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Analyzing the effects of short-term fasting on transcriptome and epigenome signatures compared with food consumption in healthy subjects

Submission date
06/12/2021

Recruitment status
No longer recruiting

Registration date
09/12/2021

Overall study status
Completed

Last Edited
03/11/2022

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Several studies in animals and some in humans have reported that dietary interventions based on intermittent fasting or on time-restricted feeding lead to promising improvements in the cardiometabolic risk profile (decreasing body weight, reducing blood sugar and fat, etc). However, although some investigations in humans have associated these beneficial effects with epigenetic modifications (changes that modify the activation of certain genes, but not the genetic code sequence of DNA), mainly with DNA methylation and changes in gene expression in key genes related to metabolism, very few studies have analyzed the changes in the transcriptome (gene expression) and in the epigenome (mainly focusing on DNA methylation) at the genome-wide level. Therefore the main aim of this study is to explore the changes in the transcriptome at the genome-wide level in healthy subjects from a Mediterranean population after a short-term fasting period (24 hours) in comparison with frequent food consumption in the same period, and to establish the corresponding transcriptome and methylome signatures that identify the main differentially expressed and or methylated genes depending on the fasting or on the frequent food consumption status in the short-term intervention.

Who can participate?
Men and women (white European) from the general Mediterranean Spanish population (aged 18-50 years)

What does the study involve?
Each participant receives both interventions in a random order. One intervention will consist of a period of 24 hours fasting (only water will be allowed) and the other intervention will consist of a frequent meal pattern (6 times a day, every 3 hours) for the equivalent 24-hour period. In this food consumption intervention, the participant will be provided with typical foods of the Mediterranean diet: fruits, vegetables, legumes, extra virgin olive oil, fish, white meat and nuts). There will be a 2-week break between the interventions.

What are the possible benefits and risks of participating?
There are no direct medical benefits of participating in the study. Participants will be informed that there are no benefits and risks expected.

Where is the study run from?
University of Valencia (Spain)

When is the study starting and how long is it expected to run for?
January 2020 to December 2022

Who is funding the study?
Generalitat Valenciana and University of Valencia (Spain)

Who is the main contact?
Prof. Carolina Ortega-Azorín
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
PTRC_1521410

Study information

Scientific Title
Effect of fasting for 24 hours compared to frequent food consumption on anthropometric, biochemical and gene expression and methylation variations in the general population (AYUGEN)

Acronym
AYUGEN

Study objectives
The hypothesis is that fasting for 24 hours can change gene expression and DNA-methylation profiles at the genome-wide level in comparison with a pattern of food consumption, allowing us to identify the transcriptome and methylome signatures associated with fasting and frequent food consumption in a Mediterranean population.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/01/2021, Ethics Committee on Human Research at the University of Valencia (Avda. Blasco Ibanez 13, Valencia, 46010, Spain; +34 (0) 963864109; vicerec.investigacio@uv.es), ref: CR_1521410

Study design
Interventional randomized cross over trial

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Community

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Short-term fasting

Interventions
This is a short-term cross-over intervention trial in 25 participants (including men and women). Two interventions related to food consumption will be carried out. All participants will receive both interventions. Participants will be randomly assigned 1:1 to the order of the two interventions by a computer-generated randomization procedure. The interventions will consist

of:
1. Fasting for 24 hours (water allowed)
2. Consumption of foods for the equivalent 24-hour period

The frequent food consumption intervention pattern includes eating 6 times a day every 3 hours. In this food consumption intervention, participants will be provided with typical foods of the Mediterranean diet: fruits, vegetables, legumes, extra virgin olive oil, fish, white meat and nuts). A wash-out period of 2 weeks between interventions will be carried out.

Intervention Type
Behavioural

Primary outcome measure
Comparative genome-wide gene expression and methylation profiles in leukocytes (using DNA and RNA isolated from blood) to identify transcriptome and methylome signatures (detection of differentially expressed genes and DNA methylation sites) of 24-h fasting versus frequent food consumption after both interventions in healthy subjects from a Mediterranean population. Blood samples will be obtained at baseline and after 24 h of the corresponding intervention (fasting or food consumption). RNA and DNA will be isolated by standard procedures and quality control measures will be carried out. Transcriptome-wide human arrays will be used to analyze differential gene expression and RT-PCR will be used for validation. Methylation will be analyzed by arrays and for selected CpG sites by Massarray according to the standard protocols. Differential gene expression and CpG methylation sites will be statistically analyzed and the combination of the most relevant differentially expressed genes and DNA-methylation sites will be combined by computational analyses to build specific signatures for each intervention.

Secondary outcome measures
1. Plasma glucose and biochemical parameters (lipids) measured by standard procedures at baseline, at 6 h and after the 24 h interventions in both groups
2. Height, weight, waist circumference and body composition by bioimpedance measured by validated methods at baseline and after the interventions
3. Blood pressure and heart rate measured by standard protocols at baseline and after 24 h intervention in both groups
4. Selected gene expression (from the genome-wide transcriptome array) measured by RT-PCR at baseline, at 6 h and after the 24 h interventions
5. Selected DNA methylation measured by MASSARRAY at baseline, 6 h and 24 h after interventions
6. Analysis of differentially expressed genes, methylation sites and pathways (GO and KEEG) at baseline and after interventions in the whole sample and by sex/gender
7. Food intake (assessed with food frequency questionnaires) and adherence to the Mediterranean diet (measured by the 14-item score for adherence) at baseline
8. Physical activity measured using the short form of the Minnesota physical activity questionnaire at baseline
9. Sleep characteristics measured using the Pittsburgh Sleep Quality Index questionnaire and the Epworth questionnaires at baseline
10. Chronotype measured using the Horne and Östberg questionnaire at baseline
11. Additional analysis (depending on the budget) of plasma/urine metabolites (lipids, amino acids, inflammatory markers measured using a standard high-throughput nuclear magnetic resonance metabolomics platform) at baseline and after the interventions

Overall study start date

01/01/2020

Completion date
31/12/2022

Eligibility

Key inclusion criteria
Current inclusion criteria as of 25/07/2022:
1. White European subjects (men and women) recruited from the Mediterranean population
2. Age ranging from 18 to 50 years old
3. BMI between 21 and 34 kg/m²

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Previous inclusion criteria:
1. White European subjects (men and women) recruited from the Mediterranean population
2. Age ranging from 18 to 50 years old
3. BMI between 23 and 33 kg/m²

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
25

Total final enrolment
28

Key exclusion criteria
1. Diabetic subjects
2. Other chronic diseases (cardiovascular, cancer, respiratory diseases, liver diseases, kidney diseases, etc)
3. Subjects with food allergies or food intolerances
4. Alcohol abuse or addiction
5. Immunodeficiency, HIV-positive status, COVID-19 positive status or other acute infections
6. Serious psychiatric disorders: schizophrenia, bipolar disease, eating disorders, depression, etc
7. Any severe co-morbid condition
8. History of major organ transplantation
9. Concurrent therapy with immunosuppressive drugs or cytotoxic agents

10. Current treatment with systemic corticosteroids
11. Current use of weight loss medication
12. Any other condition that may interfere with the completion of the study protocol

Date of first enrolment
20/12/2021

Date of final enrolment
31/10/2022

Locations

Countries of recruitment
Spain

Study participating centre
Unviversity of Valencia
School of Medicine
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46010

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CIBEROBN
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Sponsor type
University/education

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Funder(s)

Funder type
Government

Funder Name
Conselleria de Innovación, Universidades, Ciencia y Sociedad Digital, Generalitat Valenciana

Alternative Name(s)
Conselleria of Innovation, Universities, Science and Digital Society, Valencia, Conselleria d'Innovació, Universitats, Ciència i Societat Digital, CIUCSD

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Spain

Funder Name
Universitat de València

Alternative Name(s)
University of Valencia, 85|86

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Spain

Results and Publications

Publication and dissemination plan
Findings will be published in international journals. Posters and oral communications in related scientific meetings are planned. No other documents will be available at this stage.

Intention to publish date
01/06/2023

Individual participant data (IPD) sharing plan
Data will not be available outside the core research group as the informed consent form signed by participants stated that individual-level data will not be publicly available. Researchers who are interested in this study can contact the main investigator (Dr Carolina Ortega; carolina.ortega@uv.es) if they have any questions regarding the data or are interested in further collaborations.

IPD sharing plan summary
Not expected to be made available