ALBERT EINSTEIN COLLEGE OF MEDICINE
MONTEFIORE MEDICAL CENTER

DOCUMENTATION OF INFORMED CONSENT AND HIPAA AUTHORIZATION

Introduction

You are being asked to participate in a research study **Use of Functional MRI to Assess Functional Hypothalamic Activation in Response to Diazoxide.** Your participation is voluntary -- it is up to you whether you would like to participate. It is fine to say "no" now or at any time after you have started the study. If you say "no," your decision will not affect any of your rights or benefits or your access to care.

The researcher in charge of this project is called the "Principal Investigator." Her name is Dr. Meredith Hawkins. You can reach Dr. Hawkins at:
Office Address: 1300 Morris Park Avenue
Bronx, NY 10461
Telephone #: 718-430-3186
For questions about the research study, or if you believe you have an injury, contact the Principal Investigator or the IRB.

The Institutional Review Board (IRB) of the Albert Einstein College of Medicine and Montefiore Medical Center has approved this research study. The IRB # is in the stamp in the upper right hand corner. If you have questions regarding your rights as a research subject you may contact the IRB office at 718-430-2253, by e-mail at irb@einstein.yu.edu, or by mail:

Einstein IRB
Albert Einstein College of Medicine
1300 Morris Park Ave., Belfer Bldg #1002
Bronx, New York 10461

Support for this research study is provided by the National Institute of Health (NIH).

Why is this study being done?

The goal of this study is to understand how activating control centers of the brain can affect how much glucose (sugar) is produced by the liver. This is particularly important for people with diabetes who have very high production of glucose, since this could be at least in part due to impaired regulation of the liver by the brain.

This study will use functional MRI, a way of imaging the blood flow to parts of the brain, to observe how activating areas of the brain is linked to regulation of blood sugar.

Why am I being asked to participate?

You are being asked to participate in this study because you are a healthy volunteer.

How many people will take part in the research study?

You will be one of about **15** people who will be participating in this study.

How long will I take part in this research?

It will take you between 2 weeks and 2 months to complete this research study. During this time, we will ask you to make 2 study visits to Albert Einstein College of Medicine.

What will happen if I participate in the study?

The Screening Visit will take about 1.5 hours. During this visit, we will do some tests and procedures to see if you eligible to take part in this research study. The study doctor will review the results of these tests and procedures. If you aren't eligible, the study doctor will tell you why. At this visit we will:

- Ask you about your medical history
- Give you a physical exam, including height, weight, and "vital signs" (blood pressure, temperature, heart and breathing rates)
- Draw a blood sample
- Take an EKG
- Ask you for a urine sample
- Test your urine for certain drugs
- Test your urine for pregnancy, if you are a female able to become pregnant. Pregnant women cannot take part in this research study.

To obtain the blood sample, we will wipe the skin on your arm with alcohol to clean it. Then, we will insert a small needle into a vein. 4-5 tubes of blood will be drawn, which is about 7 teaspoons. If you are eligible for the study, you will be asked to maintain a consistent diet for 3 days prior to the study.

If you are not eligible, you will be informed by phone or in writing and records of the evaluation will be forwarded to you, if you'd like them.

If you are eligible for the study, we will assign you by chance (like a coin toss) to first receive either diazoxide or placebo. You and the study doctor cannot choose your study order. You will have an equal chance of being assigned to diazoxide or placebo on your first study visit.

Diazoxide is an FDA approved medication used to treat hyperinsulinism (a condition where your pancreas secretes too much insulin, causing low blood sugar). Please note that the amount of diazoxide given in this study will be lower than the daily doses typically used in a clinical setting.

This research study will compare diazoxide to placebo. The placebo looks exactly like diazoxide, but contains no drugs. During this study you may get a placebo instead of diazoxide. Placebos are used in research studies to see if the results are due to the study drug or due to other reasons.

Study Visit 1:

- You will come to the GCRC Study Room at Jack D. Weiler hospital on the morning of the study at around 8:00AM. You will be asked to not exercise the day before the study or eat after 10 PM the night before the study (but you can drink water). An MRI safe intravenous catheter will be inserted into your arm. Blood samples will be collected every hour for up to 8 hours for measurements of your blood sugar and other hormones.

- You will then be escorted to the Gruss Magnetic Resonance Research Center of the Albert Einstein College of Medicine.
- At approximately 9AM on the morning of the study, you will be asked to lie in the MRI scanner for approximately 30 minutes. During this time, the MRI pictures will be taken.
- You will then be given diazoxide orally at a dose of 4mg/kg-7mg/kg once **or** placebo.
- You will then return to the MRI scanner at approximately 2 hour intervals for approximately 30 minutes each interval. You will rest in a separate room in between MRI measurements. There will be up to 3 MRI measurements during one day. The number of scans you will receive will depend on the results of the data analysis collected from previous studies. You will be told how many scans you will receive when you are scheduled for the study.
- Your vital signs (blood pressure and heart rate) will be monitored before and after each MRI scan.
- Following the final scan, you will be given a meal, and discharged home.
- The anticipated length of the study is about seven hours including preparation, study, and post study observation.

Study Visit 2: Study Visit 2 will take place after the previous study. It will be identical to the first study, with the exception that you will receive the study drug you did not receive on the first study visit (e.g. if you received diazoxide on the first study visit, you will receive placebo on this visit).

Magnetic Resonance Imaging (MRI) is a test that uses magnets and radio waves to make pictures of organs and structures inside the body. For an MRI test, the area of the body being studied is placed inside a machine that contains a strong magnet. Pictures from an MRI scan are saved and stored on a computer for more study. Although the MRI you will have in this study is being done for research purposes only, it is possible that doctors may notice something that could be important to your health. If so, we will contact you to explain what was seen and tell you whether you should consult your doctor. We will make the MRI report available to your doctor, and if you want, we will talk with your private physician or refer you to someone for follow-up.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Genetic Testing

This study will not involve genetic research or genetic testing.

Specimen Banking (Future Use and Storage)

We will store your specimens and information about you in a “biobank”, which is a library of information and specimens (tissue and blood) from many studies. These specimens and information cannot be linked to you. In the future, researchers can apply for permission to use the specimens and information for new studies to prevent, diagnose, or treat disease, including genetic research. Your specimens and information may be kept for a long time, perhaps longer than 50 years. If you agree to the future use, some of your de-identified genetic and health

information (not linked to you) may be placed into one or more scientific databases. These may include databases maintained by the federal government.

You can choose not to participate in the biobank and still be part of the main study and this will not affect your treatment at this facility.

INITIAL ONE (1) OF THE FOLLOWING OPTIONS
_____ I consent to have my specimens and information about me used for future research studies.
_____ I do NOT consent to have my specimens and information about me used for future research studies. Information about me will be kept as long as required by regulations and institutional policy, but will not be used for future studies.

Will I be paid for being in this research study?

You will receive payment by Clincard Greenphire. A social security number is required. It will be kept confidential. Clincards are typically loaded with compensation within 24-48 business hours from the day of your study. You will not be reimbursed for child care expenses but only for travel expenses. You will receive $50 per MRI scan (up to 3 scans per study visit). If you choose to withdraw or cannot complete the study because you feel unwell during the study, or the study needs to be stopped due to a logistical or technical issue, the compensation will be pro-rated based on the time spent. You will be drug-tested the morning of the study before we begin any study procedures. If the drug test is positive, you will be withdrawn from the study.

Some researchers may develop tests, treatments or products that are worth money. You will not receive payment of any kind for your specimens and information or for any tests, treatments, products or other things of value that may result from the research.

Will it cost me anything to participate in this study?

There will be no cost to you to participate in the study.

What will happen if I am injured because I took part in this study?

If you are injured as a result of this research, only immediate, essential, short-term medical treatment as determined by the participating hospital, will be available for the injury without charge to you personally.

- No monetary compensation will be offered.
- You are not waiving any of your legal rights by signing this informed consent document.
- If additional treatment is required as a result of a physical injury related to the research, necessary medical treatment will be provided to you and billed to your insurance company or to you as part of your medical expenses.

Immediately report any discomforts, problems or injuries you experience during the course of your participation in the study to Dr. Meredith Hawkins (718-430-3186).

What else do I have to do?

- You must tell the research study doctor about any past and present diseases or allergies you are aware of and about all medications you are taking including "over-the-counter" remedies and nutritional supplements or herbs.
- If you do not feel well at any time, call your doctor or the research study doctor immediately.
- If you think you have become pregnant, contact your research study doctor immediately.
- You may carry out all your normal daily activities.

Confidentiality

The researchers and study staff follow federal and state laws to protect your privacy. This part of the consent form tells you what information about you may be used and shared in the research described in this form. You do not have to sign this form but, if you do not, you may not participate in the research.

The health information that we may use or disclose for the research described in this form includes information from your entire medical record, such as your name, phone number, email, medical diagnoses, dates, test results, social security number, medical record numbers, etc.

Your information and research records will be kept confidential. Your study information will be kept as long as they are useful for the research described in this form.

The only people who can see your research records are:

- the research team and staff who work with them
- the organization that funded the research
- groups that review research (the Einstein IRB, and the Office for Human Research Protections, and the US Food and Drug Administration)

The purposes of these uses and disclosures are to (1) conduct the study and (2) make sure the study is being done correctly. The information covered under this form may no longer be protected by federal privacy laws (such as HIPAA) once disclosed, and those persons who receive your health information may share your information with others without your additional permission. All of these groups have been asked to keep your information confidential.

Medical information collected during the research, such as test results, may be entered into your Montefiore electronic medical record and will be available to clinicians and other staff at Montefiore who provide care to you.

To maintain the integrity of this research study, you generally will not have access to your research-related personal health information. If it is necessary for your care, your research-related health information will be provided to you or your physician.

Certificate of Confidentiality

As a way to protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health, which is funding this study. If information from this study was requested or subpoenaed by government agencies or the courts, we will use the Certificate to attempt to legally refuse to provide it. This is rare – in only a few cases did researchers have to use the Certificate, and it was honored most of the time, but not every time. There are several

kinds of situations that the Certificate does not apply. For example, we are still required to report child abuse and some diseases, and we must make data available to the government for a review or evaluation of our research. The Certificate does not prevent you or a member of your family from voluntarily sharing information. Similarly, if an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Are there any risks to me?

Blood Draw: Rarely, the vein where we inserted the needle will become sore or red. Sometimes, a temporary harmless "black and blue" may develop. Very rarely, fainting may occur.

MRI: Some people are bothered by feelings of confinement (claustrophobia), and by the noise made by the machine during the test. You will be asked to wear earplugs and MRI compatible earphones while in the machine. You may not participate in this study if you have a pacemaker, an implanted defibrillator or certain other implanted electronic or metallic devices. It is important for you to tell the MRI staff if you have had brain surgery for a cerebral aneurysm, or if you have implanted medical or metallic devices, shrapnel or other metal, such as metal in your eye.

Diazoxide: The risk associated with higher doses of diazoxide therapy is hypotension (low blood pressure). Symptoms of low blood pressure are dizziness and light-headedness. During the study, there will be frequent monitoring of blood pressure, and if your blood pressure drops, the study will be stopped and treatment (intravenous salt solution) will be given until blood pressure returns to normal. Please note that the amount of diazoxide given in this study will be much lower than the doses which cause lowering of blood pressure. Another side effect of higher dose, long-term oral diazoxide is fluid retention and swelling.

Intravenous Catheter: The amount of blood drawn during the procedure (approximately 15 teaspoons for each separate study) is considerably less than that donated at a blood bank and will be replaced with intravenous fluid. The intravenous catheter is associated with a small risk of local bruising and discomfort.

Allergic Reaction to Study Drug
Any drug can cause an allergic reaction which could be mild or more serious and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you are having trouble breathing, call 911 immediately.

New Findings
If we learn any significant new findings during the study that might influence your decision to participate, we will contact you and explain them.

Unknown Risks
We have described all the risks we know. However, because this is research, there a possibility that you will have a reaction that we do not know about yet and is not expected. If we learn about other risks, we will let you know what they are so that you can decide whether or not you want to continue to be in the study.

Are there possible benefits to me?

You will not experience any direct benefit personally from participating in this study. We hope you will participate because this study may result in a better understanding of role of the brain in glucose production in people with diabetes.

Are there any consequences to me if I decide to stop participating in this study?

No. If you decide to take part, you are free to stop participating at any time without giving a reason. This will not affect your care and you will continue to be treated at this facility. However, some of the information may have already been entered into the study and that will not be removed. The researchers may continue to use and share the information they have already collected.

To revoke (take back) your consent and authorization, you must contact the Principal Investigator in writing at the address on page 1 of this form. However, you may first call or speak to the Principal Investigator and she will stop collecting new information about you. If you take back your consent and authorization, you will not be allowed to continue to participate in this research study.

Can the study end my participation early?

We will not let you participate in the study any more if 1) **you experience an adverse reaction to the study drug, 2) you test positive to a drug test during the screening or morning of the study.** In addition, your participation will end if the investigator or study sponsor stops the study earlier than expected.

CONSENT TO PARTICIPATE

I have read the consent form and I understand that it is up to me whether or not I participate. I know enough about the purpose, methods, risks and benefits of the research study to decide that I want to take part in it. I understand that I am not waiving any of my legal rights by signing this informed consent document. I will be given a signed copy of this consent form.

Printed name of participant	Signature of participant	Date	Time

Printed name of the person conducting the consent process	Signature	Date	Time