EFFECT OF 2-WEEK NIGHTLY MODERATE HYPOXIA ON GLUCOSE TOLERANCE IN INDIVIDUALS WITH TYPE 2 DIABETES (SLEEPDIABETES)

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CONSENT TO PARTICIPATE IN A RESEARCH STUDY FOR AN ADULT
INFORMED CONSENT - PART I

***Title of Study:* EFFECT OF 2-WEEK NIGHTLY MODERATE HYPOXIA ON GLUCOSE TOLERANCE IN INDIVIDUALS WITH TYPE 2 DIABETES (SLEEPDIABETES)**

What you should know about a research study

- We give you this consent form so that you may read about the purpose, risks and benefits of this research study.
- The main goal of research studies is to gain knowledge that may help people in the future.
- You have the right to refuse to take part, or agree to take part now and change your mind later on.
- Please review this consent form carefully and ask any questions before you make a decision.
- Your participation is voluntary.
- By signing this consent form, you agree to participate in the study as it is described.

1- Who is doing the study?

Principal Investigator: Eric Ravussin, PhD
225-763-3186

Medical Investigator: Frank Greenway, M.D.
Day Phone: 225-763-2576
24-hr. Emergency Phone Nos.:
225-763-2576 (Weekdays 7:00 a.m.-4:30 p.m.)
225-765-4644 (After 4:30 p.m. and Weekends)

Dr. Ravussin directs this study, which is under the medical supervision of Dr. Frank Greenway. We expect to enroll 10 people to participate and complete this study. Your expected time in this study will be approximately two weeks, which includes overnight stays under simulated altitude (~7500 ft) in a tent.

2- Where is the study being conducted?

This study takes place in the Outpatient Unit at the Pennington Biomedical Research Center, at the Louisiana Sleep Foundation, and at your home.

3- What is the purpose of this study?

The purpose of SLEEPDIABETES is to look at how a reduction in oxygen levels influences sugar metabolism. Reduced oxygen level is experienced at moderate to high altitude. It is expected that with 14 nights spent at a moderate altitude of ~7500 feet (like experienced in most ski resorts, as in Aspen, Colorado), sugar metabolism will be improved.

4- Who is eligible to participate in the study? Who is ineligible?

You may qualify for the study if:

- You are aged between 20 and 65 years
- Your BMI (a number calculated from your height and weight) is less than 55 kg/m^2
- You weigh 450 lbs or less
- You have type 2 diabetes and have been diagnosed < 15 years ago
- Your body weight has not changed more than 7 pounds over the last 3 months.
- You do not smoke.
- You have *either* been diagnosed with type 2 diabetes, or have a fasting blood sugar between 125 and 200 mg/dl, or a hemoglobin A1-C ≥ 6.5%.
- You provide written informed consent to participate in the study.
- You are willing to spend 14 nights (7-12 hours per night) in a tent at simulated altitude (~7500 feet over sea-level) that will be set-up and located in your home.
- You have sleep apnea and are treated with a continuous positive airway pressure (C-PAP) device, and agree to wear C-PAP device throughout nights spent in the tent
- You are willing to spend one night at a sleep laboratory (Louisiana Sleep Foundation) if you have no known diagnosis of sleep apnea
- You agree that a partner or any household member cannot sleep in the tent with you.
- You are willing to provide blood samples throughout the duration of the study.

You will not qualify for the study if:

- You have sleep apnea or have a positive screening following a home sleep test and do not have a C-PAP device to wear throughout nights spent in the tent.
- You have no known diagnosis of sleep apnea, but you have unsafe levels of oxygen in your blood following a one night sleep monitoring assessment performed at the Louisiana Sleep Foundation.
- You have a history of altitude sickness.
- You take insulin treatments.
- You are pregnant.
- You do not have access to a bed or sleeping surface equivalent to or smaller than a Queen size mattress.
- You take sulfonylureas or glitinides treatments.
- You take a GLP-1 agnosit.
- You take a non-oral diabetes medication unless approved by the medical investigator.
- You have Chronic Obstructive Pulmonary Disease (COPD).
- You have congestive heart failure.
- You have experienced prior severe cardiovascular events, such as stroke or myocardial infarction.
- If treated for type 2 diabetes with other oral agent(s), you will be excluded if have changed your treatment regimen <1 month prior to the study and the duration of the study.
- You suffer from high altitude sickness

If you are accepted into the study you must agree to the following:

- **Not to take new prescription or over-the-counter medications until you discuss the medication(s) with the study physician.**
- **Not to start an exercise, diet, or weight loss program.**

5- What will happen to you if you take part in the study?

You will first report to the clinic of the Pennington Biomedical Research Center for a screening visit, during which eligibility to participate in this study will be determined, including physical measures and a blood draw. If you have been previously diagnosed with sleep apnea and own a continuous positive airway pressure (C-PAP) device that you agree to wear throughout the nights spent in the tent, then you will next complete Phase 1 (Baseline testing) of the study. If you have no previous diagnosis of sleep apnea, you will next undergo a 2-step sleep screening process which will include a one night home sleep test as well as a monitored sleep study at a certified sleep laboratory. If you are cleared to participate in this study by the certified sleep laboratory, you will next complete Phase 1 (Baseline testing) of this study. This study will take approximately another 14 days to complete and will have 3 phases:

Phase 1: Baseline testing. This phase takes place at the beginning of the study to establish several physical and physiological studies. Measures of your body sugar metabolism (oral glucose tolerance test) will be performed. Your body composition by DXA scan will also be assessed.

Phase 2: Intervention. This phase is initiated three to four days after phase 1 and will last 14 days. You will have to spend the night in a tent under which the air will simulate an altitude of ~7500 feet over sea-level. Following the seventh night in the hypoxic tent, you will come to Pennington Biomedical to provide a blood sample.

Phase 3: Post-intervention testing. This phase will be initiated immediately after your fourteenth night spent at simulated altitude. Measures of your body sugar metabolism (oral glucose tolerance test) will be performed.

Screening visit (at Pennington Biomedical Research Center): about 60 minutes (fasting, nothing to eat or drink except water for 10 hours)

If you agree to participate, the following procedures will be done:

- A medical history including questions about medications, health status and symptoms.
- Height, weight, waist circumference, hip circumference, blood pressure, temperature (oral), and a questionnaire regarding your general health status.

If these measurements meet study requirements, the following procedures will be done:

- Blood draw (about 1 ½ teaspoons)
- Electrocardiogram (EKG)
- Urine sample for urinalysis.

If you have a known diagnosis of sleep apnea, own a C-PAP, and agree to wear this C-PAP throughout the nights spent in the tent, you will automatically proceed to Phase 1 (Baseline testing visit) following your Screening Visit.

If you have no known presence of sleep apnea, you will next be evaluated by a certified sleep laboratory (Louisiana Sleep Foundation) to determine whether or not you have sleep apnea. You will undergo a 2-step sleep screening process to confirm the presence or absence of sleep apnea:

Sleep Screening (at home, as well as at the Louisiana Sleep Foundation):
If you have no known presence of sleep apnea, you will next undergo a 2-step sleep screening process at the Louisiana Sleep Foundation to: (1) confirm that you do not have sleep apnea using a Home Sleep Test, and (2) confirm that you have safe blood oxygen levels while sleeping under the hypoxic tent at the Louisiana Sleep Foundation. First, you will travel to the Louisiana Sleep Foundation the day of your Home Sleep Test and be given instructions on how to use and conduct the Home Sleep Test on your own while sleeping at home for one single night. The Home Sleep Test is a device consisting of a belt that will be fastened across your chest and placed directly under your armpits, with both an external nasal tube that will be fixed to your nostrils and a finger probe sheath taped to the outside of your index finger. You will sleep with this device for a single night and return the device to the Louisiana Sleep Foundation the next morning. Your sleep data will then be reviewed and interpreted by a certified sleep specialist to determine whether or not you have sleep apnea. If you do not have sleep apnea following the Home Sleep Test, you will then be asked to spend one night at the Louisiana Sleep Foundation where a certified sleep specialist will monitor your blood oxygen levels and ensure that you are safe to participate in the study. If the certified sleep specialist confirms you are safe to participate in this study, your participation in the study will start within a few weeks depending on scheduling availability. If you do have sleep apnea and do not own a C-PAP, you will not be eligible to participate in this study.

The next table summarizes the different procedures and activities during your participation in this study for the baseline (Phase 1), intervention (Phase 2) and post-intervention (Phase 3) periods.

Table 1. Schedule of Procedures

	Pennington Screening	Louisiana Sleep Foundation Sleep Screening (2-Step Process)	Baseline (Day 0)	Mid-Intervention (Day 7)	Post-Intervention (Day 14)
Health questionnaire	X				
Body weight	X		X	X	X
Vital signs*	X				
Electrocardiogram	X				
Blood draw	X		X	X	X
Oral glucose tolerance test			X		X
Body composition by DXA			X		
Urinalysis	X				
Urine Pregnancy Test			X		
Oxyhemoglobin saturation**		X			

* Blood pressure, pulse, oral temperature

** Only performed if you do not have a previous diagnosis of sleep apnea. Time between screening and 2-step sleep screening, as well as 2-step sleep screening and baseline testing (Day 0), will vary depending on scheduling at Pennington Biomedical and the Louisiana Sleep

Foundation. 2-step sleep screening will include a Home Sleep Test, and an overnight sleep monitoring at the Louisiana Sleep Foundation.

Baseline visit (approximately 3.5 hours): (fasting, nothing to eat or drink except water for 10 hours)

- An oral glucose tolerance test (a procedure to measure your body's response to sugar) will be performed with blood draws.
- Females who are considered to be child-bearing potential will have a urine pregnancy test performed.
- Your body composition by DXA scan will be assessed.

Intervention (7-12 hours per night, 14 consecutive nights)

- Three to five days following the baseline testing phase, you will spend 14 consecutive nights in simulated altitude.
- Every night you will spend 7-12 hours in a tent, in which the content of the room air will be modified, simulating an altitude of ~7500 feet over sea-level, or as it would be in Mexico City or in some ski resorts. This is achieved by removing a small fraction of the oxygen and replacing it by nitrogen, a gas that already constitutes almost 80% of the room air. Nitrogen is an inert gas, e.g. it is not absorbed or exchanged in the lungs.
- Your partner or any household member should not, in any circumstance, sleep in the tent with you. Additionally, no individuals other than you should enter or sleep in the tent.
- You will be asked to record certain items from the machine (tent) and your sleep times along with any time spent outside of the tent each night. A form and further instructions will be provided to you by the study staff.

Mid-intervention visit (Approximately 30 minutes): (fasting, nothing to eat or drink except water for 10 hours)

- After the 7th night in the hypoxic tent, a blood sample will be drawn. After the 7th night of hypoxic sleep, you will come to the Pennington Biomedical clinic to provide a blood sample (~ 2 ½ teaspoons) and to measure your weight. We will also collect information of the quality of your sleep under the hypoxic tent.

Post-intervention visit (approximately 3 hours): (fasting, nothing to eat or drink except water for 10 hours)

- After obtaining your body weight, an oral glucose tolerance test (a procedure to measure your body's response to sugar) will be performed with blood draws.

Description of Study Procedures

Body Composition by DXA: (Time: 10 minutes)

This scan measures the amount of bone, muscle, and fat in your body. The scan will be performed using a whole-body scanner. You will be required to wear a hospital gown, to remove all metal-containing objects from your body, and to lie down on the table. You will be carefully positioned on the table, and your legs will be placed together using two Velcro straps. A scanner emitting low energy X-rays and a detector will pass along

your body. You will be asked to remain completely still while the scan is in progress. The scan takes approximately ten minutes.

Oral Glucose Tolerance Test (OGTT; fasting, nothing to eat or drink except water for 10 hours)
You will lie in bed and rest before the beginning of the OGTT. An IV line will be placed in your arm vein for blood draw purposes and will remain there throughout the testing. One blood sample will be drawn at 7:00 to measure blood glucose and insulin. Study archives will also be drawn at this time. You will then be required to drink a solution containing 75 grams of glucose (sugar). Blood samples will be drawn at 30, 60, 90, and 120 minutes after you drink the sugar solution to assess your glucose metabolism. (The total amount for the blood draws equals to about 8 ½ teaspoons at both Baseline and Post-Intervention visits).

Tent description
Pennington staff will visit your home and setup the hypoxic tent system. They will also instruct you on how to use the equipment. You will sleep with the hypoxic tent installed over your usual bed (must be a Queen size mattress or smaller). The device will be picked up at your home (or dropped off at our center).
Every evening and night will be spent lying in your bed placed in a plastic tent in which the air will simulate the air breathed at an altitude of ~7500 feet over sea-level. This represents approximately the air breathed in Mexico City, or in ski resorts such as in Aspen, Colorado. The tent, made out of clear plastic, is air tight and surrounds the bed. Its dimensions are 82" x 62" x 63". At any time, it is possible to exit the tent. During these stays, you will be allowed to watch TV/DVDs and perform sedentary activities such as reading, listening to music, and surfing the internet.

Blood Draw: You will have about 25 teaspoons (about half of a cup) of blood drawn from veins in your arm over the entire study. This will be done by trained staff using aseptic (sterile) technique.

6- What are the possible risks and discomforts?

The risk and discomforts associated with this study are listed below.

Procedure	Risk
EKG	There are minimal risks associated with this test. There is a small possibility there may be some redness or irritation if you happen to be allergic to the adhesive on the electrodes.
Blood Draws	There is the possibility of pain and bruising at the vein on your arm where the needle is inserted. Aseptic (sterile) technique and trained personnel minimize these risks.
Body composition by DXA	The amount of radiation used for this procedure is very small. The radiation dose for this scan is equivalent to the radiation you are naturally exposed to in the environment in less than one day. **Scans will not be performed on any subject who is pregnant, and all females should inform the DXA**

	technologist if there is any possibility that they are pregnant.
Sleeping under hypoxia (simulated altitude ~ 2400m)	You may feel a slight discomfort and feeling of claustrophobia while sleeping in an airtight tent. You will be free to exit the tent if they feel claustrophobic. There should not be any risk associated to sleeping at altitudes <2500m since: (1) you will be excluded from the study if you have diagnosed sleep apnea following your testing at the Louisiana Sleep Foundation and do not own a C-PAP that you are willing to wear during your nights spent in the tent, and (2) if you do have a previous diagnosis of sleep apnea, you will be required to wear a C-PAP during your nights spent in the tent. Furthermore, you will sleep in your usual bedroom. Recent reviews suggest an acclimatization process for higher altitudes, however you may experience acute altitude sickness nonetheless, with symptoms as headache, anorexia, and nausea, which might however be transient. High altitude pulmonary edema is very unlikely at such altitude, being known to occur at much higher altitudes and with exercise. However, Pennington staff will monitor for altitude sickness by asking you about symptoms (which usually happen in the first 12-24 hours) such as headache, nausea, vomiting, dizziness, insomnia, loss of appetite and dyspnea. Adverse events will be monitored throughout the study.
Confidentiality	Taking part in this research may involve providing information that you consider confidential or private. Efforts such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe. Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally.

In addition to the risks listed above, you may experience a previously unknown risk or side effect.

7- What are the possible benefits?

Possible benefits include receiving information about the results of your blood tests, results of the physical exam, and information about your metabolism.

8- If you do not want to take part in the study, are there other choices?

You have the choice at any time not to participate in this research study. If you choose not to participate, any health benefits to which you are entitled will not be affected in any way.

9- If you have any questions or problems, whom can you call?

If you have any questions about your rights as a research volunteer, you should call the Institutional Review Board Office at 225/763-2693 or the Executive Director of PBRC at 225/763-2513. If you have any questions about the research study, contact Dr. Eric Ravussin (PI) at 225-763-3186. If you think you have a research-related injury or medical illness, you should call Dr. Frank Greenway at 225-763-2576 during regular working hours. After working hours and on weekends you should call the answering service at 225-765-4644. The on-call physician will respond to your call.

10- What information will be kept private?

Every effort will be made to maintain the confidentiality of your study records. However, someone from the Food and Drug Administration or the Pennington Biomedical Research Center may inspect and/or copy the medical records related to the study. Results of the study may be published; however, we will keep your name and other identifying information private. Other than as set forth above, your identity will remain confidential unless disclosure is required by law.

11- Can your taking part in the study end early?

You will be withdrawn from the study if you experience acute altitude sickness and if we suspect any sleep apnea episode from your blood oxygen. Drs. Ravussin and Greenway can withdraw you from the study for any reason or for no reason. You may withdraw from the study at any time without penalty; however, all data Pennington Biomedical has previously collected cannot be removed from the study. Possible reasons for withdrawal include inability or unwillingness to complete the required testing and medical reasons making continuation not in your best interest.

12- What if information becomes available that might affect your decision to stay in the study?

During the course of this study there may be new findings from this or other research which may affect your willingness to continue participation. Information concerning any such new findings will be provided to you.

13- What charges will you have to pay?

None

14- What payment will you receive?

If you agree to take part, Pennington will pay you $350 at the completion of the study if you complete all screening, baseline, and intervention procedures over the 14 days. Conversely, you will receive $175 if you complete the mid-intervention visit (Day 7) but do not complete the post-intervention visit (Day 14). And finally, you will receive $50 if you enroll in the study, but do not complete the mid-intervention visit (Day 7). Your check will be requested from the LSU payroll department when you complete the study or at the appropriate milestone. Compensation will be mailed to you within 4 weeks of study completion.

15- Will you be compensated for a study-related injury or medical illness?

No form of compensation for medical treatment or for other damages (i.e., lost wages, time lost from work, etc.) is available from the Pennington Biomedical Research Center. In the event of injury or medical illness resulting from the research procedures in which you participate, you will be referred to a treatment facility. Medical treatment may be provided at your expense or at the expense of your health care insurer (e.g., Medicare, Medicaid, Blue Cross-Blue Shield, Dental Insurer, etc.) which may or may not provide coverage. The Pennington Biomedical Research Center is a research facility and provides medical treatment only as part of research protocols. Should you require ongoing medical treatments, they must be provided by community physicians and hospitals.

16- Specimen Storage for Future Research or Use

Biospecimens for future research:

You are being asked to allow some of your blood to be stored and used for research at a later time. These bodily materials are called biospecimens. The donation of biospecimens in this study is optional. No matter what you decide to do, it will not affect your study participation. You will still be allowed to take part in the study even if you don't want your specimens to be collected and used for future research. Some biospecimen samples will be stored and used for the study and other biospecimen samples will be stored for future studies. The collection of samples may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent diseases. If you agree to have your samples stored, you can change your mind later.

The samples will be stored indefinitely. If you agree to donate your samples, they may be given to other investigators for future research as well. The future research may take place at Pennington Biomedical and may involve Pennington Biomedical Researchers in this study. The future research may not take place at Pennington Biomedical Research Center and may not be reviewed by Pennington Biomedical Research Center's Institutional Review Board. For privacy and confidentiality, your biospecimens will be labeled with a unique series of letters and numbers. Pennington Biomedical will store your biospecimens with this unique identifier and the minimum number of personal identifiers to meet laboratory standards. The research done with your specimens may help to develop new products in the future, or may be used to establish a cell line or test that could be patented or licensed. You will not receive any financial compensation for any patents, inventions or licenses developed from this research.

Making your choice about future research:

Please read about each biospecimen below. It is your choice which samples will be collected, stored and used for future research for this study or future studies. After reading about each below, sign next to "Yes" or "No" to show your choice about the collections for this research study and for future research studies.

Blood

If you give permission, approximately 6 teaspoons of blood will be collected and stored by this study. Your stored samples may be tested at Pennington Biomedical Research Center or other locations used in future research. Do you give permission for your blood to be collected and used in future research by this study?

Yes, I give permission _____ _____
Signature Date

No, I do not give permission _____ _____
Signature Date

If you decide you would like to withdraw your consent to use your samples, you must provide a written request to have your samples destroyed. In the event you withdraw your consent, it will not be possible to destroy samples that have already been given to researchers.

For destruction of your samples, you can contact the Principal Investigator at:

Eric Ravussin, Ph.D.
Pennington Biomedical Research Center
6400 Perkins Road
Baton Rouge, LA 70808

17- Signatures

The study has been discussed with me and all my questions have been answered. I understand that additional questions regarding the study should be directed to the study investigators. I agree with the terms above and acknowledge that I will be given a copy of this signed consent form.

With my signature, I also acknowledge that I have been given either today or in the past a copy of the Notice of Privacy Practices for Protected Health Information.

_____
Printed Name of Volunteer

_____ _____
Signature of Volunteer Date

_____
Printed Name of Person Administering Informed Consent

_____ _____
Signature of Person Administering Informed Consent Date

Eric Ravussin
Principal Investigator

Frank Greenway
Medical Investigator