Official Title: Modulating Glucose Tolerance With Dietary Tyrosine

Unique Protocol ID: AAAS2124

Registration Identifier: NCT03872557

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Columbia University Consent Form

Protocol Information

Attached to Protocol: IRB-AAAS2124
Principal Investigator: Judith Korner (jk181)
IRB Protocol Title: Modulating glucose tolerance with dietary tyrosine

General Information

Consent Number: CF-AABM9040
Participation Duration: 8 weeks
Anticipated Number of Subjects: 12
Research Purpose: Type 2 diabetes can be rapidly reversed by metabolic surgery by an as yet unclear mechanism. This research study will examine one possible mechanism that involves the natural dietary amino acid tyrosine. The central problem of type 2 diabetes is poor regulation of blood glucose levels reflecting difficulties in the production and secretion of sufficient amounts of insulin by the pancreas and/or insensitivity to the insulin hormone. Our studies have shown that the natural amino acid Tyrosine and its metabolic by-products may be important regulators of insulin secretion. In this research we would like to study whether tyrosine, in the form of a capsule (typically available OTC at nutritional supplement stores), affects how the body processes glucose (administered in the form of a sugar solution drunk by the study volunteer). If successful, this research may lead to novel therapies to control abnormal glucose levels and non-surgical methods to improve type 2 diabetes.

Contacts

Contact	Title	Contact Information
Judith Korner	Principal Investigator	Phone: 212-305-3725 Email: jk181@cumc.columbia.edu
Rachel Arakawa	Investigator	Email: rya2103@cumc.columbia. edu

Information on Research

INTRODUCTION

The purpose of this form is to give you information to help you decide if you want to take part in a research study. This consent form includes information about:

- why the study is being done;
- the things that you will be asked to do if you are in the study;
- any known risks involved;
- any potential benefit;
- options, other than taking part in this study, that you have.

If at any time you have questions about the study, please ask a member of the study team. Take all the time you need to decide whether you want to take part in this research study.

The purpose of this research is described below in the 'What is Involved in This Study?' section of this consent form.

WHY IS THIS STUDY BEING DONE?

We are doing this research study to find out whether the natural amino acid Tyrosine and its metabolic by-products regulate insulin secretion. Insulin is a hormone produced in the pancreas and is known to regulate blood sugar levels.

The requirements of this study are:

1. 18 – 65 years old, male or female, capable of giving written as well as oral informed consent.

2. A fasting plasma glucose level (FPG) of less than 126 mg/dL (less than 7.0 mmol/L) and a hemoglobin A1C (Hb1ac) less than 6.4 %. Fasting is defined as no caloric intake for at least 8 hours.

3. Body Mass Index in the range of 18-35 kg/m^2.

4. Normal blood, renal and liver function tests.

In addition to the above criteria, you must not have

1. Current use of antacids or proton pump inhibitors (e.g.,Prilosec Prevacid, Dexilent, Aciphex, Protonix, Nexium, Vimovo, Zegerid)

2. Current use (or within 6 months) of antipsychotic, anti-anxiety, or antidepressant medications (eg MAO inhibitors, 5HT inhibitors, tricyclic antidepressants, L-DOPA), reserpine, β_2-receptor agonists (eg,terbutaline), steroids, weight loss medication, anticoagulant medication, over-the-counter nutritional supplements other than standard vitamin and mineral supplements.

3. Previous or current use of cocaine, methamphetamine, ecstasy (MDMA, 3-4 methylenedioxymethamphetamine)

4. History of Phenylketonuria, Tyrosinemia or other inherited disorders of amino acid metabolism.

5. History of movement disorder such as Parkinson's disease or Huntington's disease.

6. History of or psychiatric illness such as major depression, bipolar disease, anxiety or schizophrenia.

7. Female of child-bearing age, currently pregnant, breastfeeding or not using a form of birth control.

8. Current daily intake of caffeine greater than 500 mg/day (greater than 4-5 cups of coffee; greater than ten 12-oz cans of soda).

9. Consumption of more than 1 alcoholic drink per day or smoking more than 5 cigarettes/day.

10. Recent history (in the past three months) of more than a 3% gain or loss in body weight

11. Difficulty in swallowing capsules.

About 12 people are expected to be enrolled in this study at Columbia Presbyterian Medical Center.

WHAT YOU WILL BE ASKED TO DO IF YOU ARE IN THE STUDY

We expect your participation to last for no more than 8 weeks representing the interval between your first study visit for history, physical examination and laboratory testing and the last of 2 visits for oral glucose tolerance test.

Study participation will involve 3 visits.

The first visit is to the Columbia University Weight Control Center for baseline evaluation, including a physical exam, the collection of medical history data, drawing of blood samples for metabolic testing and obtaining written informed consent. The total amount of blood to be drawn at this time is 10 ml or 4 teaspoons.

If you are recruited (by meeting all inclusion and exclusion criteria), you will be scheduled for visit 2.

Once scheduled for a visit, you will be given a written set of instructions. On this information sheet, you will be given specific instructions about how you should modify your normal diet before your visit to the Columbia University Weight Control Center.

For forty-eight (48) hours prior to the visit, we will request that you avoid foodstuffs known to be enriched in Tyrosine or its metabolic derivative L-DOPA. These foods include Turkey, Chicken, Velvet beans, fava beans, Ricotta cheese, Parmesan cheese, Mustard Greens, walnuts, bananas, seaweed, oatmeal, wheat germ, red wine or dark chocolate. Keep a note of what you ate, how much and when. On the evening prior to your visit we will request that you substitute your normal meal and snack for three prepackaged tyrosine-phenylalanine free liquid meals called Tyr cooler, which we will supply. Tyr cooler is available from Nestle' Health Science and is a low volume, ready to drink, tyrosine and phenylalanine free medical food. The dinner (2 pouches) and snack (1 pouch) Tyr cooler liquid meal consists of 92 calories per pouch, representing 15 grams protein and 7 grams carbohydrate. The snack is to be consumed before 10 pm on the night preceding the visit. You may still feel hungry after consuming these liquid meals. After 10 pm we request that you fast (drinking water is OK) until you visit to the Medical center.

On the day of Visit 1

You will be asked to report to the Weight Control Center at Columbia Presbyterian Medical Center, having fasted since 10 pm the night before. In the following order we will ask you to

1. Lay on the exam bed in a semi recumbent position (like watching TV in bed)

2. To make the taking of blood easier for the test, allow us to place an i.v. catheter in the crook of your right or left arm. The i.v. catheter is an an intravenous needle with a plastic tube (IV) placed in a vein in your arm. At this time, we will take a blood sample. These blood samples will be used for baseline measurements of glucose and hormones made by your pancreas.

3. Next, we will ask you to take 4 capsules of tyrosine with a minimal amount of water (about 10 mls). These capsules will be similar or identical to those available in the nutritional supplement aisle at large retail pharmacies (e.g. CVS, GNC, Duane Reed, Walgreens).

4. About 45 minutes later, you will then be given a 300ml bottle of glucose to drink (similar to sweet lemonade or orangeade). You will be asked to drink the complete bottle within 5 minutes. After you finish the drink, about 1 teaspoon of blood (5 ml) will be drawn through the IV line. A clock with an alarm will be started as soon as you drink the last mouthful of glucose & this will be set for 2 hours. This drink will raise your blood sugar and cause your body to produce insulin. After you drink the sugar solution, some subjects report nausea, stomach ache and / or headache. These side effects subside during the test.

5. You will be required to rest during this period and not eat or smoke. You may sip water however.

6. When the alarm sounds you will have another sample of blood taken. Blood sampling will be at 15, 30, 60, 90, and 120 minutes. The total time for the test will be about 2 hours. The total amount of blood taken will be about 15 tablespoons (200 ml).

7. After you have completed the study, your results will be made available to you. The test will last about 3 hours.

Forty-eight hours before Visit 2.

We will ask that you once again follow the same instructions that you were given for visit one. We will request that you avoid foodstuffs known to be enriched in Tyrosine or its metabolic derivative L-DOPA. These foods include Turkey, Chicken, Velvet beans, fava beans, Ricotta cheese, Parmesan cheese, Mustard Greens, walnuts, bananas, seaweed, oatmeal, wheat germ, red wine or dark chocolate. If possible, using the notes you prepared prior to visit one, eat the same foodstuffs, the same amounts and at the same time.

On the evening prior to your Visit 2.

We will request that you substitute your normal meal and snack for three prepackaged tyrosine-phenylalanine free liquid meals called Tyr cooler, which we will supply. The snack is to be consumed before 10 pm on the night preceding the visit. You may still feel hungry after consuming these liquid meals. After 10 pm we request that you fast (drinking water is OK) until you visit to the Medical center.

On the day of Visit 2

You will be asked to report to the Weight Control Center at Columbia Presbyterian Medical Center, having fasted since 10 pm the night before. At this time you will undergo the same Oral Glucose Tolerance testing procedure that occurred on Visit 1.

On visit 2, you will not be asked to consume the Tyrosine capsules. Following the two hour blood sampling procedure (total amount of blood of 15 tablespoons), you will be released from the clinic.

The total amount of blood withdrawn for the entire study will be approximately the amount taken for a standard blood donation.

Risks

Occasionally study volunteers report minor discomfort associated with the following procedures:

Intravenous Needle. There may be the minor discomfort of having the IV placed in your arm. In about one out of ten cases, a small amount of bleeding under the skin will produce a bruise. Some people may also faint. The risk of a blood clot forming in the vein is about one in 100. The risk of infection or major blood loss is about one in 1000. To minimize bruising when the catheter is removed, pressure will be applied for at least 15 minutes

Oral Glucose tolerance testing. The sweet sugar drink used in this test has no known side effects, but you may not like the taste, feel some nausea, stomachaches or head ache. These discomforts subside during the test.

There are no published reports of any adverse side effects of use of medical food liquid formulas without phenylalanine and tyrosine (i.e. TYROS 2, Tyr cooler). Nor are there published reports of adverse effects from taking the tyrosine dietary supplement used in this study.

Loss of confidentiality

A risk of taking part in this study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your personal information shared with someone who is not on the study team and was not supposed to see or know about your information. The study team plans to protect your privacy. Their plans for keeping your information private are described in the Privacy section of this consent form

Benefits

You will not benefit as a result of participation in this study except if results of the tests, which will be communicated to participants, assist them and their physicians in management of their healthcare. However, the information collected from this research may help others in the future. The tests may be used for commercial profit but you will not share in this commercial profit if relevant.

Alternative Procedures

You may choose to not participate in this study for any reason.

Confidentiality

The health information that we may collect and use for this research may include medical history that may be considered sensitive. Such information includes mental health information and history of alcohol and drug use.

Any information collected during this study that can identify you by name will be kept confidential. We will do everything we can to keep your data secure, however, complete confidentiality cannot be promised. Despite all of our efforts, unanticipated problems, such as a stolen computer may occur, although it is highly unlikely.

Your private health information will be assigned a code number, and separated from your name or any other information that could identify you. The research file that links your name to the code number will be kept in a locked file cabinet and only the investigator and study staff will have access to the file. When the study is completed and the data has been analyzed, this list will be destroyed. Your name will not be used in any report or published material.

Once the samples are taken, they will forever be separated or unlinked from your name. This will protect your identify and preserve anonymity. However, once you donate the samples, you will not be able to withdraw your tissues from the research because the samples will not be traceable after the data is analyzed. If permission is given, we will keep your samples and they may be used for other studies.

Use of data/specimens for future research

The researchers may want to use or share your blood samples with other investigators both inside and outside of Columbia University so that additional research studies can be done now or in the future. If you agree to have the investigator or research team to store your samples for future research, they may be kept forever. In some research using human blood or tissue, the samples allow researchers to develop medical tests or treatments that have commercial value. If this occurs, there are no plans to pay you.

You have the right to have your unused samples or information kept about you for research purposes destroyed at any time. You can request this by contacting Dr. Judith Korner at 212-305-3725.

Please initial below to indicate whether or not you give permission.

YES___ NO___ I agree to have my specimens (blood) stored indefinitely and/or shared with other investigators doing research which is related to this study or my condition.

YES___ NO___ I agree to have my specimens (blood) stored indefinitely and/or shared with other investigators doing different kinds of research not related to this study or my condition.

Access to your records will be limited to those who absolutely need to see them, including the members of the research team, the University's Institutional Review Board, and the government authorities, as required. The following individuals and/or agencies will be able to look at and copy your research records

- The investigator, Columbia University Medical Center study staff and other medical professionals who may be evaluating the study
- Authorities from Columbia University, including the Institutional Review Board ('IRB')

- The Office of Human Research Protections ('OHRP') and the United States Food and Drug Administration ('FDA'); Certificate of Confidentiality

To help us protect your privacy, we received a Certificate of Confidentiality from the National Institutes of Health (NIH). With this Certificate, we cannot be forced to provide information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. We will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate of Confidentiality does not stop you or a member of your family from telling others about yourself or your involvement in this research. If an insurer, employer, or other person gets your written consent to receive research information, then we cannot use the Certificate to withhold that information.

The Certificate cannot be used to resist a demand for information from representatives of the United States Government that is used for auditing or evaluation of projects they are responsible for overseeing or for information that must be provided in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should also know that this Certificate does not protect you from our responsibility to report certain communicable diseases, suspected child abuse, or danger of physical or mental harm, to appropriate agencies or authorities.

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

Compensation

Compensation is for time and travel. Subjects will be paid $75 for the completion of each oral glucose tolerance visit (up to two) after the final visit. Payment in the form of a check will be sent to your home address approximately 6 to 8 weeks after the study completion.

Additional Costs

There are no additional costs associated with participation in this study

Research Related Injuries

Taking part in this research study may result in injury or harm to you. In the event of an injury resulting from your participation in this study, you should seek appropriate medical care and inform the study doctor. In the event of an emergency you should go to an emergency room.

If you are injured or harmed as a result of participating in the study and receive medical care through the NewYorkPresbyterian Hospital (NYPH), a Columbia doctor, or any other health provider, you will be sent a bill for whatever medical care you receive. All or part of your bill may be paid by your health insurance.

By providing financial or other assistance, neither Columbia University nor the researchers are stating that they are legally responsible for the injury.

Further information regarding compensation for injured research subjects may be obtained from the IRB Office.

Voluntary Participation

Taking part in this study is your choice. You can decide not to take part in or stop being in the study at any time. Your choice will not affect the treatment you receive from doctors and staff at Columbia University Medical Center.

You should know that we will not let you participate in the study any more if you fail to meet the inclusion and exclusion criteria. In addition, your participation will end if the investigator stops the study earlier than expected.

Taking part in this study is your choice. You may refuse to take part in the study or withdraw from the study at any time without jeopardizing your employment, student status, or any other rights. The investigator may withdraw you at his/her discretion if he or she feels that you have not followed the study instructions.

Additional Information

This document explains your rights as a research subject. If you have questions regarding your participation in this research study or if you have any questions about your rights as a research subject don't hesitate to speak with Dr. Paul Harris at 212 305-7363 or Dr. Judith Korner at 212-305-5568.

You have the right to ask any questions concerning the potential and/or known hazards of this study at any time. You are also encouraged to ask any and all questions which come to your mind about the study.

The staff of the research program will be happy to discuss any questions or concerns with you. For questions about study procedures or to report a study-related injury, you should call Dr. Dr. Judith Korner at 212-305-5568.

What are my rights if I take part in this study?

Taking part in this study is your choice. You can decide not to take part in or stop being in the study at any time. Your choice will not change the treatment you receive from doctors and staff at Columbia University Medical Center.

Please tell one of the Researchers listed at the beginning of this consent form if you decide to leave the study before it is finished.

Your participation will also end if the Researchers stops the study earlier than expected or if you do not follow the study procedures.

Who can I call if I have questions?

If you have any questions about your rights as a research participant, or if you have a concern about this study, you may contact the Institutional Review Board listed below.

Human Research Protection Office
Institutional Review Board
Columbia University Medical Center
154 Haven Avenue, 1st Floor
New York, NY 10032
Telephone: (212) 305-5883 irboffice@columbia.edu

Statement of Consent

I have read this consent form. The research study has been explained to me. I agree to be in the research study described above.

A copy of this consent form will be provided to me after I sign it. Another copy will be placed in my medical record.

By signing this consent, I have not given up any of the legal rights that I would have if I were not a participant in the study.

If you sign this paper, it means that you want to be in this study. If you do not want to be in the study, do not sign this paper.

Signatures

Participant Signature Lines

Study Subject

Print Name _____ Signature_____

Date & Time _____

Person obtaining consent

Print Name _____ Signature_____

Date & Time _____