

**University of California, San Diego
Consent to Act as a Research Subject**

**Evaluating the effects of magnesium
on arterial compliance and cerebral blood flow**

Investigators and Sponsor

Thomas Liu, Ph.D., Ryan Bradley ND, PHD and Laura Redwine, Ph.D. are conducting a research study. You have been asked to participate in this study because you are an English-speaking adult and have a history of obesity and metabolic syndrome. Metabolic syndrome is a group of risk factors (including high cholesterol levels and high blood pressure) that raises the risk of heart disease, diabetes, stroke, and other health problems. We will attempt to enroll a total of 51 participants. The research study is being funded by the Krupp Endowed Fund. All of the procedures and tasks to be performed are considered experimental and not part of routine patient care.

Purpose of Study: The main purpose of this study is to find out if taking magnesium supplements for 12 weeks has effects on blood vessels and blood flow in the brain for individuals who have metabolic syndrome and also have low levels of magnesium and vitamin D.

Overview: The overall study consists of three visits, consisting of an initial testing visit to confirm eligibility and two additional visits that will be scheduled if the initial test results indicate that you are eligible. The initial testing visit will take about 30 minutes, while each of the additional visits will take about 3 hours. Participation in all three visits will take place over the course of 3 to 4 months, with a spacing of 3 months between the two additional visits.

Procedures To Be Followed During the Study If you agree to participate, the following will happen to you:

1. You will be asked to have a blood test for screening purposes performed at Dr. Redwine's laboratory at the UCSD School of Medicine to assess magnesium levels, vitamin D-levels, fat levels, kidney function, levels of blood sugar, electrolytes and other chemicals in your body (grouped into a report that is called a metabolic panel), blood insulin, and a complete blood count. You will also have your height, weight, and waist circumference, and blood pressure measured.
2. Based on the initial test results, you may be asked to return for two additional visits if it is determined that you have low magnesium and vitamin D levels and are confirmed to have metabolic syndrome.

3. Each of the additional visits will consist of a blood test, blood pressure measurement, height, weight, and waist circumference measurements, and an MRI scan. The blood test will assess magnesium levels, kidney function, vitamin D-levels, fat levels, levels of blood sugar, electrolytes and other chemicals (known as a metabolic panel), blood insulin, and a complete blood count. The visits will be separated by 12 weeks.
4. During the period between the two visits you will be asked to take a daily dose of magnesium citrate (450 mg per day taken as 3 150mg capsules) and 5 drops of a vitamin-D supplement.
5. You will be asked to keep a daily log of your intake of the supplements and to return the supplement bottles at the end of the study.
6. Since MRI uses a large magnet, it may be dangerous for you to enter the scanning room if you have metallic implants, devices, objects, or materials in or on your body. No such known cases will be scanned. You will be asked about medical conditions, work history, and other situations that suggest MRI may harm you. Additionally, as hearing aids must be removed and you will need to follow verbal instructions during the scans, you must be able to hear adequately without hearing aids.
7. You will be scheduled for a **60-90 minute MR imaging session** at the UCSD fMRI Center on the UCSD campus in La Jolla, CA. During this session you will receive a series of MRI scans of your brain or heart.
 - You will be placed in a large, donut-like machine called a magnetic resonance scanner.
 - You must be able to lie still, flat on your back within the MRI for 60-90 minutes.
 - For brain scans, your head will be within a helmet-like structure and padding will be placed alongside your head to reduce motion.
 - While no one will be in the scanner room with you during the study, you will remain in direct verbal contact with the investigator running the MRI scanner via an intercom, and a squeeze bulb placed in your hand will allow you to sound an alarm if you have any concerns.
8. For each visit,
 - i) You will be asked to refrain from eating and drinking all beverages except water after 10 pm on the night before both the initial testing visit and the additional visits.
 - ii) You will have a blood sample (25 ml) collected at 8 am, after which you may consume a light breakfast and your standard morning beverage.
 - iii) You will consume no more than one alcoholic drink the night before and abstain from drinking caffeinated beverages (e.g. coffee, tea, energy drink) during the 2 hours prior to lying down in the scanner.

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Blood collected during this study may be stored with a coded label that does not identify you and may be investigated later for other metabolic-related biomarkers. Dr. Thomas Liu will have solitary control of the stored specimens. Your blood will not be shared with anyone outside of this study. The specimens will be stored for an indefinite period of time. The research with the specimens collected from you may have significant therapeutic value. You consent to such uses. You may notify the Principle Investigator, Dr. Thomas Liu to withdraw consent for your blood to be stored and analyzed later. If you withdraw your consent for later blood analysis, the sample will immediately be disposed of in a biohazardous waste container.

There are no plans to provide any compensation to you for potential commercial values. No DNA or genetic testing will be done on your saved blood. By initializing below, you are accepting or declining to have your blood saved for future tests but are willing to participate in other parts of this study.

- Yes, you may save my blood for future analyses.
- No, you may not save my blood for future analyses.

_____Initials of Subject.

You have the alternative to not participate in this study.

If at any time during the entire study you experience anxiety, excessive shortness of breath or headaches, or wish to stop the study, you may squeeze the squeeze bulb, and the operator will stop the scan immediately.

Your heart rate and blood oxygenation level may be monitored during the exam by a device that fits on your fingertip. If your heart rate significantly increases or your blood oxygen saturation level drops, the study will be discontinued. Your breathing may be monitored by an elastic belt placed around your mid-section.

The series of scans being completed are experimental and not sufficient for clinical diagnosis or treatment planning. They will not routinely be reviewed by a radiologist. If any abnormal findings occur, however, you will be notified, and any images collected can be transferred to your physician at your discretion. Additional medical tests and treatment may result in further costs to you. De-identified samples of your blood plasma will be banked in a -80 C freezer in Dr. Redwine's laboratory.

Benefits of the Study

There will not be any direct benefit to you from this study, but we hope to learn more about the effect of magnesium on cerebrovascular health.

Risks and Discomforts If you participate, you may experience the following:

1. Discomfort from lying flat on your back in the scanner for at least 60 minutes.
2. Anxiety or apprehension associated with being in a confined, close space. If you feel anxious or claustrophobic during the study, you can stop the procedure at any time.
3. Banging noises that the machine makes while it is taking pictures. You will be given earplugs and/or headphones to reduce the noise to safe levels.
4. Although there are no known risks to pregnant women or fetuses involved with MRI, please tell us if there is any possibility that you could be pregnant at this time. If so, we request that you not participate in the research at this time.
5. As the scanner exerts a strong magnetic force on some objects, individuals with pacemakers, some surgical clips or implants, and other items on the list above will be excluded from participation. Serious injury or death can result from complications associated with these items. Your honest completion of the screening questionnaire is for your protection.
6. You may experience diarrhea from the magnesium supplements. If this is the case, we will ask that you spread out taking the dose over the course of the day. If the diarrhea persists, we will ask you to reduce the dosage to 300 mg per day (2 capsules per day).
7. If you take more than the prescribed dose of magnesium you may experience diarrhea. If this is the case, we will ask that you discontinue the magnesium supplements until the diarrhea resolves and that you notify the study staff. If the diarrhea does not resolve after a few days, we ask that you contact your primary care physician and notify the study staff. If you suffer more severe symptoms such as severe abdominal, pelvic, or lower back pain; chest pain or pressure; confusion or loss of consciousness for even a brief moment; rapid heart rate (tachycardia); and shortness of breath we ask that you seek immediate medical attention.
8. If you take more than the prescribed dose of Vitamin D, will ask that you notify the study staff and resume the prescribed dose.
9. There is a potential loss of participant confidentiality.
10. If you are unable to remain relatively still during the MRI scan session we may ask that you discontinue participation in the study.
11. There may be risks that are currently unforeseeable.
12. Over the course of the study, you will be provided with any significant research findings relevant to your continued participation.

Care if Harmed

If you are injured as a direct result of participation in this research, the University of California will provide any medical care you need to treat those injuries. The University will not provide any other form of compensation to you if you are injured. You may call

the UCSD Human Research Protections Program at (858) 246-4777 for more information about this, to inquire about your rights as a research subject, or to report research-related problems.

Subject Rights and Study Withdrawal

Participation in research is entirely voluntary. You may refuse to participate or withdraw at any time without jeopardy to the medical care you receive at this institution or loss of benefits to which you are entitled. To withdraw, you can simply tell anyone on the study team during the procedure that you no longer wish to continue.

_____ has explained this study to you and answered your questions. If you have other questions or research related problems, you may reach Dr. Liu at (858) 822-0542.

Subject Cost/Payment for Participation

You will be paid \$25 for the initial blood test screening visit. For additional blood tests and MRI scans, you will receive \$25 for each visit. In addition, you will be given \$10 per visit to defray transportation and parking costs.

There is no cost to you for participation in this study.

Confidentiality

Research records will be kept confidential to the extent provided by law. The results of this study will be seen only by other professional researchers and for teaching purposes and if appropriate, may be published in scientific journals or be presented at scientific meetings but your name will not be identified. In addition, research records may be reviewed by the UCSD Institutional Review Board. All study data will be stored in password protected accounts on a server located at the UCSD Center for fMRI or in a locked cabinet in Dr. Redwine’s laboratory. We will assign each participant a numerical code, so that acquired data will thus nowhere be associated with your name and will be kept confidential.

Your signature below indicates that you agree to participate in this study and you have received the UCSD Experimental Subject's Bill of Rights and a copy of this consent document to keep.

Subject's signature

Person Obtaining Consent

Date

Your response to the following option does not impact your ability to participate in this study.

- YES, I would like to be contacted by Dr. Liu or his colleagues for future studies.
- NO, I would not like to be contacted by Dr. Liu or his colleagues for future studies.