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Influence of a very low-carbohydrate diet on the body's responses and adaptations to intense exercise in healthy young adults

Submission date 14/07/2026	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 17/07/2026	**Overall study status** Completed	
Last Edited 17/07/2026	**Condition category** Other	

Plain English summary of protocol

Background and study aims
Physical exercise improves health and fitness, but people do not always respond to exercise in the same way. One factor that may influence these responses is diet, particularly the amount of carbohydrate consumed. Very low-carbohydrate diets have become increasingly popular, but scientists still do not fully understand how they affect the body's responses and adaptations to exercise. This study aims to compare a very low-carbohydrate diet with a high-carbohydrate diet and determine how these diets influence exercise performance, oxygen transport, metabolism, muscle adaptation and overall physiological responses to high-intensity exercise.

Who can participate?
Healthy physically active men and women aged 18 to 35 years who meet the study eligibility criteria.

What does the study involve?
Participants will attend several laboratory visits at the University of Las Palmas de Gran Canaria. After screening and familiarisation sessions, participants will undergo a series of baseline assessments, including exercise tests, blood sampling, body composition measurements and other physiological evaluations.

Participants will then be randomly assigned to either a very low-carbohydrate diet or a high-carbohydrate diet. Before starting the diet, they will complete an exercise session designed to reduce the amount of carbohydrate stored in their muscles. The assigned diet will then be followed for approximately three days under close supervision by the research team.

Participants will complete detailed physiological testing, including blood sampling, exercise testing and muscle biopsies. They will then undertake a two-week supervised sprint interval training programme while continuing their assigned diet. At the end of the training period, the main assessments will be repeated.

What are the possible benefits and risks of participating?
Participants will receive detailed information about their body composition, exercise capacity, blood volume, haemoglobin mass and other health-related measurements. The study may also contribute to improving scientific knowledge about how nutrition influences exercise adaptation and human health.

Potential risks include discomfort, bruising or bleeding associated with blood sampling, temporary soreness following muscle biopsies, and fatigue or discomfort during exercise testing. All procedures will be performed by experienced researchers following approved safety procedures.

Where is the study run from?
The study is conducted by the Human Performance, Physical Exercise and Health Research Group, which belongs to the Institute of Biomedical and Health Research (IUIBS) of the University of Las Palmas de Gran Canaria (ULPGC), Spain. Participant testing and experimental procedures are performed at the Human Performance Laboratory of the Faculty of Physical Activity and Sport Sciences (FCAFD).

When is the study starting and how long is it expected to run for?
Recruitment began in February 2026 and continued until June 2026. Data collection is expected to be completed by July 2026.

Who is funding the study?
The study is primarily funded by the Spanish Ministry of Science, Innovation and Universities through the State Research Agency (AEI) project. Additional support is provided through the AEI Proof of Concept project and Government of the Canary Islands through the ULPGC pre-competitive research project.

Who is the main contact?
Associate Professor Dr. Marcos Martin-Rincon, University of Las Palmas de Gran Canaria, marcos.martinrincon@ulpgc.es

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Additional identifiers

Spanish State Research Agency (AEI) grant number
PDC2025-165723-I00

Spanish Ministry of Science, Innovation and Universities through the State Research Agency (AEI) project grant number
PID2024-156206OA-I00

Government of the Canary Islands ULPGC pre-competitive research project grant number
SD-24/03

Study information

Scientific Title
Randomized controlled parallel-group mechanistic study of the impact of a very low-carbohydrate dietary intervention on acute and chronic physiological, metabolic and molecular responses to high-intensity exercise in healthy females and males

Acronym
GLYDEX

Study objectives
To determine the effects of a very low-carbohydrate dietary intervention on acute and chronic physiological, metabolic and molecular responses to high-intensity exercise in healthy physically active females and males.

The study aims to examine the effects of dietary carbohydrate availability on substrate metabolism, skeletal muscle signalling pathways, mitochondrial adaptations, oxygen transport, blood volume regulation, exercise performance, and molecular biomarkers involved in exercise adaptation and intrinsic motivation towards physical activity.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 19/01/2026, Human Research Ethics Committee, University of Las Palmas de Gran Canaria (CEIH-ULPGC) (c/ Juan de Quesada, 30, Las Palmas de Gran Canaria, 35001, Spain; +34 928 451072; secv.investigacion@ulpgc.es), ref: CEIH-2024-18-R

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Parallel

Purpose
Basic science

Study type(s)

Health condition(s) or problem(s) studied
Physiological, metabolic and molecular adaptations to exercise and a very low-carbohydrate dietary intervention in healthy physically active adults

Interventions
Following screening, familiarization and baseline assessments, participants will be randomly allocated to one of two dietary intervention groups:

1. Very low-carbohydrate diet (VLChD) providing less than 5% of total daily energy intake from carbohydrates.

2. High-carbohydrate control diet providing approximately 65–70% of total daily energy intake from carbohydrates.

Randomization was stratified by sex, with participants matched into pairs within each sex according to relative aerobic capacity (VO_2max normalized to leg lean mass). Allocation within

each matched pair was determined by a coin toss performed by the principal investigator in the presence of a witness. This was an open-label study, and group allocation was known to participants and the research team.

No masking was used, as the dietary interventions cannot be concealed from participants or investigators. Dietary adherence was independently verified through real-time meal monitoring, and nutritional ketosis was confirmed biochemically by capillary blood β-hydroxybutyrate measurement, independent of participant or investigator report.

Before the acute experimental trial, participants will complete a glycogen depletion exercise protocol. The assigned dietary intervention will start immediately after completion of the glycogen depletion protocol and will be maintained until the invasive experimental trial conducted after 3 days of dietary intervention. During this period, participants will refrain from exercise and all dietary intake will be individually prescribed. Compliance will be monitored in real time: participants will photograph and send images of each meal before and after consumption, including the weighed portions and the empty plate, and any missing or substituted food items will be followed up directly by the research team by phone.

The chronic phase consists of a 2-week sprint interval training programme performed under the assigned dietary condition, including six supervised sprint interval training sessions. After the training period, physiological, metabolic and molecular outcome measures will be reassessed, including blood sampling, skeletal muscle biopsies, haemoglobin mass and blood volume assessment, DXA-derived body composition assessment, and exercise performance testing.

Intervention Type
Other

Primary outcome(s)
1. Leg respiratory quotient (RQ) during submaximal cycling exercise at 50% VO_2max measured using femoral arteriovenous oxygen and carbon dioxide content differences, from which RQ is calculated according to the Fick principle at the acute invasive trial, after glycogen depletion and 3 days of dietary intervention; and the post-training invasive trial, after 2 weeks of sprint interval training

Key secondary outcome(s)
1. Leg respiratory quotient (RQ) during submaximal cycling exercise at 65% VO_2max measured using femoral arteriovenous oxygen and carbon dioxide content differences, from which RQ is calculated according to the Fick principle at the acute invasive trial, after glycogen depletion and 3 days of dietary intervention; and the post-training invasive trial, after 2 weeks of sprint interval training

2. Skeletal muscle signalling responses to exercise measured using immunoblotting (Western blotting) of vastus lateralis muscle biopsy samples, assessing AMPK, p38 MAPK, CaMKII, Nrf2 /Keap1 and ACE2/Ang-(1-7)/MasR-related targets at baseline before the dietary intervention; during the acute invasive trial after glycogen depletion and 3 days of dietary intervention (at rest before exercise, 10 seconds after completion of the functional reserve test, and 30 minutes after completion of the full exercise protocol); and during the post-training invasive trial after 2 weeks of sprint interval training (same timepoints)

3. Mitochondrial and oxidative capacity responses to exercise measured using high-resolution mitochondrial respirometry of vastus lateralis muscle biopsy samples at baseline before the

dietary intervention; during the acute invasive trial after glycogen depletion and 3 days of dietary intervention (at rest before exercise and 10 seconds after completion of the functional reserve test); and during the post-training invasive trial after 2 weeks of sprint interval training (same timepoints)

4. Muscle glycogen content and distribution measured using biochemical glycogen assays and transmission electron microscopy of vastus lateralis muscle biopsy samples (with additional exploratory proteomic, metabolomic and molecular analyses on stored samples subject to supplementary funding availability) at baseline before the dietary intervention; during the acute invasive trial after glycogen depletion and 3 days of dietary intervention (at rest before exercise, 10 seconds after completion of the functional reserve test, and 30 minutes after completion of the full exercise protocol); and during the post-training invasive trial after 2 weeks of sprint interval training (same timepoints)

5. Aerobic capacity and substrate oxidation measured using VO_2max, maximal fat oxidation, VO_2 /intensity relationship, lactate thresholds and cycling economy, assessed via incremental exercise testing and indirect calorimetry, at 50-65% VO_2max at baseline before the dietary intervention; during the acute invasive trial after glycogen depletion and 3 days of dietary intervention; during the post-training invasive trial after 2 weeks of sprint interval training; and during post-training non-invasive performance assessments performed 3 days after the final training session and on the following day

6. Time to exhaustion and functional reserve measured using constant-load cycling exercise at 50% VO_2max (endurance performance) and repeated supramaximal exercise performed to exhaustion (functional reserve test) at baseline before the dietary intervention; during the acute invasive trial after glycogen depletion and 3 days of dietary intervention; during the post-training invasive trial after 2 weeks of sprint interval training; and during post-training non-invasive performance assessments performed 3 days after the final training session and on the following day

7. Sprint and Wingate performance measured using 10-second sprint testing following vascular occlusion, and Wingate testing (peak and mean power output) at baseline before the dietary intervention; during the acute invasive trial after glycogen depletion and 3 days of dietary intervention; during the post-training invasive trial after 2 weeks of sprint interval training; and during post-training non-invasive performance assessments performed 3 days after the final training session and on the following day

8. Cardiovascular and oxygen transport responses to exercise measured using cardiac output, leg blood flow, systemic and leg oxygen delivery, and muscle oxygen extraction, via femoral arterial and venous catheterization with transpulmonary thermodilution at the acute invasive trial (continuous monitoring throughout), after glycogen depletion and 3 days of dietary intervention; and the post-training invasive trial (continuous monitoring throughout), after 2 weeks of sprint interval training

9. Haemoglobin mass and blood volume measured using carbon monoxide rebreathing at baseline before the dietary intervention; during the acute invasive trial, after glycogen depletion and 3 days of dietary intervention; and during the post-training invasive trial, after 2 weeks of sprint interval training

10. Cerebral and muscle oxygenation during exercise measured using near-infrared spectroscopy at baseline before the dietary intervention; during the acute invasive trial after glycogen depletion and 3 days of dietary intervention; during the post-training invasive trial after 2 weeks

of sprint interval training; and during post-training non-invasive performance assessments performed 3 days after the final training session and on the following day

11. Circulating biomarkers and molecular mediators of exercise adaptation measured using circulating IL-6, IL-15, FGF21, miR-29 family members, and selected inflammatory, metabolic and renin-angiotensin system biomarkers, via venous, arterial and femoral venous blood sampling, biochemical assays, immunoassays and RT-qPCR analyses at baseline before the dietary intervention; and during the acute and post-training invasive trials at rest before exercise, during submaximal exercise at 50% VO_2max, and 30 minutes after completion of the full exercise protocol

12. Intrinsic motivation, subjective exercise experience, mood state and sleep quality measured using Behavioural Regulation in Exercise Questionnaire (BREQ-3), Subjective Exercise Experience Scale (SEES), Profile of Mood States (POMS), Pittsburgh Sleep Quality Index (PSQI), and polysomnography-derived sleep architecture and physiological sleep variables at baseline before the dietary intervention; after glycogen depletion and 3 days of dietary intervention; after completion of the 2-week sprint interval training intervention; and before and after training sessions when applicable

Completion date
31/07/2026

Eligibility

Key inclusion criteria
1. Healthy male and female adults aged 18 to 35 years
2. Physically active individuals performing regular exercise training at least 3 times per week
3. Body mass index between 18.5 and 29.9 kg/m²
4. Free from diagnosed cardiovascular, metabolic, respiratory, neuromuscular, or endocrine disease
5. Non-smokers and not taking medications or supplements known to affect metabolism, exercise performance, or hormonal responses
6. Willingness to comply with the prescribed dietary intervention and all experimental procedures
7. Ability to perform maximal exercise testing and repeated muscle biopsy/blood sampling and other physiological assessment procedures
8. Written informed consent provided

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 Years

Upper age limit
35 Years

Sex

All

Total final enrolment
24

Key exclusion criteria
1. History of cardiovascular, metabolic, pulmonary, renal, hepatic, endocrine, or neuromuscular disorders
2. Current smoking or use of recreational drugs
3. Current use of medications or nutritional supplements affecting substrate metabolism, appetite regulation, hormonal function, coagulation, inflammation, or exercise performance
4. Use of hormonal contraceptives in female participants
5. Pregnancy or breastfeeding
6. Body mass index ≥30 kg/m² or clinically significant underweight
7. Clinically significant anaemia, iron deficiency requiring treatment, abnormal coagulation, or abnormal screening blood results considered incompatible with study participation
8. Musculoskeletal injury, surgery within the previous 6 months, or any limitation preventing maximal exercise testing
9. Known food allergies, dietary restrictions, or intolerance that could interfere with compliance with the prescribed diets
10. Inability or unwillingness to undergo muscle biopsy, blood sampling, femoral arterial/venous catheterization, carbon monoxide rebreathing, DXA, or other physiological assessment procedures
11. Contraindication to maximal exercise testing, femoral arterial/venous catheterization, local anaesthesia, muscle biopsy, DXA, or carbon monoxide rebreathing
12. Failure to comply with pre-study standardization requirements or with the prescribed dietary intervention
13. Any medical condition or investigator-assessed circumstance that could compromise participant safety, adherence to the protocol, or data quality

Date of first enrolment
15/02/2026

Date of final enrolment
15/06/2026

Locations

Countries of recruitment
Spain

Study participating centre
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Sponsor information

Organisation
Universidad de Las Palmas de Gran Canaria

ROR
https://ror.org/01teme464

Funder(s)

Funder type

Funder Name
Agencia Estatal de Investigación

Alternative Name(s)
Spanish State Research Agency, Spanish Agencia Estatal de Investigación, AEI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Spain

Funder Name
Consejería de Educación, Universidades, Cultura y Deportes, Gobierno de Canarias

Alternative Name(s)
Ministry of Education, Universities, Culture and Sports, Government of the Canary Islands, Ministry of Education, Universities, Culture and Sports of the Canary Islands Government

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Spain

Funder Name
Universidad de Las Palmas de Gran Canaria

Alternative Name(s)
University of Las Palmas de Gran Canaria, ULPGC

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Spain

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon reasonable request from Dr Marcos Martín Rincón (marcos.martinrincon@ulpgc.es) following publication of the primary study results. Participant-level data will be coded and stored securely on password-protected institutional computers and servers at the University of Las Palmas de Gran Canaria. Only de-identified data will be considered for sharing. Access requests will be evaluated on a case-by-case basis for legitimate scientific research purposes, subject to applicable ethical, legal and data protection requirements.

IPD sharing plan summary
Available on request