Improving Sleep and Alzheimer's Disease (AD) Biomarkers: A Pilot Randomized Clinical Trial (RCT) of Citicoline

NCT06029894

Date: 18 June, 2025

STUDY00006047

You Are Being Asked to Be in a Research Study
Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study, you will be one of 100 people who are being studied at Emory.

Why is this study being done?
This study is being done to answer the question: Does citicoline dietary supplement impact sleep and biomarkers, a marker of your biological condition?

Do you have to be in the study?
It is your decision to be part of this research study. You do not have to be in it. Your choice will not affect your access to medical care for your condition. Before you make your decision, you should take time to learn about the study.

What do I have to do if I choose to participate in this study?
If you are eligible and want to be part of the study, you will be asked to participate in two study visits. At the first visit, the researchers will ask you to do the following: review and sign the consent form, complete questionnaires about your sleep health and cognition. We will also instruct you on how to use the sleep and activity devices. At this time, you will also be given instructions on how to begin taking citicoline supplements or placebo pills once daily for 3 months. If you have Alzheimer's blood biomarker data available from a prior research study in the past year, we will use this data as your baseline level and obtain a blood sample (approximately 3 teaspoons) at baseline. At the follow-up visit we will collect approximately 4 teaspoons of blood. Should you have spinal fluid Alzheimer's biomarker data from prior research cohorts in the past year, spinal fluid will not need to be taken at the baseline visit, and we will obtain spinal fluid (2 tablespoons) at the follow-up visit at 3 months only. We will collect about 4 teaspoons of blood at both your baseline and follow-up visit. Should you have neither blood nor spinal fluid collection from a prior research study, we will collect approximately 4 teaspoons of blood at baseline and at follow-up. The blood collection for this study may take place on a separate visit from the baseline visit (within an approximately 1-week time window). At the 3-month follow-up, we will assess your sleep health and cognition.

How is this study going to help you?
If you are in the study, you will be helping the researchers answer the study question. The main purpose of the research studies is to gain knowledge. This knowledge may be used to help others.

What are the risks or discomforts I should know about before making a decision?
The study will take time. The supplement that is being tested may not work any better than regular care. All studies have some risks. Some risks are relatively small, like being bored or losing time. Some are more serious – for this study, include loss of privacy, and breach of confidentiality. A full list of expected risks, their frequency and severity are in the "What are the possible risks and discomforts?" section of this document.

Alternatives to Joining This Study
Since this is not a treatment study, the alternative is not to participate.

Costs
You WILL NOT have to pay for any of the study procedures.

What Should I Do Next?
Read this form, or have it read to you. Make sure the study staff explains the study to you. Ask questions (e.g., about exact time commitment, about unfamiliar words, more details on specific procedures, etc.) Make sure

you understand which parts of the are research and which are standard care that you would have even if you did not join the study. Take time to consider this and talk about it with your family and friends.

Emory University
Consent to be a Research Subject / HIPAA Authorization

Title: Improving Sleep and AD Biomarkers: A Pilot RCT of Citicoline

IRB #: IRB # STUDY00006047

Principal Investigator: [redacted] PhD, MS, MTR

Sponsor: NIH

Introduction

You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

A description of this clinical trial will be available on http://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.

What is the purpose of this study?

You are being asked to volunteer to participate in this research project because you have a neurocognitive disorder or suspected neurocognitive disorder, or your spouse, family member, or non-kindred associate has a neurocognitive disorder or suspected neurocognitive disorder. The purpose of the research is to learn more about whether a dietary citicoline supplement will impact sleep and cognition. Cognitive disorders include such things as memory disorders, mild cognitive impairment, and Alzheimer's disease (AD). We are studying persons with mild cognitive impairment (MCI) or suspected MCI. For this population, we will test to see whether citicoline also impacts biomarkers, a marker of your biological state, in your body.

We are interested in learning more about a dietary supplement called citicoline and how it helps sleep, cognition, and markers of Alzheimer's. Previous studies have tested this dietary supplement in Alzheimer's disease and shown that citicoline may impact cognitive decline. We would like to see if citicoline will also impact sleep and markers of Alzheimer's. The citicoline that will be provided to you is made by Kyowa Hakko Pharma Chemical Company. This dietary supplement has been tested in Alzheimer's disease and found to be well tolerated. Citicoline has previously been used safely in other Alzheimer's disease populations at the same dosage.

What will I be asked to do?

You will complete sleep questionnaires and cognitive assessment questionnaires at the first and follow-up (3 months after) visits. These visits can take place either in person, at the study visit, or remotely as applicable.

- Identifiable Data Access: If you are a patient at Emory University your entire medical record, including any information obtained during your regular clinic evaluations or during your hospitalization, such as examination findings and test results may be reviewed. We will collect data on your prior medical history. We will also interview on your past medical history at your baseline appointment.

  All study participants' information will be entered into a computer database. You will be asked for permission to share your data with other investigators conducting research under an IRB-approved protocol.

  Medical history/medications/supplement intake will be asked at the baseline visit, and you will also have the option to provide this information remotely within approximately 1 week of your baseline visit.

- Questionnaires (takes approximately 1 hour to complete)
  - Sleep questionnaires: you will be asked to fill out questionnaires assessing your sleep-you will have the option to take this questionnaire remotely from home if preferred. If you have already taken the sleep questionnaires as part of screening for this study, these questionnaires will not be retaken at the baseline visit (the day that pills are given to the participant).
  - Cognitive assessment questionnaires: You will be asked to fill out a questionnaires to measure your cognitive assessment. This questionnaire can also be taken remotely from home via arranging a HIPAA compliant video Zoom call with study team if preferred.
  - Food frequency questionnaire: You will be asked to fill out a questionnaire to measure your choline intake. This measure can also be taken remotely from home within approximately 1 week before your baseline visit if preferred.

- Assignment to citicoline supplement or placebo for 3 months.
  - Participants in one group will be provided with 1000 mg of citicoline (to be taken once per day with or without food) and those in the other group will receive the placebo (to be taken once per day with or without food). Neither you nor the researchers will know which of the two study related drugs (citicoline or placebo) that you are given. This information will be in our study files, but we will not look at these files until after the study completion. This allows us to see the true effects of citicoline without being influenced by biases. Should you prefer to be remote, we can offer to have the research pharmacy send the pills directly to your home.
  - Some participants in the study will not be provided with the citicoline supplement- these individuals will instead be provided with a placebo pill. There is no known risk associated with the placebo pill. A placebo pills look like a real supplement, but they are pretend supplements. It has no effect on a person. Citicoline and the placebo pill will have the same appearance in our study.
  - In order to determine the true effectiveness of citicoline, we will need to compare the results from the participants who took citicoline against those who took placebo. This involves assigning the study participants to two groups. Each participant will be assigned randomly.

If you agree to participate, you will allow the researchers to use the information gathered during your research visits for this study. Your records will be placed in a database designed to store data for future use for an indefinite period of time. A total of 100 people will participate in this research. Participation in this study requires two visits: once at baseline and another time at your 3-month follow up visit. At each visit, we would like to ask you to complete cognitive and sleep surveys. We will also provide you with a side effect checklist to fill out and return at 3 months follow up. We will also be providing reminder phone calls, emails, and or texts at 1 week after your initial visit, at 4 and 8 weeks, to ensure continued adherence and address any concerns or questions you may have.

You will be administered the sleep and cognitive assessment questionnaires as described above. We will also provide you with a 7-day sleep diary to take home to assess sleep patterns and training on how to fill out this questionnaire. We also will provide an electronic version of the sleep diary should you wish. You will also be asked to fill out a socioeconomic status and quality-of-life questionnaire to measure how you feel about your health and well-being at the baseline visit or remotely emailed the questionnaires at least 1 week in advance of your visit.

Objective sleep and activity measures. You will be administered the sleep profiler to measure your sleep over night. This FDA approved device is applied over your head and worn for 2 nights at baseline and 2 nights at follow up (at 3 months). You will also wear a wristwatch to measure activity for 2 days to measure how you sleep and your activity level at your baseline visit and your follow up at 3 months. We reserve the right to determine whether to provide this equipment for the study visit or not based on individual circumstances. We will also offer the option of delivering the devices to your home directly. If provided, you are expected to return the equipment back to the study team as instructed via a pre-paid Fedex box to deliver to the Fedex store, or we would arrange to pick up the equipment directly from you. We will send a reminder email to you on when to send us back the equipment or arrange for pick up as appropriate.

Blood draw. If you have Alzheimer's blood biomarker data available from a prior research study in the past year, we will use this data as your baseline blood biomarker level. We will also obtain a blood sample at baseline (3 teaspoons) and blood (4 teaspoons) at the follow-up visit at 3 months. If you have not participated in a prior research study that collects blood AD biomarkers in the past year, we will obtain about 4 teaspoons (approximately 20 ml) of blood from a vein in your arm at both the baseline and follow-up visit at 3 months. We will also offer a travel phlebotomist as a potential option to collect blood.

Spinal Fluid. Should you have spinal fluid biomarker data for Alzheimer's biomarkers from prior research cohorts in the past year, spinal fluid will not need to be taken at the baseline visit, and we will obtain spinal fluid (2 tablespoons) at the follow-up visit at 3 months only. The collection will take place at the 3 month visit only if you have spinal fluid collection data from your participation in a prior research study. If you do not have spinal fluid biomarker data from a prior research cohort, we will not collect spinal fluid data from you in our study.

Here is the procedure for the lumbar puncture.

> Lumbar Puncture (LP): The LP is also called a "spinal tap". This procedure involves collecting a small amount of the spinal fluid that surrounds the brain and spinal cord which is removed by inserting a needle in the lower back. You will be positioned lying on your side and curled up in a ball, or sitting up and bent forward, depending on your comfort level and what you prefer. Your lower back will be cleaned with antiseptic. A numbing medicine (lidocaine, 1%) will be injected into the skin of your lower back. Once this area is numb, a thin needle will be inserted into the spinal canal in the lower back, below the level where the spinal cord ends. Approximately 2 tablespoons of spinal fluid will be removed. The fluid will be analyzed and stored. After this procedure, the spinal fluid will be replaced naturally by your body within approximately 1-2 hours. Your spinal fluid will be measured for biomarkers and stored indefinitely. After the procedure is completed, you will be asked to stay in the room for approximately 30 minutes. You will be offered something to eat and drink before you leave. Do not do any strenuous physical activity for 24 hours. This involves bending, doing housework, exercises such as jogging or riding your bicycle, and gardening.

Permission to Contact: We will also ask for your permission to keep your contact information in a database so that we may contact you by telephone, mail or email to update our records and to inform you about other research opportunities.

How will my supplements be provided?
The supplements that you will take will be dispensed by the pharmacy and delivered to the principal investigator or study team member. The principal investigator or study coordinator on his/her research team will provide the supplements to you. If you have questions about the supplements, you should ask the study coordinator or pharmacy.

Who owns my study information?
If you join this study, you will be donating your study information. If you withdraw from the study, data that were already collected may still be used for this study.

We will store all the data and biospecimens that you provide using a code. We need this code so that we can keep track of your data over time. This code will not include information that can identify you (identifiers). Specifically, it will not include your name, initials, date of birth, or medical record number. We will keep a file that links this code to your identifiers in a secure location separate from the data.

We will not allow your name and any other fact that might point to you to appear when we present or publish the results of this study.

Your data and biospecimens may be useful for other research being done by investigators at Emory or elsewhere. We may share the data and biospecimens linked by the study code, with other researchers at Emory, or with researchers at other institutions that maintain at least the same level of data security that we maintain at Emory. We will not share the link between the study code and your ide*ntity.*

What are the possible risks and discomforts?

Confidentiality. All information about you will be kept confidential and there are practices in place to protect your personal information. However, there is always a risk to your privacy when you share information about yourself.

Sleep and cognitive tests. Evaluation of sleep and cognitive status may be frustrating to take part in.

Side effects of dietary supplement. Side effects with this dietary supplement include possible nausea or diarrhea that occur in less than 5% of the population studied.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Blood draw. Removal of blood may result in pain or bruising. You may feel dizzy or faint. There is also a risk of infection. We will have experienced medical staff to draw the blood in order to minimize this risk. This visit will take place at our study site at Emory or we may potentially be able arrange to provide a travel phlebotomist to come to your home.

Lumbar puncture. You may have temporary pain or discomfort. Headache may occur. If headache does not go away, you may need additional treatment. A blood patch which is an injection of some blood into the lumbar puncture site may be needed to patch the spinal fluid leak if needed. It is possible you may have an allergic reaction to lidocaine 1% which is a numbing medication. There are rare risks of puncture which includes infection and nerve damage. This procedure is performed by a clinician trained to perform this in order to reduce this risk. This procedure is only conducted at follow-up for those who had lumbar puncture available from participation in a prior research study cohort. For those who did not have this done from a prior study, lumbar puncture is not taken.

Will I benefit directly from the study?

There is no direct benefit to you by participating in this research study. Scientists may learn new things that will help individuals with neurological conditions impact their sleep.

Will I be compensated for my time and effort?

You will be asked to fill out a tax form, including your Social Security or Taxpayer Identification Number, and address information, in order to be reimbursed, depending on the amount and method of payment. Some payment methods involve mail coming to your house, which may be seen by others in your household. You can decline payment if you are concerned about confidentiality, or you can talk to the study team to see if there are other payment options. Compensation will be a total of $300 in the form of a gift card at the follow up visit if you complete all study visits.

What are my other options?

You may choose not to participate in this study. This choice will not affect your current or future care or that of any of your family members.

How will you protect my private information that you collect in this study?

Emory will keep any research records that it creates private to the extent that this is required to do so by law. Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Certain offices and people other than the researchers may look at your medical charts and study records. Emory overseeing proper study conduct may look at your study records. Study sponsors and people or companies they use to carry out the study may also look at your study records. Emory will keep any research records we create private to the extent we are required to do so by law. A study number rather than your name will be used on study records wherever possible. Your name and other facts that might point to you will not appear when we present this study or publish its results.

Certificate of Confidentiality

The Certificate of Confidentiality helps us to keep others from learning that you participated in this study. Emory will rely on the Certificate of Confidentiality to refuse to give out study information that identifies you. For example, if Emory received a subpoena for study records, it would not give out information that identifies you.

The Certificate of Confidentiality does not stop you or someone else, like a member of your family, from giving out information about your participation in this study. For example, if you let your insurance company know that you are in this study, and you agree to give the insurance company research information, then the investigator cannot use the Certificate to withhold this information. This means you and your family also need to protect your own privacy.

The Certificate does not stop Emory from making the following disclosures about you:

- Giving state public health officials information about certain infectious diseases,
- Giving law officials information about abuse of a child, elderly person or disabled person.
- Giving out information to prevent harm to you or others.

Giving the study sponsor or funders information about the study, including information for an audit or evaluation.

Storing and Sharing your Information

De-identified data from this study (data that has been stripped of all information that can identify you), including your de-identified genetic information, may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data. We will use your data only for research.

The information in the database may be shared with Emory and non-Emory investigators to help them study diseases. These studies will require authorization of the PI and a committee comprised of Emory clinicians and researchers. Researchers requesting your data for future studies will be reviewed by the IRB, if applicable.

Information and materials that may be released to researchers may include, but are not limited to: medical information, age, gender, ethnic background, and family history. Appropriate material transfer agreements will govern all biological material provided to researchers at other institutions. Identifiers, such as names and addresses, will not be released. All efforts will be made to keep identities confidential. The study results will not be shared with the participants. Incidental findings such as previously unknown positive AD biomarkers, will be relayed to you and your provider.

Medical Record

If you have been an Emory Healthcare patient before, then you already have an Emory Healthcare medical record. If you have never been an Emory Healthcare patient, you do not have one.

The results of all study tests and procedures will be used only for research purposes and will *not* be placed in your medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

Costs

There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities. If the study procedures result in any medical complications, the cost of treatment for these complications may be charged to you or your insurance.

Withdrawal from the Study

You have the right to leave a study at any time without penalty. We will collect the study outcome measures from those who choose to withdraw, if the representatives are willing. For your safety, however, you should consider the study doctor's advice about how to go off the study drug. The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. As part of this study, we will be requesting health care entities who are covered by the Health Insurance Portability and Accountability Act and regulations (HIPAA) to provide us with health information that identifies you ("individually identifiable health information" or "IIHI"). Because the health care entities are covered by HIPAA, we must have your authorization to obtain your IIHI from them. However, the researchers who get your IIHI from the health care entities are not covered by HIPAA. Once they receive your IIHI from the health care entities, they will put it in a separate research record that is not a part of your medical record. IIHI placed in the separate research record is not covered by HIPAA.

Purpose of this Authorization:
By signing this form, you give us permission to get your IIHI from health care entities and to use and share your IIHI as described in this document. You do not have to sign this form. If you do not sign this form, then you may not participate in the research study.

Research-Related Treatment
There is no research-related treatment involved in this study. You may receive any non-research related treatment whether or not you sign this form.

Main Study

IIHI that Will be Used/Disclosed:
The IIHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your IIHI Will be Used/Disclosed:
We will use and share your IIHI for the conduct and oversight of the research study. Once we have your IIHI we will keep it in a separate research record that will be used for the conduct of the study. We will use and share your IIHI to provide you with study related treatment and for payment for such treatment. We will also use and share your IIHI to conduct normal business operations. We may share your IIHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your IIHI to determine your health, vital status or contact information. We will use and disclose your IIHI for the administration and payment of any costs relating to subject injury from the study.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your IIHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults.

Authorization to Use IIHI is Required to Participate:
By signing this form, you give us permission to use and share your IIHI as described in this document. You do not have to sign this form. If you do not sign this form, you may still receive non-research related treatment

People Who will Use/Disclose Your IIHI:
The following people and groups will use and disclose your IIHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your IIHI to conduct the study and give you study related treatment.
- Emory may use and disclose your IIHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your IIHI with other people and groups to help conduct the study or to provide oversight for the study. This includes sharing your IIHI with people and groups at other sites who are helping conduct the study.
- Emory's Alzheimer's Disease Research Center and the NIH is the Sponsor of the study. The Sponsor may use and disclose your IIHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your IIHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The research team and the Sponsor may use and disclose your IIHI, including disclosure to insurance carriers to administer payment for subject injury.
- The following people and groups will use your IIHI to make sure the research is done correctly and safely:
    - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory University and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Other researchers and centers that are a part of this study.
    - Government agencies that regulate the research including: Office for Human Research Protections
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your IIHI may be shared with that new institution and their oversight offices. IIHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your IIHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at: [redacted]

At that point, the researchers would not collect any more of your IIHI. But they may use or disclose the information you already gave them described in this authorization so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the main study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. HIPAA does not apply to research that does not include treatment that is billed to insurers or government benefit programs. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. The Sponsor, and

people and companies working with the Sponsor on this study are not covered by the Privacy Rules. They will only use and disclose your information as described in this Consent and Authorization.

To maintain the integrity of this research study, you generally will not have access to your IIHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your IIHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your IIHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers is not subject to HIPAA and may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information

Contact [redacted] or [redacted]:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, or concerns about the research

Contact the Emory Institutional Review Board at [redacted] or [redacted] or [redacted]:

- if you have questions about your rights as a research participant.
- if you have complaints about the research or an issue you rather discuss with someone outside the research team.

You may also let the IRB know about your experience as a research participant through our Research Participant Survey at [redacted].

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in this research study, and any future studies you initialed below. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____
Signature of Subject (18 or older and able to consent) **Date** **Time**

_____ _____
Signature of Legally Authorized Representative or Study Partner **Date** **Time**

_____
Relationship of Study Partner or authority of legally authorized representative to subject (i.e. spouse, son, daughter, or friend)

_____

Please choose one:

If you are willing to volunteer for future research, in the boxes below, please put a check mark next to yes if you agree to the statement or no if you do not agree

Yes _____

No _____

TO BE FILLED OUT BY STUDY TEAM ONLY

_____
Name of Person Conducting Informed Consent Discussion

_____ _____
Signature of Person Conducting Informed Consent Discussion **Date** **Time**

_____