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Effects of acute heat stress and regular exposure to hot environments on the oxidation of carbohydrates consumed during exercise

Submission date 19/01/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 01/02/2022	**Overall study status** Completed	
Last Edited 18/06/2024	**Condition category** Other	

Plain English summary of protocol

Background and study aims

During prolonged and strenuous exercise, the body relies on carbohydrate fuel stores located in muscles and the liver to support energy production and allow the muscles to keep working. Those carbohydrate stores are small and when they become low, fatigue can occur. Many sportspeople eat or drink carbohydrate-containing foods or drinks during exercise to provide an additional source of energy, which helps to delay the onset of fatigue. However, when exercise is performed in hot conditions (i.e. acute heat stress) the body's capacity to use carbohydrate that is fed during exercise for energy (i.e., exogenous carbohydrate oxidation) appears to be reduced, and this nutritional strategy is less effective. This is a particular problem as exercising in the heat places even more demands on the body's existing carbohydrate reserves, so being able to use carbohydrate that is fed during exercise is even more important for sustaining exercise.

It is not known why exogenous carbohydrate oxidation is reduced during exercise in the heat. If we can understand the physiological processes that are affected, we might be able to develop different nutritional strategies to enhance the effectiveness of carbohydrate feeding during exercise in the heat. On the other hand, it is well established that regular exposure to hot environments (i.e., heat acclimation) results in adaptations to the body that improve heat tolerance and the body's responses to exercise in the heat. Heat acclimation could therefore be a way to improve exogenous carbohydrate oxidation during exercise in the heat, but this has not been investigated.

This study seeks to understand the mechanisms by which exogenous carbohydrate oxidation is reduced during exercise in the heat, and to test whether heat acclimation can overcome limitations to exogenous carbohydrate oxidation. The findings of this study could have implications not only for sportspeople but also for people in occupations that can require strenuous physical effort in hot conditions (e.g., firefighters, military personnel).

Who can participate?

Healthy non-smoking individuals aged 18-45 years who have good general health and no history of cardiometabolic disease and who are participating in endurance-based activities at least three times a week.

What does the study involve?
The study consists of 19 visits spread over a 4-6 week period depending on the timing between visits. This includes four fitness test visits, three familiarisation exercise visits, nine heat acclimation visits and three experimental trial visits.

Visit 1 - Screening and baseline testing (Duration: ~1 h; Time of the day: Any time of the day)
This visit will be used for consenting and screening and to determine the participants' fitness. Upon arrival, the study will be fully explained to the participant and he/she will then be asked to sign an Informed Consent Form if decided to take part. A general health questionnaire will need filling in and body height and body mass will be measured. If they successfully complete the questionnaire and meet the eligibility requirements participants will then have their aerobic fitness determined using a test that will take place on a stationary bicycle. The test starts at a very easy work level and gets harder every 3 minutes and participants are asked to keep cycling for as long as they can (typically this takes between 10- 25 minutes). During the test, participants will be wearing a facemask connected to a computerised gas analysis system that will measure how much oxygen they are using. If their test results meet the set criterion, they will be scheduled for subsequent visits. If the criterion is not met, they will not be eligible to continue taking part in the study.

Visits 2, 3 and 4 – Familiarisation (Duration: ~2 h each; Time of the day: Any time of the day)
The purpose of the familiarisation visits is to get participants acquainted with the type of exercise that will follow during the rest of the study. They will be asked to visit the laboratory on three occasions, each separated by at least 1 day, over the course of a week. During Visit 2 they will undertake 90 minutes of continuous moderate-intensity exercise on a stationary bicycle, whilst also being asked to consume a carbohydrate drink. During Visits 3 and 4 they will undertake 15 minutes of high-intensity (sprint) interval exercise followed by 75 minutes of continuous moderate-intensity exercise, again on a stationary bicycle. They will be able to drink water during exercise.

Visits 5, 7 and 18 – Pre-trial standardisation (Duration: ~1 h each; Time of the day: morning)
The purpose of the pre-trial standardisation visits is to ensure participants' physiological status is as consistent as possible before each subsequent main experimental trial. They will be asked to come in the morning at ~08:00 after an overnight fast. The researchers will measure their body weight, and then ask them to undertake the same fitness test that they completed at Visit 1. After this, they will ask them to refrain from any strenuous physical activity for the remainder of the day and the next day (i.e., leading up to the experimental trial). The researchers will also provide them with food packages for this period and ask them to only consume the food and drinks provided. All food will be prepared by the research team at the study site kitchen facility. All of the food will be pre-packed and labelled with clear instructions for storage and when they should consume each item.

Visits 6, 8 and 19 – Experimental Trials (Duration: ~3 h each; Time of the day: morning)
Participants will be asked to come in the morning at ~07:30-8:00 after an overnight fast. When they arrive they will be asked to go to the toilet and urinate (i.e., empty their entire bladder) into a container that the researchers will use to take an instantaneous measure of their hydration status. Next, while they are lying down on a plinth, a muscle biopsy sample (about the size of a small pea) will be collected from their thigh under local anaesthetic (please note: a total of 6 muscle biopsies will be performed [two biopsies during visits 6, 8 and 19]).
Once the muscle biopsy has been obtained, a number of procedures will be carried out to facilitate data collection during the subsequent exercise test. This includes 1) a cannula (tube) will be fitted into an arm vein on each arm, with one cannula used for blood sampling and the

other for stable isotope tracer infusion; 2) probes will be attached to the skin at four sites (chest, triceps, thigh, and calf) to allow continuous measurement of skin temperature; 3) alone, and in private, they will be asked to insert a medical-grade, flexible, sterile and disposable rectal thermistor to a depth of 10 cm to enable measurement of body core temperature; 4) they will be fitted with a chest-strap that will allow measurement of heart rate. They will then be asked to go to the toilet once more and urinate before being asked to measure, in private, their own nude body weight.
Next, a cannula will be fitted into one of the arm veins to allow blood sampling throughout the rest of the trial. Another cannula will be fitted to one of the veins in the other arm to enable the researchers to infuse a sterile, salt solution (saline) containing a trace amount of a stable isotope of glucose ('heavy' glucose) into the bloodstream during exercise. This allows the measurement of carbohydrate metabolism during exercise in detail. The infusion will commence and they will be asked to undertake 90 minutes of moderate-intensity exercise on a stationary bike. During the exercise they will be asked to consume a carbohydrate drink containing glucose and water at regular intervals. The drink will also contain a small amount of a stable isotope of glucose, and this will be used to measure how much of the drink is being used for energy whilst they exercise. The researchers will collect blood samples (10 ml or around 2 teaspoons each time) and expired breath samples at regular intervals during exercise, and they will be asked to rate how hard they feel the exercise is, how comfortable they find the temperature and if they are experiencing any stomach discomfort. Immediately after the exercise the researchers will obtain another muscle biopsy under local anaesthetic. The researchers will remove the cannulas from their arms and they will be asked to go to the toilet once more and urinate before being asked to measure, in private, their own nude body weight. Once they have recovered from the exercise and experimental procedures they will be free to leave the laboratory. Exercise will be undertaken in a purpose-built environmental chamber. For Visits 6 and 8, one of the exercise bouts will be performed under normal environmental temperature (i.e., 20°C, 20% Relative Humidity [RH]) and the other under hot conditions ((i.e., 40°C, 20% Relative Humidity [RH]). For Visit 19, which occurs after the heat acclimation period, the exercise will be undertaken under hot conditions ((i. e., 40°C, 20% Relative Humidity [RH]).

Visits 9-17 – Heat Acclimation (Duration: ~2 h each; Time of the day: Any time of the day)
The purpose of this period is to give a regular and repeated exposure to performing exercise in hot conditions in order to produce adaptations that improve their tolerance to exercise in the heat (i.e., heat acclimation). For these visits participants will attend the laboratory on 9 consecutive days or 9 days within a 10-day period, allowing for one 'rest' day (these consecutive days are including of weekends). They will be asked to perform exercise during each visit, and the exercise will take place undertaken under hot conditions ((i.e., 40°C, 20% Relative Humidity [RH]). The exercise will consist of a brief warm-up and then 15 minutes of high-intensity (sprint) interval exercise followed by 75 minutes of continuous moderate-intensity exercise, again on a stationary bicycle. They will be able to drink water during exercise. Before and after exercise they will be asked to go to the toilet and urinate before being asked to measure, in private, their own nude body weight. Before exercise the researchers will ask them to place a rectal thermistor for core temperature measurement as described above, and will be fitted with a chest-strap that will allow measurement of heart rate. During each exercise bout they will be asked to rate how hard they feel the exercise is, how comfortable they find the temperature and if they are experiencing any stomach discomfort. Once they have recovered from the exercise and experimental procedures they will be free to leave the laboratory.

What are the possible benefits and risks of participating?
Participants will get to know their physiology better. The most obvious risks will involve the muscle biopsy (tissue sample), lidocaine administration, exercise testing and heat stress, blood sampling and stable isotope infusion.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
April 2021 to June 2024

Who is funding the study?
US Army Medical Research and Development Command (USA)

Who is the main contact?
Dr Tim Podlogar
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Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
301502

Protocol serial number
RG_20-094, IRAS 301502

Study information

Scientific Title
Effects of acute heat stress and heat acclimation on exogenous carbohydrate oxidation during steady-state aerobic exercise

Acronym
HEAT-CARB

Study objectives
Heat acclimation will increase exogenous carbohydrate oxidation rates that have been reduced as a result of heat stress

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/11/2021, London - Fulham Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8109; fulham.rec@hra.nhs.uk), REC ref: 21/PR/1319

Study design
Non-randomized controlled study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Acute heat stress and heat acclimation

Interventions
The study consists of 19 visits spread over a 4-6 week period depending on the timing between visits. This includes four fitness test visits, three familiarisation exercise visits, nine heat acclimation visits and three experimental trial visits.

Visit 1 - Screening and baseline testing (Duration: ~1 h; Time of the day: Any time of the day) This visit will be used for consenting and screening and to determine their aerobic fitness. Upon arrival, the study will be fully explained to the participant he/she will then be asked to sign an Informed Consent Form if decided to take part. A general health questionnaire will need filling in and body height and body mass will be measured. If they successfully complete the questionnaire and meet the eligibility requirements participants will then have their aerobic fitness determined using a VO_2max test which will take place on a stationary bicycle. The test starts at a very easy work level and gets harder every 3 minutes and participants are asked to keep cycling for as long as they can (typically this takes between 10- 25 minutes). During the

test, participants will be wearing a facemask connected to a computerised gas analysis system that will allow the determination of how much oxygen they are using. If their test results meet the set criterion (i.e., men – 45 ml/kg/min; women - 40 ml/kg/min), they will be scheduled for subsequent visits. If the aerobic fitness criterion is not met, they will not be eligible to continue taking part in the study.

Visits 2, 3 and 4 – Familiarisation (Duration: ~2 h each; Time of the day: Any time of the day)
The purpose of the familiarisation visits is to get participants acquainted with the type of exercise that will follow during the rest of the study. They will be asked to visit the laboratory on three occasions, each separated by at least 1 day, over the course of a week. During Visit 2 they will undertake 90 minutes of continuous moderate-intensity exercise on a stationary bicycle, whilst also being asked to consume a carbohydrate drink. During Visits 3 and 4 they will undertake 15 minutes of high-intensity (sprint) interval exercise followed by 75 minutes of continuous moderate-intensity exercise, again on a stationary bicycle. They will be able to drink water during exercise.

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The purpose of the pre-trial standardisation visits is to ensure participants' physiological status is as consistent as possible before each subsequent main experimental trial. They will be asked to come in the morning at ~08:00 after an overnight fast. The researchers will measure their body weight, and then ask them to undertake the same aerobic fitness test that they completed at Visit 1. After this, they will ask them to refrain from any strenuous physical activity for the remainder of the day and the next day (i.e., leading up to the experimental trial). The researchers will also provide them with food packages for this period and ask them to only consume the food and drinks provided. All food will be prepared by the research team at the study site kitchen facility. All of the food will be pre-packed and labelled with clear instructions for storage and when they should consume each item.

Visits 6, 8 and 19 – Experimental Trials (Duration: ~3 h each; Time of the day: morning)
Participants will be asked to come in the morning at ~07:30-8:00 after an overnight fast. When they arrive they will be asked to go to the toilet and urinate (i.e., empty their entire bladder) into a container that the researchers will use to take an instantaneous measure of their hydration status. Next, while they are lying down on a plinth, a muscle biopsy sample (about the size of a small pea) will be collected from their thigh under local anaesthetic (please note: a total of 6 muscle biopsies will be performed [two biopsies during visits 6, 8 and 19]).
Once the muscle biopsy has been obtained, a number of procedures will be carried out to facilitate data collection during the subsequent exercise test. This includes 1) an indwelling intravenous cannula will be fitted into an arm vein on each arm, with one cannula used for blood sampling and the other for stable isotope tracer infusion; 2) skin thermistor probes will be attached to the skin at four sites (chest, triceps, thigh, and calf) to allow continuous measurement of skin temperature; 3) alone, and in private, they will be asked to insert a medical-grade, flexible, sterile and disposable rectal thermistor to a depth of 10 cm to enable measurement of body core temperature; 4) they will be fitted with a chest-strap that will allow measurement of heart rate. Once these procedures have been implemented, they will be asked to go to the toilet once more and urinate before being asked to measure, in private, their own nude body weight.

Next, a venous cannula will be fitted into one of the arm veins to allow blood sampling throughout the rest of the trial. Another cannula will be fitted to one of the veins in the other arm to enable the researchers to infuse a sterile, salt solution (saline) containing a trace amount of a stable isotope of glucose (‘heavy’ glucose) into the bloodstream during exercise. This allows the measurement of carbohydrate metabolism during exercise in detail. The infusion will

commence and they will be asked to undertake 90 minutes of moderate-intensity exercise on a stationary bike. During the exercise they will be asked to consume a carbohydrate drink containing glucose and water at regular intervals. The drink will also contain a small amount of a stable isotope of glucose, and this will be used to measure how much of the drink is being used for energy whilst they exercise. The researchers will collect blood samples (10 millilitres or around 2 teaspoons each time) and expired breath samples at regular intervals during exercise, and they will be asked to rate how hard they feel the exercise is, how comfortable they find the temperature and if they are experiencing any stomach discomfort. Immediately after the exercise the researchers will obtain another muscle biopsy under local anaesthetic. The researchers will remove the cannulas from their arms and they will be asked to go to the toilet once more and urinate before being asked to measure, in private, their own nude body weight. Once they have recovered from the exercise and experimental procedures they will be free to leave the laboratory. Exercise will be undertaken in a purpose-built environmental chamber. For Visits 6 and 8, one of the exercise bouts will be performed under normal environmental temperature (i.e., 20°C, 20% Relative Humidity [RH]) and the other under hot conditions ((i.e., 40° C, 20% Relative Humidity [RH]). For Visit 19, which occurs after the heat acclimation period, the exercise will be undertaken under hot conditions ((i.e., 40°C, 20% Relative Humidity [RH]).

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The purpose of this period is to give a regular and repeated exposure to performing exercise in hot conditions in order to produce adaptations that improve their tolerance to exercise in the heat (i.e., heat acclimation). For these visits participants will attend the laboratory on 9 consecutive days or 9 days within a 10 day period, allowing for one 'rest' day (these consecutive days are including of weekends). They will be asked to perform exercise during each visit, and the exercise will take place undertaken under hot conditions ((i.e., 40°C, 20% Relative Humidity [RH]). The exercise will consist of a brief warm-up and then 15 minutes of high-intensity (sprint) interval exercise followed by 75 minutes of continuous moderate-intensity exercise, again on a stationary bicycle. They will be able to drink water during exercise. Before and after exercise they will be asked to go to the toilet and urinate before being asked to measure, in private, their own nude body weight. As well, before exercise the researchers will ask them to place a rectal thermistor for core temperature measurement as described above, and will be fitted with a chest-strap that will allow measurement of heart rate. During each exercise bout they will be asked to rate how hard they feel the exercise is, how comfortable they find the temperature and if they are experiencing any stomach discomfort. Once they have recovered from the exercise and experimental procedures they will be free to leave the laboratory.

Intervention Type
Other

Primary outcome(s)
Exogenous carbohydrate oxidation from a carbohydrate drink consumed during exercise, measured using a stable isotope tracer every 15 minutes during exercise

Key secondary outcome(s))
1. Fluid absorption from a carbohydrate drink consumed during exercise, measured using the appearance of deuterated water in the bloodstream every 15 minutes during exercise after the 30-min timepoint
2. Self-rated gut comfort measured using visual analogue scales before and after exercise as well as every 15 min during exercise
3. Blood glucose regulation measured using analysis of plasma glucose concentrations every 15 min during exercise as well as before and after exercise

4. Muscle glycogen concentrations measured using biochemical analysis of glucose-6-phosphate after the breakdown of glycogen using hydrochloric acid just before and after exercise

Completion date
17/06/2024

Eligibility

Key inclusion criteria
1. Men or women
2. Aged 18 – 45 years
3. Compliance: understands and is willing, able and likely to comply with all study procedures and restrictions
4. Consent: demonstrates an understanding of the study and willingness to participate as evidenced by voluntary written informed consent
5. In good general health with no previous history of cardiometabolic disease
6. Body mass index in the range 18.5 – 27.5 kg/m²
7. Aerobically trained (i.e., participates in endurance-based exercise [e.g. cycling, running, rowing] at least three times per week)
8. Aerobic fitness: VO_2max >45 ml/kg/min (men), >40 ml/kg/min (women)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
All

Key exclusion criteria
1. Lidocaine allergy
2. Current participation in another scientific/clinical study
3. Pregnant or breastfeeding
4. Bleeding disorder/s
5. Current or recent smoker to include vaping (last 60 days)
6. Existence of food intolerances
7. Poor recent health as indicated in the general health questionnaire
8. Engage in uncommon eating practices (e.g. sustained periods of fasting)
9. Following a low dietary carbohydrate lifestyle

Date of first enrolment
01/02/2022

Date of final enrolment
17/06/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Birmingham
School of Sport, Exercise and Rehabilitation Sciences
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
U.S. Army Medical Research and Development Command

Alternative Name(s)
U.S. Army Medical Research & Development Command, United States Army Medical Research and Development Command, The U.S. Army Medical Research and Development Command, The United States Army Medical Research and Development Command, Army Medical Research and Development Command, Medical Research and Development Command, USAMRDC, MRDC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Gareth Wallis (g.a.wallis@bham.ac.uk) based on a reasonable request and in line with the ethics approval.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version 2.0	19/11/2021	20/01/2022	No	Yes
Participant information sheet	version 3	12/01/2022	16/03/2023	No	Yes