BUTLER HOSPITAL CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

Effects of L-theanine on Motor Cortex Excitability in Healthy Subjects:
A Paired-Pulse TMS Study

Sponsorship

This study is being paid for by internal funds at Butler Hospital.

Research Project Summary

L-theanine, a green tea extract, is an over-the counter "nutritional supplement" that has been shown to have anti-anxiety, anti-depression effects. This study aims to understand the effects of L-theanine on the brain, by testing how a single dose of L-theanine impacts excitability of neurons (nerve cells) in the brain. You are invited to participate in this study because you are a healthy adult and not taking medications that impact brain excitability. This study will require you to complete 3 visits in a research clinic at Butler Hospital over a period of 2-3 weeks. Being in the study will take you about 7 hours (1-3 hours per visit) in total. You will have an interview with one of our research staff to confirm your healthy status, and then attend two visits, each of which involves taking one dose of either L-theanine or placebo (sugar pill). Your brain excitability will be measured with a procedure called "paired-pulse transcranial magnetic stimulation (ppTMS)" and we will tell you more information about this below. You will be paid for participation in the study. This green tea extract is very safe and it has few bad effects after taking one dose. The main side effects from the TMS procedure include discomfort from sitting a prolonged period, and discomfort from the sensation of magnetic pulses on your head. There is also an extremely small chance of seizure and it will be discussed below.

In order to decide whether or not you wish to be a part of this research study, you should know enough about its risks and benefits to make an informed judgment. This consent form gives you detailed information about the research study which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, risks associated with the procedures, possible benefits of participation, and possible alternatives. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form. This consent may contain words that you do not understand. Please ask the investigator or the study staff to explain any words or information that you do not clearly understand.

Description of Procedures

If you decide to participate, you will have 3 visits to Butler Hospital:

The first visit: You will have a talking session with the researcher to discuss this consent and to review your health history, to see if you qualify to participate in the study. You will be asked to provide a consent for us to contact your primary care physician to ensure you are free of any conditions that may prevent you from participating in the study.

The second visit:

1) You will participate in a procedure called "paired-pulse transcranial magnetic stimulation (ppTMS)", which is a pulse of energy delivered by a piece of magnet over the scalp. It sends stimulation to the brain area that controls your hand movement. In the meantime, your right-hand muscle movement (electromyography, EMG) will be recorded by 2 stickers with small pieces of metal on them. This procedure will take about 30-45 minutes; You will need to not eat or drink during the experiment but can drink water.
2) Then you will be given a capsule of either 400mg L-theanine (a green tea extract) or 400mg placebo (lactose), followed by 30 minutes of relaxation time sitting in a quiet room; You will not

know which (L-theanine or placebo) you received, to ensure a fair result. You will be able to stretch and walk around for a short period of time if you wish after taking the capsule.
3) Then the ppTMS procedure in 1) will be repeated, which will take another 30-45 minutes. There will be assessments of safety before/during/after each ppTMS procedure.

The third visit:
1) Just like the second visit, you will first have the ppTMS procedure, which will take about 30-45 minutes; You will need to not eat or drink during the experiment but can drink water.
2) Then you will be given a capsule of what you did not receive in the second visit. In other words, if you received L-theanine in the second visit, you will get placebo this time; or if you received placebo in the second visit, you will get L-theanine this time. But you still will not know which (L-theanine or placebo) you received, to ensure a fair result. This is again followed by 30 minutes of relaxation time sitting in a quiet room; You will be able to stretch and walk around for a short period of time if you wish after taking the capsule.
3) Then the ppTMS procedure in 1) will be repeated, which will take another 30-45 minutes. There will be assessments of safety before/during/after each ppTMS procedure.

Risks and Inconveniences

Risks of ppTMS procedure include:
1) Mild headache or scalp discomfort (5%-10%), usually mild if it happens and it typically gets better when you get used to the feeling of stimulation.
2) Seizure, very rare, with an estimated risk of 2-3 in 100,000. You will be carefully screened for any risks of seizure before the study and closely monitored during the procedure.
3) Dizziness or fainting. Usually due to anxiety about the procedure or dehydration. You will be closely monitored during the procedure.
4) Hearing damage. This would not likely occur if you wear ear plugs that we provide to you during the procedure.

Risks of taking L-theanine include:
1) Allergic reaction, extremely rare.
2) Sleepiness, increased length of sleep or increased dream activity, rare.
3) The agent is given by mouth, hence an extremely rare risk of choking on the capsule.

Risks of the placebo (because it will be lactose) include:
1) Allergic reaction, extremely rare.
2) Lactose intolerance. Please let the staff know if you have ever had diarrhea, gas or stomach upset after you drink milk.
3) The placebo is also given by mouth, hence an extremely rare risk of choking on the capsule.

There is a risk of loss of confidentiality. However, the study team will have procedures to protect your privacy and identity, by assigning you a study ID, and destroying all information that could be use to identify you personally once the study is completed.

Potential inconveniences include:
The study will take about 7 hours in total of your time, divided into 2-3 visits (1-3 hours each visit). During the second and third visit, you will sit with your head still in a chair for most of the 3 hours; you may become tired or uncomfortable, but we will give you time to stretch. You will need to travel to Butler Hospital for each visit, and we are not able to pay you for travel expenses but there is free parking on the hospital campus. You will also be asked to stop taking any caffeinated food/drink, stop using marijuana,

tobacco or any other drugs and over-the-counter supplements for 7 days before you receive the TMS procedures.

Any medical treatment or procedure may have unforeseen side effects. You should know that the prediction of effects from a treatment or procedure for any individual cannot be done with certainty, and unexpected potentially harmful effects occasionally occur with the administration of any type of treatment. If you have questions about investigational procedures or treatments, or if you have any disturbing side effects during participation in this study, please tell our staff. In the event of any unexpected, potentially harmful effects of any treatment or procedure given in this study, we will monitor your condition closely and institute appropriate treatment. If significant new knowledge is obtained through the course of the research which may change your mind about whether you would like to continue being in part of this study, you will be informed of this knowledge.

Women Please Note:
ppTMS procedure may be harmful to a growing fetus. Therefore, you may be tested for pregnancy at the time of your admission to the study. Prior to your beginning the study we will discuss with you in more detail the importance of avoiding pregnancy. We will specifically ask you to let us know if you change your mind and decide to become pregnant during the study.

Benefits
While it is unlikely that a single dose will have a significant effect, you may experience mild beneficial effects from the green tea extract L-theanine, including a sense of calm, relaxation, and reduced level of anxiety, on the day you are given the active drug.

Economic Considerations
You will be paid in the form of gift cards as follows: $20 for completion of the first visit; $50 for completion of the second visit and $80 for finishing the third and last visit. Therefore, you will receive $150 in total if you completed the whole study (for about 7 hours in total of your time). All monetary compensation will be given to you in a form of gift cards. The one dose of L-theanine or placebo will be provided by the researchers.

Alternative Treatments/Alternative to Participation
N/A. No treatments are being offered in this study.

In Case of Injury
We will offer you services in Care New England facilities as needed to treat any injury that results directly from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for any injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed on the last page of this consent form.

Financial Disclosure
N/A. There is no industry support for this research study

Voluntary Participation

You are free to decide whether or not to participate in this study, and you are free to withdraw from the study at any time. A decision not to participate or to withdraw from the study will not adversely affect your current or future interactions with Butler Hospital or Care New England. Your participation in the study may be terminated by the researchers without regard to your consent; in that case, you are entitled to an explanation of the conditions leading to that decision.

Confidentiality

Personal identifiers will be removed from any identifiable private information about you in the final research dataset created by this study. You will not be personally identified in any reports or publications that may result from this study. The confidentiality of the information you provide to us will be maintained in accordance with state and federal laws. If you tell us something that makes us believe that you or others have been or may be physically harmed, we may report that information to the appropriate agencies. To keep your information safe, all data will be stored on password protected computers, as well as on Care New England's REDCAP secure database and research servers.

General information about this study has been or will be submitted to the federal clinical trial registry databank, which can be accessed on the Internet at www.ClinicalTrials.gov.

Authorization for use/disclosure of your Identifying Health Information, to Conduct this Research Study

If you sign this document, you give permission to the researchers (Dr. Shiwen Yuan, Dr. Linda Carpenter, and the Neuromodulation Research Facility Assistants) at Butler Hospital to use your health information that identifies you, for the purpose of conducting the research study described above.

Your health information may also be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability, and conducting public health surveillance, investigations, or interventions.

Butler Hospital is required by law to protect your health information. Individuals outside of Butler that receive your health information may not be required by Federal privacy laws (such as the HIPAA Privacy Rule) to protect it, so we cannot guarantee that they will not share it without your permission.

Please note that:

- You do not have to sign this consent form, but if you do not, you may not participate in or receive research-related treatment in this study.
- Butler Hospital may not withhold treatment or refuse to treat you, based on whether you sign this consent form.
- You may change your mind and revoke (take back) this consent and authorization at any time. If you no longer want to give us permission to use your health information for this research study, you must contact the Principal Investigator, Dr. Linda Carpenter, and you will be instructed to provide a written statement.
- Even if you revoke (take back) this consent and authorization, Butler researchers may still use or share health information about you that they already have obtained, when doing so is necessary to maintain the integrity or reliability of the current research.
- You generally will not have access to your personal health information related to this research until the study is completed. At the conclusion of the research and at your request, you will have access to your health information that Butler Hospital maintains in a designated record set, according to the Notice of Privacy Practices provided to you by Butler Hospital. The designated

record set includes medical information or billing records used by doctors or other health care providers at Butler Hospital to make decisions about individuals.
- Your health information will be provided to you or to your physician if it is necessary for your care.
- If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

This Authorization does not have an expiration date.

Questions

Taking part in this study is entirely voluntary. We urge you to discuss any questions about this study with our staff members. You should take as much time as you need to make your decision. If you decide to participate, you must sign this form to show that you want to take part.

Authorization:
I have read this form and decided that I _____
(printed name of participant)
will participate in the project described above. Its general purposes, the nature of my involvement, and possible hazards and inconveniences have been explained to my satisfaction.
I have received a copy of this consent form.

_____ _____
Signature of Participant Date

_____ _____
Signature of Principal Investigator Date
~or~

_____ _____
Signature of Person Obtaining Consent Date

Telephone Number of Principal Investigator or Person Obtaining Consent_____

If you have further questions about this project or about research-related injuries, please contact Shiwen Yuan, M.D. at 401-455-6436 or Linda Carpenter, M.D. at 401-455-6349. If you have questions about your rights as a research subject, please contact Paul F. Malloy, Ph.D., Vice Chair, Butler Hospital Institutional Review Board, at 401-455-6355.

THIS FORM IS NOT VALID UNLESS THE FOLLOWING BOX HAS BEEN COMPLETED BY THE IRB OFFICE

THIS FORM IS VALID UNTIL

DATE:

IRBNET ID#

BUTLER IRB REFERENCE#

BY (ADMINISTRATOR):