Influence of Graded Hypercapnia on Endurance Exercise Performance

NCT05116397

Informed Consent

Document Approval Date 10 Sep 2021

Document Version Date 27 Aug 2021

U.S. Army Research Institute of Environmental Medicine

CONSENT TO PARTICIPATE IN RESEARCH

Title of Protocol: Influence of graded hypercapnia on endurance exercise performance

Principal Investigator: Benjamin Ryan, Ph.D.

You are being asked to participate in a research study. As you think about your decision, you should consider all of the information in this informed consent form.

Introduction: You are being asked to participate in this research study because you are healthy and physically fit. You do not have to take part in this research. It is your choice.

The table below summarizes some **key** points to think about. After reading this summary, if you think you might be interested in participating, read the rest of the consent form for more details about the study.

RESEARCH SUMMARY	
Informed Consent	It is important that you understand this research study so that you can make an informed decision. This process is called informed consent. • Please ask questions about anything you do not understand. • Feel free to talk with your family, friends, or others before you decide. • After your questions have been answered, you will be asked if you want to participate. If you agree, you will sign this consent form. • You will be given a copy of this form to keep.
Voluntary Participation	You do not have to take part in this research. It is your choice. You can also choose to stop participating at any time during the study.
Purpose	To determine the effects of different levels of carbon dioxide in the air (0, 2, and 4% carbon dioxide (CO_2)) on endurance performance.
Duration	You will be in this study for 6 hours over the course of ~2-4 weeks.
Procedures	While you are in the study, you will complete **visits 1-3 for familiarization (FAM) and baseline testing** before completing **visits 4-6 for performance testing days**. • Treadmill tests while breathing either **0%, 2%, or 4% CO_2** combined with **normal** levels of oxygen **(21%)** • Collect small amount of blood **3** times each performance testing day (total of **9** finger sticks) • maximal fitness test • Lung function tests

Restrictions	During the course of the study, you will be asked to: • **No** strenuous exercise **36** hours before each study visit • **No** exercise **24** hours before each study visit • **No** alcohol **24** hours before each study visit • **No** caffeine, food or beverages (unless water) until after testing on familiarization and performance trial days (visits 2-6). • Have **8** hour sleep opportunity (e.g. lights out 2200; lights on 0600) each night before each familiarization or performance trial. • Eat the **same types** and **amounts** of food in the **2** days before each familiarization and performance trial.
Risks	The **main** risks from being in this study are: • Breathing air that contains higher amounts of carbon dioxide (CO_2) than normal (feeling out of breath, headache, nausea, lightheadedness, fatigue) • Strenuous exercise (cardiovascular risk, musculoskeletal strains) • Fingersticks (Minor discomfort and/or fainting) • Wearing the breathing mask while exercising (Claustrophobia)
Benefits	There is no direct benefit to you for participating in the study, except the information gathered from this research may benefit Soldiers in future subterranean (underground) operations.
Payment	You will be paid for your participation in this study.
COVID-19 risk mitigation	Study staff and volunteers will comply with all COVID-19 risk mitigation procedures in place at USARIEM during the time of data collection. As such, volunteers may be asked to wear face masks and use hand sanitizer during data collection activities (in accordance with prevailing recommendations at the time of data collection) and may be asked to wear gloves (i.e., nitrile gloves) during data collection activities. You also may be asked to undergo COVID-19 testing (via nose swab performed at USARIEM) within the 72 hours prior to each visit.

WHY IS THIS RESEARCH BEING DONE?

Hypercapnia (an increased amount of CO_2 in the air) has been identified as an important environmental stress that Warfighters may encounter while operating in a subterranean (underground) setting. Understanding the impact of extreme environmental factors, such as hypercapnia, on performance is important to inform mission planning. However, the impact of higher levels of CO_2 in the air on exercise performance is unknown. The purpose of this research is to determine the effect of different amounts of carbon dioxide (CO_2; 0%, 2% and 4%) on endurance performance.

WHAT WILL HAPPEN DURING THIS RESEARCH?

If you agree to participate in this research, you will be asked to do the following:
You will first need to be cleared by our Office of Medical Support and Oversight (OMSO) at United States Army Research Institute of Environmental Medicine (USARIEM) to make sure you are in good health. This will consist of ~1-2 days (~1 hour each) in which the medics and doctors will have you provide urine and blood samples, as well as complete a physical. If you are cleared to participate in this study, you will complete 6 visits of ~1 hour duration each at our lab over a period of ~2-4 weeks (**See Table 1**). All 6 visits will occur at least 36 hours apart and be done in USARIEM (Building 42).

Table 1. Overview of study visits

Study Visit	**1**	**2**	**3**	**4**	**5**	**6**
Lung Function Testing	X					
Maximal Fitness Test	X					
Familiarization Trials		X	X			
Performance Trials				X	X	X

Baseline Testing (Visit 1)
During the visit, we will have you complete a series of lung function tests where you'll take a maximal breath in and out through a mouthpiece while wearing a nose clip. You will then complete a maximal fitness test to measure how well your body uses oxygen to exercise. The maximal fitness test involves you selecting a comfortable running speed and then we will increase the treadmill grade by 2% every 2 minutes until you are too tired to continue. During the maximal fitness test, you will wear a mask covering your nose and mouth and we will measure the oxygen and carbon dioxide in the air you breathe out. We will also measure your heart rate. This visit will last a total of about 1 hour.

Diet and hydration prior to Visits 2-6
You will complete a diet log prior to visit 2 and asked to repeat a similar (same types and amount of food) diet 2 days before each of the remaining visits.

You will be provided 1 liter of water to drink the night before each Familiarization or Performance visit (in addition to your normal water drinking). We will also ask you arrive at the laboratory in the morning after a 10 hour overnight fast and to provide a urine sample the morning of testing to make sure you are hydrated. During the visits, you can drink as much water as you like, but will not be allowed any food until after the testing session is done.

Familiarization (FAM, Visits 2 & 3)
During the FAM visits, we will familiarize you with the exercise protocol we will be using in the performance testing days. We will have you will walk on the treadmill for ~10 minutes (at about 40% of your maximal effort) before completing a self-paced 2-mile run time trial on the treadmill.

During the time trial, you will be allowed to change the speed at any time, but you will not be allowed to see how fast you are going or how long you have been going. You will be notified when you have reached half-mile intervals (i.e. ½, 1, 1 ½, and 2 miles completed) but you will not receive any other feedback during the time trial.

During the FAM visits, we will be measuring body weight and your heart rate (via heart rate strap), oxygen usage, carbon dioxide production, and ventilation via a machine that collects the air you breathe through a facemask. We will ask you about how hard you feel you're working, how much does your head hurt, and how you describe your breathing. The FAM visits will last about 1 hour.

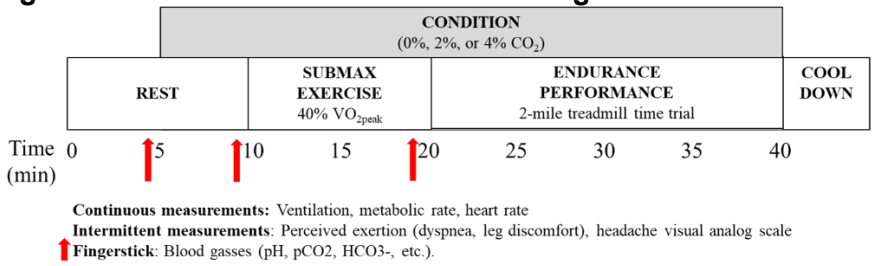
Performance Testing Days (Visits 4, 5, & 6)
If you are a female, a pregnancy test will be done for you using the same urine sample you provided for measuring hydration status. During the testing days, you will complete the same exercise protocol as above (walking on the treadmill for ~10 minutes before completing a self-paced 2-mile time trial on the treadmill).

While completing the exercise protocol, you will be breathing normal levels of oxygen (21%) combined with either 0%, 2%, or 4% CO_2. The testing gas is kept in large bags and will be given to you via a facemask/mouth piece that is connected to the bags by a tube. Throughout the test, there will be an additional tube that will carry your exhaled gases to a computer that will collect and analyze it for oxygen usage, carbon dioxide production, and ventilation. We will also be measuring your heart rate (via heart rate strap), and ask you about how hard you feel you're working, how much does your head hurt, and how you describe your breathing. See Figure 1 for a picture of the Performance Testing set-up.

Figure 1. Performance Testing Set-up

After you complete the 2-mile time trial, we will remove the mask suppling the gas mixture and allow you to cool down on the treadmill for 5 minutes while breathing room air. We will monitor you for additional 25 minutes while you recovering in the lab. See Figure 2 for an overview of the performance testing timeline.

Figure 2. Overview of Performance Testing Timeline



The percentage of CO_2 you will be given on each of the 3 performance testing days will be randomized (not occur in any particular order). You will not know which gas mixture percentage you are breathing on which performance trial, however the study staff will be aware of which gas mixture you are being given. You will be breathing the test gas for about 45 minutes.

There will be 3 finger sticks to collect a small (less than 1/10 teaspoon per finger stick) blood sample on each of the 3 performance testing days. One will be before you begin exercising while you are breathing room air, the second will be after you have been breathing the test gas at rest for ~5 minutes, and the third will be during walking on the treadmill. There will be a total of 9 finger sticks over the course of the study for a total amount of less than 1/3 teaspoon.

HOW LONG WILL I BE IN THE STUDY?

Testing will occur over the course of 2-4 weeks with 6 total visits of 1 hour duration per visit (total of ~6 hours of participation).

WHAT PRECAUTIONS DO I NEED TO TAKE?

- No strenuous exercise in the 36 hours before each study visit.
- No exercise of any kind in the 24 hours before each study visit.
- No alcohol in the 24 hours before each study visit.
- No caffeine, food or beverages (unless water) until after testing on familiarization and performance trial days.
- Give yourself an 8 hour sleep opportunity (e.g. lights out 2200; lights on 0600) each night before the familiarization and performance trials.
- Eat the same types and amounts of food in the 2 days before each familiarization and performance trial.

HOW MANY PEOPLE WILL BE IN THE STUDY?

Complete data will be collected on 12 healthy individuals.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Source of Risk	Risk(s)	How We Will Minimize
Breathing higher levels of CO_2	Headache Feeling out of breath (dyspnea) Nausea Lightheadedness Fatigue Fainting	• Study staff will be monitoring you throughout testing • You will be able to immediately stop breathing the gas mixture if your symptoms become intolerable • You will remain in the laboratory for at least 30 minutes after breathing the gas mixture to be monitored by study staff

Treadmill Exercise	Cardiovascular risk Musculoskeletal strains Lightheadedness Fatigue Claustrophobia	• CPR-certified study staff will be monitoring you throughout testing • Exercise testing will be separated by at least 36 hours to allow for recovery • Medical staff is available to treat you in the event of an injury
Heart rate monitoring	Skin irritation/chaffing	• Study staff will monitor your skin for irritation • Medical staff is available to treat you in the event of skin irritation
Finger sticks	Pain Dizziness Fainting Infection Bruising Tenderness Swelling Skin irritation Nausea Vomiting	• Finger sticks will be preformed using sterile techniques • Study staff will monitor you throughout the finger stick

WHAT ARE THE POSSIBLE BENEFITS FROM BEING IN THIS RESEARCH?

There are no direct benefits from you participating in this research study. However, information gathered from this research may benefit Soldiers in future subterranean operations.

WHAT IF UNEXPECTED INFORMATION IS LEARNED ABOUT MY HEALTH?

If any unexpected health information is found during screening process or your participation, the information will be documented and a copy provided to you, the Principal Investigator (PI) will direct you to OMSO (for military individuals) or your primary care physician (PCP; for civilian individuals). No diagnoses will be made by study staff; therefore, no findings will be reported to PCP or authorities.

WILL RESEARCH RESULTS BE SHARED WITH ME?

Yes, we will be able to share the result of your maximal fitness test and lung function test upon request. No other information will be shared.

WHAT ARE MY OTHER OPTIONS IF I DO NOT PARTICIPATE IN THIS STUDY?

The only alternative is to not participate in the study.

WILL I HAVE TO PAY FOR ANYTHING IF I TAKE PART IN THIS RESEARCH?

There are no anticipated costs for this study. We will not reimburse you for expenses paid (travel, etc.) related to participation in the study.

WILL I BE PAID TO TAKE PART IN THIS RESEARCH?

No compensation will be offered for the blood draw performed by OMSO as part of the medical clearance. You will receive $25 for each successful finger stick blood collection. There are a total of 9 finger stick blood collections during the entire study, so you will receive $225 if you complete the entire study. You will be paid for every finger stick blood sample you complete regardless of if you withdraw or are withdrawn from the study. If you choose to withdraw prior to the completion of the study, compensation will be pro-rated. It may take up to 6 weeks to receive payment for study participation. All payments will be sent in the form of direct deposit to a bank account.

Your Social Security Number (SSN) will be needed to process your payment, as required by law. This information will be carefully protected. The Defense Finance and Accounting Service will report total payments of $600 or more within 12 months to the Internal Revenue Service (IRS). This may require you to claim the compensation that you receive for participating in this study as taxable income.

WHAT HAPPENS IF I AM INJURED AS A RESULT OF TAKING PART IN THIS RESEARCH?

If at any time you believe you have suffered an injury or illness as a result of participating in this research, please contact the Principal Investigator (PI) of the study (Benjamin Ryan, benjamin.j.ryan14.civ@mail.mil; 508-206-2408).

If you are injured because of your participation in this research and you are a DoD healthcare beneficiary (e.g., active duty military, dependent of active duty military, retiree), you are entitled to medical care for your injury within the DoD healthcare system, as long as you remain a DoD healthcare beneficiary.

If you are injured because of your participation in this research and you are not a DoD healthcare beneficiary, you are entitled to care for your injury at DoD hospitals or clinics, but care for your injury may be limited to a given time period, and your insurance may be billed. It cannot be determined in advance which DoD hospital or clinic will provide care. If you obtain care for research-related injuries outside of a DoD hospital or clinic, you or your insurance will be responsible for medical expenses.

For DoD healthcare beneficiaries and non-DoD healthcare beneficiaries: Transportation to and from hospitals or clinics will not be provided. No reimbursement is available if you incur medical expenses to treat research-related injuries. No compensation is available for research-related injuries. You are not waiving any legal rights. If you believe you have sustained a research-related injury, please contact the PI. If you have any questions, please contact the PI (Benjamin Ryan, benjamin.j.ryan14.civ@mail.mil; 508-206-2408).

HOW WILL YOU PROTECT MY PRIVACY AND THE CONFIDENTIALITY OF RECORDS ABOUT ME?

The principal investigator will keep records of your participation in the research. To protect your privacy, all of your research-related records including data sheets will be labeled or “coded” with

an assigned research participant number that will not include any identifiable information such as your name or social security number. Dr. Ryan will keep the link between your participant number and your name in a locked cabinet or password-protected computer on a restricted-access folder on our shared drive. The principal investigator and study coordinator are the only people who will be able to match your research participant number with any of your personal identifying information. The key code will be destroyed upon study closure.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity to others. Specific permission to use photographs or video recordings of you and the manner in which they may be used will be requested and documented in an Audio/Visual Image Release form. If you do not sign the photo release form, no photos of you will be taken. If any photographs or video recordings are taken of you inadvertently, they will be destroyed immediately. You do not have to sign a photo release to participate in this study.

Authorized representatives of the following groups may need to review your research and/or medical records as part of their responsibilities to protect research participants:

- US Army Medical Research & Development Command Institutional Review Board responsible for review and oversight of human research
- DoD and other Federal offices charged with regulatory oversight of human research
- US Army Research Institute of Environmental Medicine's Office of Research Quality and Compliance

Once information that personally identifies you is removed from your data, then your de-identified data may be used for future research studies or given to other researchers for future research studies without additional permission from you to do so. No biological samples will be saved for future use.

Complete confidentiality cannot be promised for military personnel, because information bearing on your health may be required to be reported to appropriate medical or command authorities.

WHAT IF I DECIDE NOT TO PARTICIPATE IN THIS RESEARCH?

It is your choice whether you want to participate in this research. You can choose not to be in the study now without any penalty or loss of benefits to which you are entitled.

If you decide to participate, you can stop taking part in this research at any time without any penalty or loss of benefits to which you are entitled. Deciding not to participate now or withdrawing at a later time does not harm, or in any way affect future relationships with USARIEM.

You may withdraw by verbally, emailing, or telephoning to the study PI (Benjamin Ryan, benjamin.j.ryan14.civ@mail.mil; 508-206-2408)

If you do decide to withdraw, your compensation will be pro-rated based on the number of hours/blood samples collected you completed. Data collected prior to your withdrawal will be used for analysis.

WHAT COULD END MY PARTICIPATION IN THE RESEARCH?

The Principal Investigator may withdraw you from participating in this research if circumstances arise which warrant doing so such as if you are unwilling or unable to complete the study procedures or requirements. The Principal Investigator will make the decision and let you know if it is not possible for you to continue. Your taking part in the study may be stopped without your consent if it is determined by the Principal Investigator that remaining in the study might be dangerous or harmful to you.

WHAT IF ANY NEW INFORMATION IS FOUND OUT?

During the course of the research, the investigators will tell you of any new findings that might cause you to change your mind about continuing in the study. If new information is provided to you, the investigators will obtain your consent to continue participating in this study.

WHO SHOULD I CALL IF I HAVE QUESTIONS OR CONCERNS ABOUT THIS RESEARCH?

If you have questions about the research at any time, you should contact the PI (Benjamin Ryan, benjamin.j.ryan14.civ@mail.mil; 508-206-2408).

If you have questions regarding your rights as a research participant, you may contact the HQ USAMRDC IRB Office at 301-619-6240 or by email to usarmy.detrick.medcom-usamrmc.other.irb-office@mail.mil. Alternatively, you can also contact the USARIEM Office of Research Quality and Compliance at 508-206-2371 or by email to usarmy.natick.medcom-usariem.mbx.usariem-rqc-protocol@mail.mil.

By signing below, I agree that I have been provided time to read the information describing the research study in this consent form. The content and meaning of this information has been explained to me. I have been provided with the opportunity to ask questions. I voluntarily consent to participate in this study.

By signing this form, I have not given up any of my legal rights as a research participant.

SIGNATURE OF RESEARCH PARTICIPANT

Printed Name of Participant

Signature of Participant | Date

CONSENT DISCUSSION CONDUCTED BY:

Printed Name	Date Received