

The importance of non-essential amino acids for maintaining skeletal muscle protein synthesis rates in healthy young men

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The purpose of this study is to determine if a diet lacking NEAA, with or without being replaced by additional EAA, influences skeletal muscle protein synthesis rates and whole-body metabolism in healthy young men.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Muscle disorders
Study type	Interventional

Summary

ID

NL-OMON53839

Source

ToetsingOnline

Brief title

NEAA Study

Condition

- Muscle disorders

Synonym

muscle anabolism, Muscle growth

Research involving

Human

Sponsors and support

Primary sponsor: Universiteit Maastricht

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Amino acids, Metabolism, Muscle, Protein

Outcome measures

Primary outcome

Skeletal muscle protein synthesis rates

Secondary outcome

- Skin protein synthesis rates
- Muscle mass
- Resting energy expenditure
- Blood pressure and heart rate
- Plasma profiles (lipids, insulin, amino acids, inflammatory markers)
- Urine markers of protein breakdown
- Skeletal muscle mitochondrial respiration
- Organ volumes
- Biochemical signaling pathways in skeletal muscle

Study description

Background summary

Muscle tissue consists of proteins. These proteins are built up of small building blocks: amino acids. Some amino acids must be consumed through the diet because they cannot be made within the body (essential amino acids), while some amino acids can be made within the body (non-essential amino acids). Regardless of the source, all amino acids are required for complete muscle protein building. Therefore, if non-essential amino acids are not consumed through foods, they must be made adequately in the body, which is a process that requires energy. However, it is not yet known how a diet lacking

non-essential amino acids changes muscle building, energy metabolism, and muscle metabolism. The goal of this study is to investigate if non-essential amino acids are an important component of a human diet.

Study objective

The purpose of this study is to determine if a diet lacking NEAA, with or without being replaced by additional EAA, influences skeletal muscle protein synthesis rates and whole-body metabolism in healthy young men.

Study design

Randomized, parallel design, double-blind, dietary intervention study in which males will consume a standardized low-protein diet supplemented with various amounts of essential amino acids and non-essential amino acids (in the form of free amino acid drinks) for 10-days.

Intervention

All subjects will consume a standardized low-protein diet (<2% energy as protein) supplemented with various amounts of EAA and NEAA in the form of free amino acid drinks. Subjects will be randomized to either 1) a conventional diet group (standardized diet supplemented with 7% energy as EAA + 10% as NEAA), 2) a diet lacking NEAA (supplemented with 7% EAA + 0% NEAA), or 3) a diet lacking NEAA and replaced by additional EAA (supplemented with 17% EAA + 0% NEAA, isonitrogenous with conventional diet). The dietary intervention will be 10 days in duration and deuterium oxide will be consumed throughout the intervention period.

Study burden and risks

The risks involved in participating in this experiment are minimal. The blood sample will be comparable to a normal blood draw and the only risk is a small local hematoma. This is also true for muscle biopsies. Muscle biopsies will be taken through a small (5 mm) incision, following local anaesthetic of the skin and muscle fascia, and will heal completely. Muscle biopsies will only be obtained by an experienced physician. Skin biopsies will be taken from the buttocks using a small (4 mm) punch. Skin biopsies are frequently used method for diagnostic and therapeutic purposes and will heal completely. The ingestion of deuterium oxide has been applied in numerous published studies and is entirely safe and non-toxic in the amounts provided in the present study. We will take 4 blood samples (80 mL total) during the experimental trial. For the experimental trials (D2O dosing day, Test Day 1, Test Day 2, test Day 3), participants have to be fasted, so they are not allowed to eat and drink (except for water) from 22:00 the evening before. Also, 3 days prior to the experimental trial participants should keep their diet as constant as possible,

should not perform any type of intense physical exercise, and should not consume alcohol. Furthermore, we will ask the participants to fill out a dietary and activity record for 3 days prior to the experimental trial. The time investment is 2 hours (screening), 4 hours (D2O Dosing Day), 2 hours (Test Day 1), 0.5 hours (Test Day 2), 2.5 hours (Test Day 3) and filling in the food and activity dairies diaries (30 minutes per day). There are some risks of discovering an incidental finding when performing an MRI, however if the participant does not want to receive such information, they cannot participant in the research. If there are unexpected findings in the form of abnormal values/structures identified during the MRI (and any other research tests performed), the participant will be informed.

The diet lacking NEAA is expected to pose no risk to participants, as it has been shown that a prolonged diet very low in protein does not lower fat-free mass (diet composed of 5% energy from protein) or lower muscle protein synthesis rates (diet composed of 9% energy from protein), suggesting that a very low protein intake does not compromise muscle mass maintenance. The experimental diets contain normal commercially available nutritional ingredients that are safe for human consumption and for this reason do not form any health risks. Furthermore, the diets are tailored to the participant*s energy and macronutrient needs, and composed according to the dietary guidelines of the Dutch National Health Council.

There is no direct benefit for the participants, only their contribution to scientific knowledge of the role of nutritional components in a diet. The current study will provide valuable information about the role of essential and non-essential amino acids in the human diet. A small benefit for the participants is that they will get insight into their body composition (MRI).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Inclusion criteria

- Male
- Age between 18 and 35 y inclusive
- BMI between 22 and 30 kg/m²
- Non-smoker
- Having given informed consent

Exclusion criteria

- Participating in a structured (progressive) exercise program
- Smoker
- Diagnosed GI tract disorders or diseases
- Diagnosed musculoskeletal disorders
- Diagnosed metabolic disorders (e.g. diabetes)
- Cardiovascular disease
- Hypertension (blood pressure above 140/90 mmHg)
- Donated blood 3 months prior to test day
- Use of any medications known to affect protein metabolism (i.e. corticosteroids, non-steroidal anti-inflammatories).
- Chronic use of gastric acid suppressing medication
- Chronic use of anti-coagulants
- Any intolerance to foods included in the standardized diet intervention

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	14-11-2024
Enrollment:	64
Type:	Actual

Ethics review

Approved WMO	
Date:	31-08-2023
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO	
Date:	11-11-2024
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	NL83031.068.22