Sleep Disturbance and Emotion Regulation Brain Dysfunction as Mechanisms of Neuropsychiatric Symptoms in Alzheimer's Dementia

Informed Consent Form

NCT04100057

August 5, 2025

Looking to Understand Neuropsychiatric Symptoms in Alzheimer's Disease (LUNA Study)

Participant Consent Form

Are you participating in any other research studies? _____ **Yes** _____**No**

Summary of Key Points

- Consent is being sought for your participation in a research study.
- Participation in this study is voluntary and you are free to withdraw at any time. You have the right to refuse to answer any particular question.
- The purpose of this study is to research how sleep disruption and brain circuits relate to neuropsychiatric symptoms in those with mild cognitive impairment and mild Alzheimer's dementia. The study is being conducted only for the purposes of research.
- If completing the entire study, your total involvement will be 14 visits over nine months, six of which can be completed over Zoom:
  - Screening session: one two-part session
  - Baseline session: one two-part session
  - Therapy: six sessions over eight weeks
  - End of Therapy Session: one two-part session
  - Six-Month follow-up Session: one two-part session
- This study entails two MRIs, four PSG sleep recordings, one saliva sample, various questionnaires, standardized clinical interviews, and cognitive tasks.
- Both the EEG and fMRI are safe and have been used on many other participants.
- You will be randomized into one of two therapies. Both groups will meet with a therapist for six sessions over eight weeks. Therapy can be done in-person at Stanford or virtually, via Stanford Zoom.
- CBT-I targets behaviors and cognitions that sustain or add to patients' sleep problems.
- DT-I targets anxiety provoking associations that are activated when patients are trying to sleep and interfere with the sleep onset process.
- This study has minimal risks, but includes the risks associated with neuroimaging which are described below.
- The potential benefit of this study is a possible improvement in sleep.
- The alternative to participating in this study is to seek treatment from your physician for your insomnia symptoms.
- You will be compensated up to $650 for completing the study.

PURPOSE OF RESEARCH

You are invited to participate in a research study on how sleep and brain circuits relate to neuropsychiatric symptoms including anxiety, depression, agitation, irritability, and apathy. We hope to learn whether improving sleep will also improve brain function and reduce neuropsychiatric symptoms in those with or at high risk for developing Alzheimer's disease.

You may be a good fit for this study if you are between the ages of 50-90, experiencing memory problems that are consistent with MCI or mild Alzheimer's disease, having trouble sleeping, and also experiencing symptoms such as anxiety, depression, agitation, irritability, and/or apathy. In order to participate, you also need to have a spouse, friend, or relative—in other words, a "study partner"—who is willing to tell us about your functioning during the nine-month period of this study.

You have already completed a telephone interview about joining this research study. You are now receiving this consent form for you to read and think about before you participate further. The study staff will review the consent form with you and answer any questions you may have.

If you decide to terminate your participation in this study, you should notify Dr. Goldstein-Piekarski at (650) 721-4780.

This research study is looking for 150 participants with signs of mild cognitive impairment (MCI) or mild Alzheimer's disease dementia who are experiencing sleep disturbances. All participants will be enrolled in California. All 150 participants will complete study visits at Stanford University.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you are entitled. You have the right to refuse to answer particular questions.

DURATION OF STUDY INVOLVEMENT: How long will I be in the Study?

If you are eligible and agree to participate, you will be in the study for about nine months—including an eight-week period of receiving the study therapy, and a six-month period of follow-up.

PROCEDURES: What will happen if I take part in this research study

If you choose to participate, Dr. Andrea Goldstein-Piekarski and her research study staff will begin your participation in the study. Your participation would normally involve a total of 14 study visits which include two in-person visits for screening (including today), two in-person visits for baseline measurement, six in-person or virtual visits for therapy over eight weeks, two in-person visits at the end of therapy, and two in-person visits six months after completion of therapy for follow-up. You are required to have a study partner who can accompany you to some session visits in order to participate in this study. A study partner may not need to be present at therapy sessions.

SCREENING SESSION

There are two in-office screening sessions during evaluation. During the screening session, we will ask you to complete a number of cognitive and psychological tests and questionnaires about the nature of your sleep problem, memory impairment, and mood. You will also have a chance to bring up issues you believe are relevant to your sleep problem. We will also complete a modified, detailed medical history questionnaire and a standard evaluation of your sleep issues to determine if your sleep problem has a physiological basis.

- Medications: you may not take medications, drugs, herbal remedies, or hormones specifically prescribed for treating sleep disturbances while participating in the Therapy and End of Therapy phases of the study. Other medications, including those with sleep and mood side-effects, are acceptable if stable (at least 4 weeks of same dose/timing/formulation) at the time of recruitment.
- Sleep Reports: During the in-office session, we will show you how to complete daily sleep reports. A sleep report is designed to gather information about your daily sleep pattern. You will be asked to keep a daily sleep report for the night of the overnight screening, one week prior to the baseline visit, the entire eight-week therapy period, until the end of therapy visit, and for one week prior to the six-month follow-up session.
- Overnight Sleep Apnea Screen and Sleep Recording: As part of the screening session, you will complete a one-night ambulatory, overnight sleep recording that that will be set up by our study team at the lab for you to go home and sleep in. The sleep equipment is similar to a snug fitting swim cap with electrodes that connect to a small machine. In addition to the electrodes on the cap, there will also be small electrodes attached to your chin, jaw, and one each on your right collarbone and lower left rib. The machine connected to the wires will be put inside of a

fanny pack for your convenience. We will also fit a net over the cap to ensure that everything stays in place at night. You will also be set-up with portable equipment to measure your breathing while you sleep (Apnealink). Study staff will show you how to wear the Apnealink and send you home with instructions. You will return to the lab the next morning to have the sleep recording equipment removed. You will not be permitted to drive yourself while wearing the sleep recording equipment. If you are not able to arrange a ride with a friend or family member, we can provide transportation via a ride service (e.g., Lyft, Uber, etc.) for when you are wearing the equipment. In situations where you cannot arrange transportation to or from the lab for the screening session or any other study visit, we may also provide transportation via a ride service.

- Actigraphy Watch: You will be given an actigraphy watch to wear during the overnight sleep recording. This watch contains a small motion sensor, which is used to estimate your sleep and daily activity patterns. This watch does not track or record your location in any way; it only senses movement on your hand and light levels in the room.
- **Audio/Video Recording**: If you check "yes" below, we will make an audio/video recording of each assessment and therapy session, which will be evaluated by a research psychologist for quality control and training new staff. Therapy and assessments done in-person will be audio-recorded; assessments and therapy done over Stanford Zoom will be video-recorded. All audio/video recordings will be kept on a secure Stanford server or in a locked cabinet for the required period of six years after study closure, then destroyed. The team will always ask first before starting a recording and will not record without your knowledge.

_____ Yes, I give permission for audio/video recordings to be made, as set forth above.

_____ No, I do not give permission for audio/video recordings to be made.

If you choose to participate, Dr. Goldstein-Piekarski and her research study staff will enroll you into study procedures which include a baseline visit, therapy phase, and follow-ups.

BASELINE VISIT

If you are eligible to be in the study, you can enroll and move on to the Baseline Visit. The purpose of the Baseline Visit is to collect initial measurements of your sleep, mood, and brain functioning:

- On the evening before the full baseline visit you will complete a one-night ambulatory, overnight sleep recording that you will have set up in our lab and sleep with in your own home. You will return to the lab the next morning to have the equipment removed and complete the rest of the baseline visit. You will not be permitted to drive yourself while wearing the sleep recording equipment. If you are not able to arrange a ride with a friend or family member, we can provide transportation via a ride service (e.g., Lyft, Uber, etc.) for when you are wearing the equipment. In situations where you cannot arrange transportation to or from the lab, we may also provide transportation via a ride service.
- On the morning after the sleep recording you will be given written tests of your memory and thinking. You and your study partner will be asked to answer questions about your daily functioning, your sleep, your mood, and your behavior. You can skip any questions you do not want to answer. You can take breaks if needed.
- You will also undergo an MRI scan to take electronic pictures of your brain. MRI scanning is described in more detail later in this consent form.
- You will provide a saliva sample at this time. Please refer to the Genetic Testing section of this consent form for more information.
- You will be asked to complete two brief questionnaires regarding the COVID-19 Pandemic and related shelter-in-place restrictions. These questionnaires will ask you about your experience, thoughts, and feelings about the Pandemic.
- Actigraphy Watch: You will be given an actigraphy watch to wear continuously throughout the day and while you are sleeping until the end of therapy visit, and again for one week prior to the six-month follow-up visit. This will be sent to you in the mail approximately one week prior to the scheduled baseline visit. You will also be asked to wear this the night of the screening visit. This watch contains a small motion sensor, which is used to estimate your sleep and daily activity patterns. This watch does not track or record your location in any way; it only senses movement on your hand and light levels in the room. Anytime you will need a new actigraphy watch, you have the options for mail delivery or in-person pick-up/drop-off. If you prefer mail delivery, we will send you the new watch in a package, along with a return label for you to mail your old watch back to our lab office, if applicable. If you prefer an in-person handoff, you can visit the lab office during business hours to pick up/drop off a watch. Or, you can arrange an off-site pick-up/drop-off with us, in which two of our staff will meet you at an agreed location to give you a new watch, and collect the old watch, if applicable.

THERAPY PHASE

The Therapy Phase involves the following procedures:

Randomization to Therapy:

- You will have a fifty percent chance to be assigned to one of two therapies: Cognitive Behavioral Therapy for Insomnia (CBT-I) or Desensitization Therapy for Insomnia (DT-I). The two therapies teach you different skills and techniques to help reduce insomnia symptoms.
- You will not know which therapy you are randomized into until you have completed the study.
- Cognitive Behavioral Therapy for Insomnia (CBT-I): This therapy addresses thoughts and behaviors that can interfere with sleep. Thoughts and behaviors that develop in response to insomnia can result in heightened anxiety about sleep and the development of coping strategies that can ultimately worsen insomnia. This therapy aims to alter behaviors that contribute to sleep problems, and correct the beliefs that drive those behaviors. Therapy will also include sleep education.
- Desensitization Therapy for Insomnia (DT-I): This therapy addresses the heightened state of alertness that can occurs when experiencing difficulty sleeping. This heightened state of arousal develops over time in response to insomnia, and can make falling asleep more difficult. Since this response is learned, it can also be unlearned. This therapy teaches skills to reduce the heightened arousal that contributes to insomnia. Therapy will also include sleep education.

Therapy Scheduling:

- The therapy part of the study lasts eight weeks and you will complete a sleep report for each day during therapy. You have the option to complete therapy over Stanford Zoom or in-person at Stanford University. During the therapy, you will meet with the therapist for a total of six sessions over eight weeks. Each session lasts approximately 60 minutes.

Procedures for Therapy Visits:

- At each visit, we will ask you about any changes in medicines you might be taking. We will also ask you about any changes in health, mood, or behavior since your last visit, which may or may not be related to the study therapy. We will also confirm you have been wearing the actigraphy watch and check the battery levels.
- You will meet with a therapist for approximately an hour over Zoom or in-person.
- Your study partner will be invited to attend all therapy sessions with you.

- As described above, we will make an audio/video recording of each assessment and therapy session, which will be evaluated by a research psychologist for quality control and training purposes. In person sessions will be audio-recorded and Zoom sessions will be video-recorded. All audio/video recordings will be kept on a secure Stanford server or in a locked cabinet for the required period of six years after study closure, then destroyed.

END OF THERAPY VISIT

Approximately a week after your last therapy session, we want to repeat the tests you did at your baseline. The End of Therapy Visit is very important so that we can measure changes in your sleep, memory, mood, and brain function following therapy. At this visit you will repeat:

- Tests of memory and thinking, and questions about your mood and daily functioning.
- Overnight sleep recording
- An MRI brain scan
- A week of sleep reports

SIX MONTH FOLLOW-UP

You will return once more six months after the End of Therapy Visit. You will repeat:

- Tests of your memory and thinking. We will again ask you about your mood and daily functioning.
- Overnight Sleep Recording
- A week of sleep reports
- A week of wearing the Actigraphy Watch

- If you are still experiencing sleep difficulties after your participation in the study, we will offer personalized treatment sessions with a member of our team. In these booster sessions, we will address barriers to adherence and highlight strategies to improve sleep. You may learn some new skills to help reduce your insomnia symptoms.

MRI (MAGNETIC RESONANCE IMAGING)

An MRI machine uses a strong magnet and radiofrequency magnetic fields to take electronic pictures of your brain. The scanning procedure is very much like an X-ray or CT scan. You will be asked to lie on a long narrow couch for the scan (about 105 minutes) while the machine does its work. During this time you

will not be exposed to x-rays, but rather a strong magnetic field and radiofrequency magnetic fields, which you will not feel. You will, however, hear repetitive tapping noises that arise from the Magnetic Resonance (MR) scanner. We will provide earplugs or headphones that you will be required to wear. The space within the large magnet in which you lie is somewhat confined, although we have taken many steps to relieve the "claustrophobic" feeling.

The CNI scanner is an investigational system. The CNI scanner shares much of the same hardware and software of the FDA approved systems but has improved performance due to a better performing gradient coil. The CNI scanner has magnet strength, SAR limits, slew rates and noise characteristics consistent with the FDA approved scanners, so there is no additional risk.

Some of the radio frequency imaging coils, imaging software and devices being used in your scan are not approved by the FDA but are similar to counterparts that have been approved by the FDA. There is a small risk of heating from the cables associated with these devices. Steps will be taken to reduce the likelihood of this occurring. Please report any heating sensation to the research staff immediately.

GE Healthcare, the manufacturer of the MR scanners, will be supporting this research by providing some of the software for the MR scanner. This software provided by GE Healthcare has not been approved by the FDA and is considered to be investigational but from a safety standpoint, poses no significant risk to you. Dizziness or nausea rarely may occur if you move your head rapidly within the magnet.

IF YOU FEEL DISCOMFORT AT ANY TIME, NOTIFY THE OPERATOR AND YOU CAN DISCONTINUE THE EXAM AT ANY TIME.

The scans performed in this study are for specific research purposes and are not optimized to find medical abnormalities. The investigators for this project may not be trained to perform medical diagnosis. The investigators are not responsible for failure to find existing abnormalities with these MRI scans. However, on occasion the investigator may notice a finding on an MRI scan that seems abnormal. If this occurs, a doctor will be asked to look at the images to see if any medical follow-up is needed. If so, the investigator will contact you and recommend you inform your doctor about the findings. Because the images are taken using research settings, they will not be made available for clinical purposes.

The MRI will take about 60 minutes of actual scanning, plus another ½ hour or so to prepare. The MRI will be performed at the Stanford University Medical Center for Cognitive and Neurobiological Imaging (CNI).

In the event that the scan has poor image quality and cannot be used, we will ask you if you would be willing to repeat the MRI scan.

Risks:

Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MR scanner uses a very strong magnet that will attract some metals and affect some electronic devices. If you have a cardiac pacemaker or any other biomedical device in or on your body, it is very important that you tell the operator/investigator immediately. As metallic objects may experience a strong attraction to the magnet, it is also very important that you notify the operator of any metal objects (especially surgical clips), devices, or implants that are in or on your body before entering the magnet room. All such objects must be removed (if possible) before entering the magnet room. In some cases, having those devices means you should not have an MRI scan performed, so it is very important that you notify the operator. In addition, watches and credit cards should also be removed as these could be damaged. You will be provided a way to secure these items. If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop, or if you could be pregnant, you should notify the operator/investigator. You should also notify the operator/investigator if you have any tattoos on your body, including eyeliner and other permanent makeup. Tattoos could become warm and irritated during the scan and remain so for several days.

There is a possibility that you will experience a localized twitching sensation due to the magnetic field changes during the scan. This is not unexpected and should not be painful. However, you may have the scan stopped at any time if this occurs. There is also a possibility of tinnitus (ringing in the ears) after the MRI.

During one of the imaging tasks, you will be asked to view neutral and negative images shown on the screen. Some images may be shocking, repulsive, disturbing, or lewd. Most people will find parts of this 13-minute task difficult, unpleasant, upsetting, and stressful. As a result, engaging in this task may be difficult, frustrating, and emotionally challenging. If this happens, please tell us and we will take a break.

The MRI will make a variety of noises during the scan called acoustic noise. Problems associated with acoustic noise include simple annoyance, difficulties in verbal communication, heightened anxiety, temporary hearing loss, and, potentially, permanent hearing impairment. Acoustic noise may pose a particular hazard to specific subject groups who are at increased risk. Subjects with psychiatric disorders, the elderly and pediatric subjects may be confused or experience heightened anxiety. Various techniques have been described to attenuate noise and, thus, prevent problems or hazards associated with exposure to MRI-related acoustic noise. All participants will be required to wear earplugs while in the scanner. When properly used, earplugs can decrease noise by about

20-40 dB, which affords adequate protection for MR environments. Additional hearing protection may be provided to participants upon request.

WOMEN OF CHILDBEARING POTENTIAL

If you are a woman who is able to become pregnant, it is expected that you will use an effective method of birth control to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If you are pregnant or currently breast feeding, you may not participate in this study. You understand that if you are pregnant, if you become pregnant, or if you are breast-feeding during this study, you or your child may be exposed to an unknown risk.

If you are unsure of the possibility of being pregnant, you will be given a pregnancy test that will be provided for you.

You must accept the risk that pregnancy could still result despite the responsible use of reliable method of birth control. You agree to notify the investigator as soon as possible of any failure of proper use of your birth control method, or if you become pregnant, either of which may result in your being withdrawn from the study.

FUTURE USE OF PRIVATE INFORMATION AND/OR SPECIMENS

Future Use of Private Information, Study Data, and Specimens

Research using private information and/or specimens is an important way to try to understand human disease. You are being given this information because the investigators want to save private information and/or specimens for future research. Information from study procedures, including your imaging data and questionnaire responses may be put into one of the National Institutes of Health (NIH) databases along with information from the other research participants and will be used for future research. All data will be de-identified.

National Data Archive:

Data from this study will be submitted to the National Institute of Mental Health Data Archive (NDA) at the National Institutes of Health (NIH). NDA is a large database where coded study data from many NIH studies are stored and managed. Sharing your coded study data helps researchers learn new and important things about brain science more quickly than before.

Coded study data means that all personal information about you (such as name, address, birthdate and phone number) is removed and replaced with a code number. The study researchers will have to collect your personal information from you in order to make that code number. The code number cannot be used to identify you. The study researchers will never send your personal information to NDA.

It is possible that you will participate in more than one study that sends data to NDA. NDA can connect your data from different studies by matching the code number from each study. This data matching helps researchers who use NDA data to count you only one time. It also helps researchers who use NDA to better understand your health and behavior without knowing who you are.

During and after the study, the study researchers will share coded study data about your health and behavior to the NDA. Other researchers across the world can then request your coded study data for different research projects. Every researcher (and the institution to which they belong) who requests your coded study data must promise to keep your data safe and promise not to try to learn your identity. Experts at the NIH who know how to keep your data safe will review each request carefully to reduce risks to your privacy. Sharing your study data does have some risks, although these risks are rare. Your study data could be accidentally shared with an unauthorized person who may attempt to learn your identity. The study researchers will make every attempt to protect your identity.

You may not benefit directly from allowing your study data to be shared with NDA. The study data provided to NDA may help researchers around the world learn more about brain science and how to help others who have problems with brain science. NIMH will also report to Congress and on its website about the different studies using NDA data. You will not be contacted directly about the study data you contributed to NDA.

You may decide now or later that you do not want your study data to be added to NDA. You can still participate in this research study even if you decide that you do not want your data to be added to NDA. If you know now that you do not want your data in NDA, please tell the study researcher before leaving today. If you decide any time after today that you do not want your data to be added to NDA, call or email the study staff who conducted this study, and they will tell NDA to stop sharing your study data. Once your data is part of NDA, the study researchers cannot take back the study data that was shared before they were notified that you changed your mind. If you would like more information about NDA, it is available on-line at http://nda.nih.gov.

_____ Yes, I give permission for my de-identified data to be shared with the NDA

_____ No, I do not give permission for my de-identified data to be shared with the NDA

Saliva collection:

We may collect samples of saliva from you, which will require you to either spit into a container and/or to hold a cotton swab in your mouth for several minutes. You will be asked NOT to eat or drink anything, including water, 30 minutes prior to your saliva collection. We plan to use the saliva to extract DNA from the cells in your saliva. Your specimens will be stored in a locked drawer after collection and then in locked freezers after analysis. Any left-over saliva after doing these tests will be saved for future uses. Your sample and information about you will be labeled with a code that does not contain your name, initials, SSN, date of birth, or other ways that identify who you are. The research we conduct with your sample is being done for research purposes only and we will not tell you or your doctor about the results of the research.

You may withdraw your permission for us to use your saliva for future research at any time. Contact the investigators to withdraw your permission. If you take back your permission, the research team can continue to use information about you collected before you decided to take back your permission, but they will not collect any information about you going forward and any remaining samples and the code linking you to the samples will be destroyed. Identifiers might be removed from identifiable private information and/or identifiable specimens and, after such removal, the information and/or specimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

The research we conduct using your saliva may result in inventions or discoveries that could be used to make new products or diagnostic or therapeutic agents. These inventions and discoveries may become financially valuable. You will not receive any money or other benefits from any commercial or other products that are made using your specimens. Please initial below.

_____ Yes, I give permission for my samples to be saved for futureresearch, as set-forth above.

_____ No, I do not give permission for my samples to be saved for future research.

Genetic tests will be conducted on your samples. The tests we plan to do will allow us to study how differences in the code of your genes relates to the function of your brain circuits and to behavior. This research will inform an understanding of how differences in genetic code are reflected by differences in function in the nervous system, which may also be relevant to risk for psychiatric illness or response to therapies.

Your specimens will be stored until the sample is all used up. Both your samples and your research information will be labeled with a code that does not contain your name, initials, social security number, date of birth, or other ways that identify who you are.

The results of the study of your specimens from this project will be used for research purposes only. You will not be told the results of any of your genomic testing, even if some of the genes are related to disease risk. No information regarding your genetic or biomarker tests results will be entered in your medical records. If you are concerned about a potential genetic disorder, you should discuss this with your primary care doctor. You and your doctor may choose to test specifically for it, but this would require separate blood samples and would not be part of this research study.

Information from analyses of your coded samples and your coded medical information may be put into one of the National Institutes of Health (NIH) databases along with information from the other research participants and will be used for future research. If so, these databases will be accessible by the Internet. Only anonymous information from the analyses will be put in a completely public database, available to anyone on the Internet.

No traditionally-used identifying information about you, such as your name, address, telephone number, or social security number, would be put into the public database. While the public database will not contain information that is traditionally used to identify you, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It also is possible that there could be violations to the

security of the computer systems used to store the codes linking your genetic and medical information to you.

However, your privacy is very important to us and we will use safety measures to protect it. Despite all of the safety measures that we will use, we cannot guarantee that your identity will never become known.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

We will protect the confidentiality of your samples and information about you. Your samples will be stored in a locked area and all information about you will be stored in a locked file cabinet or on a password protected secure computer.

PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the Protocol Director and study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the Protocol Director or research study staff to reschedule as soon as you know you will miss the appointment.
- You are required to be fully vaccinated (i.e. received 2 doses of Moderna or BioNTech, Pfizer vaccines; or 1 Johnson and Johnson) and willing to provide proof (e.g., CDC COVID-19 Vaccination Card, e-Health record, etc.) if asked
- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Tell the Protocol Director or research staff if you believe you might be pregnant.
- Keep your diaries as instructed.
- Complete your questionnaires as instructed.
- Wear your actigraphy watch each day as instructed.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.
- Return all laboratory equipment that you take home.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for any condition and you will not lose any benefits to which you would otherwise be entitled.

If you decide to withdraw your consent to participate in this study, you should notify the Principal Investigator, Dr. Andrea Goldstein-Piekarski at (650) 721-4780.

If you withdraw from the study, for any reason, you must return any study-related equipment still in your possession.

The Protocol Director may also withdraw you from the study without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your participation could be harmful to you.
- Pregnancy
- You need treatment/therapy not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions. This study involves the following risks, discomforts, and possible inconveniences:
Evaluation and testing. There are virtually no risks involved in the cognitive testing and psychological measurements other than the anxiety that can be associated with any test. It is possible that you might become tired or frustrated by some of our testing. You may find answering the questionnaires annoying, boring, or repetitive. Evaluations of mood and mental status may be slightly frustrating, produce fatigue and boredom, or elicit an emotional response. If this happens, please tell us and we will take a break or skip a particularly difficult test. If the research staff has reason to believe you may be having suicidal thoughts, you will be asked to speak to a clinician trained in suicidality risk assessment.

The responses to questions concerning illegal drug use could be self-incriminating and harmful to you if they became known outside the study. As explained in the confidentiality statement of the consent, we do not intend to disclose this information.

Sleep Log and Questionnaires. There are no harmful effects to filling out the sleep log and questionnaires, but you may find answering the questionnaires annoying or boring.

Sleep recording. The ambulatory overnight recording offers minimal risk other than a certain discomfort due to the attached sensors which may slightly affect your sleep quality during that night. The tape or glue used to attach the sensors to your skin might cause a minor skin irritation (rash). If this were to occur, we recommend putting lotion on the irritation.

Additionally, it is possible that the wires from the sleep equipment could fall in your face and obstruct your view. To minimize the risk this poses, we will not allow you to drive while wearing the equipment. If you are not able to have a friend or family member drive you, we will provide transportation when you are wearing the sleep recording equipment. In situations where you cannot arrange transportation to or from the lab, we may also provide transportation via a ride service.

Actigraphy Watch. Wearing an actigraph device may cause physical discomfort, but is akin to wearing similar wristwatches, such as a Fitbit, Apple Watch, or other equivalent heart rate/activity monitors. You will be asked to adhere, to the best of your ability, to wearing the device for 24 hours a day, every day from one week prior to baseline to the end of therapy visit, and one week prior to the six-month follow-up through the six-month follow-up visit. You will be able to take off the actigraph device in case of discomfort or any other reason that may require you to do so for the amount of time you require.

Therapies. Non-pharmacological therapies for insomnia like Cognitive Behavioral Therapy and Desensitization Therapy may lead you to challenge some of your thoughts and concerns about the way you sleep. The therapy may lead you to adopt a more flexible cognitive stance regarding your sleep. Some people may find this uncomfortable. In addition, you may feel overly sleepy, cranky, or disoriented during the first few days of therapy. It is recommended that you avoid driving, operating machinery, or doing activities that require close attention for the first few days of therapy. Sleep efficiency training has been known to trigger seizures in people with seizure disorders and to have possible negative effects on mood in people with bipolar disorder. For this reason, people with these disorders are not eligible for this study.

There is always the possibility that your sleep might get worse during therapy. In general, most patients benefit from the proposed therapies, but it is always

possible that an individual can experience unwanted changes in their sleep pattern.

Audio/video recordings. The risks associated with recording audio from in-person therapy and assessments and video from Zoom therapy and assessments include: privacy and confidentiality risks and feelings of discomfort. Additionally, it may be easier for someone to identify you from a Zoom video recording as opposed to recordings from in-person sessions (audio only). Agreeing to audio/visual recordings is optional and not required to participate. Additionally, you may refuse to record any individual sessions at your discretion. The research team will always ask permission before starting a recording. As stated above, our team does everything to ensure the security of these recordings.

Personal Items. We are not responsible for any damage to personal property or any stolen personal items while you are on campus.
Magnetic Resonance Imaging. See risks of MRI imaging on page six.

Risk of COVID-19
The research staff has implemented precautions to reduce the risk of COVID-19 infection, including:

1. COVID-19 screening call: The day of the in-person study visit, a member of the research staff may call you to ask a series of questions or ask you to fill out an online questionnaire regarding COVID-19 symptoms and indicators of risk to determine if you are cleared for an in-person study visit.

2. Vaccination Requirements: The research staff have all been fully vaccinated and received their booster shots. When coming in-person to research visits, you are required to be fully vaccinated—2 doses (1 for Johnson and Johnson), 2 weeks out. You are also required to be willing to provide additional proof of your vaccination (e.g., CDC COVID-19 Vaccination Card, e-Health record, etc.) to the researcher, if asked, prior to study participation.

3. Social Distancing: Research staff and participants will practice social distancing (> six feet of separation) from individuals not in their household when possible.

4. Face Coverings: Research staff and participants will receive procedural masks on entry to CNI and they must be worn at all times.

5. Redundant Disinfection Protocols: All equipment, including the MRI system and scan accessories at CNI receive thorough cleaning twice between each study using cleaning/disinfection supplies approved by the Environmental Protection Agency (EPA) for reducing risk of infection. This is completed once at the end of

a scan, and again prior to starting a new scan. Commonly touched surfaces (door handles, faucets, counters, restrooms) also receive frequent cleaning.

6. Hand Sanitation: Research staff and participants are encouraged to practice good hand hygiene – washing their hands with soap and water or using the available hand sanitizer and to not touch their eyes, nose or mouth with unwashed hands.

These precautions are deemed to significantly reduce the risk of infection, but it is important to recognize that by increasing your contact with other individuals and physical locations, your level of risk of COVID-19 infection does increase.

It is important that you disclose to the research staff any indication of having been exposed to COVID-19, or whether you have experienced any signs or symptoms associated with COVID-19 disease.

Please select an option and initial below.

_____ Yes, I understand that by participating in this study and interacting with new physical locations and individuals that I am increasing my risk of COVID-19 infection. I also acknowledge that I could contract COVID-19 unrelated to my in-person visit at Stanford.
_____ No, I would not like to participate in this study due to the possible increased risk of COVID-19 infection.

POTENTIAL BENEFITS

There may be no direct benefits to you for participation in this study. Your sleep and mood may improve. Your participation may help us to learn more about the causes of insomnia and neuropsychiatric symptoms.

WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY DIRECT BENEFITS FROM THIS STUDY.

ALTERNATIVES

You do not have to participate in this research study in order to receive treatment for any medical condition. There are other behavioral therapies for sleep problems and neuropsychiatric symptoms, as well as various drug treatments for sleep problems and neuropsychiatric symptoms, that are not

included in this study. A study clinician can discuss any alternatives with you before you agree to participate in this study.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. If you decide not to participate, tell the Protocol Director.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

ClinicalTrials.gov

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.

CONFIDENTIALITY

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed except as authorized by you or as required by law**.** However, there is always some risk that even de-identified information might be re-identified.

Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

CERTIFICATE OF CONFIDENTIALITY

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or specimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or specimens protected by this Certificate cannot be disclosed to anyone else who is not

connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of child abuse and neglect, or harm to self or others.

Authorization To Use Your Health Information For Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?
This research study of on how sleep and brain circuits relate to neuropsychiatric symptoms including anxiety, depression, agitation, irritability, and apathy. We will compare two therapies for insomnia and we hope to learn how each therapy effects the brain circuits involved in sleep and neuropsychiatric symptoms. Your health information will be used to help us determine how sleep and brain circuits relate to neuropsychiatric symptoms.

Do I have to sign this authorization form?
You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study including receiving any research-related therapy. Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?
If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (e.g., necessary to maintain integrity of research). If

you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to: Dr. Andrea Goldstein-Piekarski at 401 Quarry Rd, Palo Alto, CA 94305 or agoldpie@stanford.edu.

What Personal Information Will Be Obtained, Used or Disclosed?
Your health information related to this study, may be used or disclosed in connection with this research study, including, but not limited to:
Full legal name, social security number, telephone number, mailing and email addresses, date of birth, place of birth, date of visit, detailed medical history and neurological assessment information, including any trauma or illness which may impact sleep; Full name and email and/or phone number of an emergency contact; Progress notes from study visits; Saliva specimens and related laboratory results; Survey and Questionnaire responses collected for this study; Psychological and cognitive test results collected for this study, and mental health notes made by study therapists; Sleep logs and overnight sleep recordings; Audio/Video recording of therapy and study assessments; Proof of Vaccination (e.g. CDC COVID-19 Vaccination Card, e-Health record, etc.) if asked; Device identifiers and serial numbers may be obtained to determine whether personal equipment, implanted devices, implants, prostheses, or prosthetics are fMRI-safe and whether the presence of the item is permissible in the fMRI scan room. Additional research records (clinical, neurocognitive, behavioral, magnetic resonance imaging (MRI), electroencephalogram (EEG), psychophysiological (including heart rate, respiration, pupil size, eye tracking, skin conductance), genetic, and combinations of the above) will be reviewed and analyzed by the research staff. Vehicle identifiers, including license plate numbers, and certificate/license numbers may be obtained for purposes regarding parking and transport around the Stanford, and will be requested in special circumstances, as described in following. Parking is heavily regulated on the Stanford campus. In rare events, parking permits that are assigned to participants have been incidentally misplaced causing the issuance of parking violation tickets. Vehicle identifiers, license plates, and certificate/license numbers are obtained for the purposes of resolving these parking-related issues when these occur.

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director Dr. Andrea Goldstein-Piekarski
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary
- Research Staff

Who May Receive or Use the Information?

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- The National Institute of Health
- The Food and Drug Administration (FDA)

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?

Your authorization for the use and/or disclosure of your health information will end on December 31, 2045 or when the research project ends, whichever is earlier.

Will access to my medical record be limited during the study?

To maintain the integrity of this research study, you may not have access to any health information developed as part of this study until it is completed. At that point, you would have access to such health information if it was used to make a medical or billing decision about you (e.g., if included in your official medical record).

_____ _____
Signature of Adult Participant Date

_____
Print Name of Adult Participant

_____ _____
Signature of Legally Authorized Representative (LAR) Date
(e.g., parent, guardian or conservator)

_____
Print Name of LAR

_____
LAR's Authority to Act for Participant
(e.g., parent, guardian or conservator)

FINANCIAL CONSIDERATIONS

Payment/Reimbursement
You will receive $50 for the screening visit.

If you are deemed eligible, you will be compensated an additional $175 for completing the baseline visit which includes an overnight sleep recording, fMRI scan, cognitive, and psychological assessments.

You will receive $175 for completing the end of therapy follow-up and an additional $100 for completing the six-month follow up visit.

Additionally, you will receive a $50 bonus after completing the end of therapy visit and a $100 bonus after study completion.

This payment is to help cover any expenses you may incur in the course of your participation, such as costs of transportation and telephone calls to our offices.

Payments may only be made to U.S. citizens, legal resident aliens, and those who have a work eligible visa. You may need to provide your social security number to receive payment.

Costs
There is no cost to you for participating in this study, other than basic expenses like transportation and the personal time it will take to come to all of the study visits.

Sponsor
The National Institute of Health is providing financial support and/or material for this study.

COMPENSATION for Research-Related Injury

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you in obtaining appropriate medical treatment. In the event that you have an injury or illness that is directly caused by your participation in this study, reimbursement for all related costs of care first will be sought from your insurer, managed care plan, or other benefits program. **You will be responsible for any associated co-payments or deductibles as required by your insurance.**

If costs of care related to such an injury are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, the Protocol Director will assist

you in applying for supplemental benefits and explain how to apply for patient financial assistance from the hospital.

You do not waive any liability rights for personal injury by signing this form.

CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of therapy, you should ask the Protocol Director, Dr. Andrea Goldstein-Piekarski. You may contact her now or later at (650) 721-4780.

Injury Notification: If you feel you have been hurt by being a part of this study, please contact the Protocol Director, Dr. Andrea Goldstein-Piekarski at (650) 721-4780.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.

Appointment Contact: If you need to change your appointment, please contact the LUNA Study Staff at lunastudy@stanford.edu or at 650-721-6089.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;

- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you about future studies that may be of interest to you?
☐ **Yes** ☐ **No**

Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

_____ _____
Signature of Adult Participant Date

_____
Print Name of Adult Participant

_____ _____
Signature of Legally Authorized Representative (LAR) Date
(e.g., parent, guardian or conservator)

_____ _____
Print Name of LAR LAR's Authority to Act for Participant
(e.g., parent, guardian or conservator)

_____ _____
Signature of Person Obtaining Consent Date

_____
Print Name of Person Obtaining Consent