Active blood donor (<3 months prior to start study)
• Use of an investigational product in another biomedical study within the previous month
• Having a history of spontaneous vagal collapse
• Having participated in a previous trial where LPS was administered

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo

Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	12
Type:	Anticipated

Ethics review

Approved WMO Date:	13-12-2021
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-07-2023
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	NL78277.068.21

Study results

Summary results
Trial never started