UNIVERSITY OF CALIFORNIA, IRVINE
CONSENT TO ACT AS A HUMAN RESEARCH SUBJECT

Enhancing memory consolidation in older adults

You are being asked to participate in a research study. Participation is completely voluntary. Please read the information below and ask questions about anything that you do not understand. A researcher listed below will be available to answer your questions.

RESEARCH TEAM
Lead Researcher
Sara C. Mednick, PhD
Department of Cognitive Sciences
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Other Researchers
Steven C. Cramer, MD – UC Irvine School of Medicine
Sara J. Stern-Nezer, MD – UC Irvine School of Medicine

STUDY LOCATION(S):
UC Irvine Institute for Clinical and Translational Science (ICTS), Irvine, CA
UC Irvine Institute for Clinical and Translational Science (ICTS), Orange, CA
Sleep and Cognition (SaC) lab in the Social Science Research building, room 380

STUDY SPONSOR(S):
National Institute of Health, Grant #: R01AG046646

WHY IS THIS RESEARCH STUDY BEING DONE?

The purpose of this research study is to understand the neural mechanisms underlying long-term memory formation in older adults. Both sleep and memory decrease with age. We are interested in discovering whether these two biological changes are related. This study is specifically focused on understanding what are the critical components of sleep that facilitate memory formation and are they impaired in older adults. We will be using the hypnotic zolpidem, a sleep drug that has been shown to increase a specific aspect of sleep that have been shown to correlate with memory improvement in young adults. The Food and Drug Administration (FDA) have approved zolpidem for use in certain sleep disorders, specifically in the treatment of sleeplessness (i.e., insomnia). In the current study, we will examine whether zolpidem (5mg), compared with placebo, increases memory-related sleep events in older adults and test the impact of these drug-related sleep changes on post-sleep memory recall.

This is a research study because we are using pharmacological interventions to investigate our hypotheses about memory consolidation. We are not investigating the efficacy of zolpidem to treat conditions for which the FDA has already approved it.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Approximately 60 participants will take part in the research at UCI.

AM I ELIGIBLE TO PARTICIPATE IN THIS STUDY?

Please note this may not be a complete list of eligibility criteria. We have included a few examples of study criteria to help you better understand how your eligibility in the study will be determined; your study team will go through the study eligibility criteria with you to verify if you qualify for participation in this study.

Inclusion Requirements
You can participate in this study if you are a healthy, English-speaking, non-smoking adult between the ages of 60 to 75 without major medical problems. You must have a regular sleep-wake schedule, defined as obtaining 6-9 hours of sleep per night, with a habitual bedtime before 2am and a habitual wake time before 10am, and must have experience with Ambien to participate in the study.

Exclusion Requirements
You cannot participate in this study if you: a) have a sleeping disorder (reported or detected on the questionnaires); b) have any personal or immediate family (i.e., first degree relative) history of diagnosed mental disorders; c) have any personal history of head injury with loss of consciousness greater than 2 minutes or seizures; d) have a history of substance dependence; e) currently use any medications that could affect sleep and/or thought processes; f) have any cardiac, respiratory or other medical condition which may affect cerebral metabolism; g) have dementia i) have non-correctable vision and hearing impairments, due to the nature of the stimulus and its presentation, will also be excluded.

HOW LONG WILL THE STUDY GO ON?
You will be involved in this study for about three weeks, although this time frame may be extended for scheduling purposes. Your involvement will include the following: in-person interview (1 hour), orientation (4 hours), medical history and physical appointment (30 mins), and two nap experimental visits (6:30am-8pm, total: 13.5 hours/visit).

The study will consist of two nap visits with at least one week in-between visits. The timing of each visit will be from 6:30am to 8pm. During both visits, you will complete cognitive testing, questionnaires/surveys, and be asked to take a nap. Before each nap, you will be given a pill (either Zolpidem or Placebo). After the nap, subjects will continue to stay in the lab to complete further cognitive testing and will be supervised and checked for any side effects.

WHAT PROCEDURES ARE INVOLVED WITH THIS STUDY?
Before you can participate in the main part of the study...
You will need to have "screening" exams, tests or procedures. The screening process helps the researchers decide if you meet the study requirements listed below. The screening procedures include:

- **In-person interview**
  You will meet with a research staff for approximately 1 hour. During this time, you will be asked about medical or psychiatric conditions you may have, family history of medical or psychiatric conditions and your use of prescription and recreational drugs, alcohol, coffee, and cigarettes. Additionally, you will be told about all study procedures.
- **Orientation**
  During this appointment, you will be given questionnaires about your sleep-wake habits, mood and psychological status, and history of psychiatric symptoms. If any part of this process makes you uncomfortable, you are not obligated to answer and may choose to skip any question. In addition, you will be expected to inform the investigators of anything that occurs during the study that may affect your ability to fully participate in the study, including starting or stopping any prescription or over-the-counter medications. Your results will only be shared with authorized research personnel to determine eligibility for this study and not for other purposes. Afterwards you will complete four tests that measure cognitive abilities that include:
    - Digit span forward: You will be presented with a list of items and will be asked to repeat them in the same order. Items may include words, numbers or letters.

- Digit span backward: You will be presented with a list of items and will be asked to repeat them in reverse order. Items may include words, numbers or letters.
- Stroop task: In this task, you will be presented with the name of a color that is printed in a color different from the name and will be asked to name the color.
- Symbol digit task: This task deals with viewing a list of digit-symbol pairs followed by a list of digits. You will then be asked to type of the corresponding symbol under each digit as fast as possible.

You will then be hooked up to an EEG cap and be given an opportunity to nap for two-hours, which is monitored.

- **Medical history and physical appointment**

  If you remain eligible after the initial screening interview, you will be scheduled for a medical history and physical appointment at the UCI Institute for Clinical and Translational Science (ICTS). During this interview, you will also be asked to provide a urine specimen sample. This sample will be used for a toxicology screen to ensure you have not engaged in recreational drug use. Prior to leaving the medical appointment, you will be loaned an actigraph, an activity monitor the size of a watch that measures movement, that needs to worn for one week prior to each test day. You will also be asked to maintain a regular sleep-wake schedule for one week prior to each test day. This means you will pick a two-hour window at night and always go to bed during that window and a two-hour window in the morning and always wake up during that window. You must follow this schedule 7 days a week, even on weekends. During the period when you are maintaining a regular sleep-wake schedule, you will be asked to log your sleep-wake schedule, caffeine, alcohol, and drug use with a daily Sleep Diary. You will also be asked to refrain from caffeine, alcohol, and any medications not approved by the study staff starting 48 hours prior to each test day. The night before each study day, you will be required to spend 8 hours time-in-bed from 10pm-6am, All of this is to assure that you have obtained an adequate amount of sleep prior to the study and that you have not consumed any substance that interferes with your sleep.

During the main part of the study...

If the screening exams, tests and/or procedures show that you can continue to be in the study, and you choose to take part, then you will have the following procedures and tests done. The main study tests and procedures include:

- **Study Day Timeline**
  - Test Session 1 - You will report to the lab at 6:30am and complete two cognitive tasks, word pair associates task and finger tapping task, starting at 7am. During the word pair associates task, you will be presented with word pairs and asked to remember them as you will be tested on them later. As for the finger tapping task, you will be shown a string of five digits and be asked to type the string of letter as quickly and as accurately as possible for 30 seconds. Each of these tasks take about 30 minutes to complete.
  - EEG Cap Setup - After completing these tasks, electrodes will be attached to your scalp and body using a conductive paste. We will use rubbing alcohol to clean your skin/scalp and remove any excess dirt, oil or makeup. Prior to attaching the electrodes, we will use an exfoliating gel and cotton swab to lightly scrub your skin/scalp to remove any dead skin cells.
  - Drug Administration - At 9am, you will be provided a snack. At 9:30am, you will be administered one of two possible drug treatments (i.e. 5mg zolpidem, or placebo (a pill that looks like the investigational drug but it includes no active ingredients). You will always be given a pill administered in a double-blind fashion, meaning that neither you nor the researcher(s) conducting the study will know which treatment you are receiving - only the research pharmacists know which treatment you are receiving.
  - Nap - Following drug administration, you will be asked to take a nap for 2 hours (from 10am-12pm) where your sleep will be monitored with routine clinical polysomnographic procedures (i.e., a sleep study). We will monitor you the entire time you are in the lab

(including monitoring vital signs after the drug ingestion) and will ask you about possible drug effects and side-effects at several time points after you take the pill.
  - Break - During your down-time in the lab you will be able to watch TV, listen to music, read, eat snacks, etc. but will not be able to leave the lab, take any additional naps, or consume caffeine or alcohol. Lunch will be served during your down-time and you will be offered an opportunity to stretch your legs, accompanied by a team member.
  - Test Session 2 -
  - At 7pm, you will have a second test session in which you will do different versions of the tasks you learned earlier that day. Once testing is completed, research personnel will complete a side effects mobility test to ensure that you are well to leave the lab. If you experience any adverse events or do not pass the mobility test, you will remain in the lab until symptom free.

- **Transportation:** During visit days, you will not be allowed to drive or operate a vehicle. You will need to be dropped off and picked up by a friend or family member at the beginning and end of your visit day.

- **Surveys/Questionnaires** – Throughout the study day, you will complete a variety of questionnaires to evaluate sleepiness, sleep quality, and mood.

- **Study Equipment:** You will be loaned an actigraph device to wear for one week prior to each test day. Instructions for caring for the actigraph are listed below:
  - Remove the actigraph only when in water (e.g., showering, swimming, etc.), if playing a high impact sport (e.g., football), or if any risk of damage. Put watch back on **immediately** after such an instance.
  - Any time you remove the actigraph, record the interval that the watch was off and why in your sleep diary.
  - Although the actigraph is not an extraordinarily delicate instrument, it must still be handled with care. Do not strike it against anything rigid and do not drop it.
  - You will sign for the particular actigraph issued to you (on a separate form). It is a valuable piece of instrumentation, and you will be responsible for its safe return.
  - While wearing the actigraph, carry on in your normal daily activities. You will quickly adjust and will soon forget about it during day-to-day activities.
  - It is extremely important that you wear the watch at night.

WHAT ARE THE POSSIBLE SIDE EFFECTS OR RISKS RELATED TO THE STUDY?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. Side effects may be mild or very serious. The researchers may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the drug. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to the research team about any side effects you experience while taking part in the study.

Risks and side effects related to **Ambien** include those which are:

Likely

- Drowsiness
- Dizziness
- Diarrhea

- Grogginess or feeling as if you have been drugged

Rare but serious

- Getting out of bed while not being fully awake and do an activity that you do not know you are doing. After taking AMBIEN, you may get up out of bed while not being fully awake and do an activity that you do not know you are doing. The next morning, you may not remember that you did anything during the night. You have a higher chance for doing these activities if you drink alcohol or take other medicines that make you sleepy with AMBIEN. Reported activities include: driving a car ("sleep-driving"), making and eating food, talking on the phone, having sex, and sleep-walking
- Abnormal thoughts and behavior. Symptoms include more outgoing or aggressive behavior than normal, confusion, agitation hallucinations, worsening of depression, and suicidal thoughts or actions. Ambien may cause serious effects, including:
- Memory loss
- Anxiety
- Severe allergic reactions. Symptoms include swelling of the tongue or throat, and trouble breathing. Get emergency medical help if you get these symptoms after taking Ambien.
- Falls, which may lead to severe injuries.

Risks and side effects related to **actigraphy devices** include those which are:

Likely

- Discomfort from wearing the actigraph device if you are not used to wearing a wrist-watch.

Risks and side effects related to the **EEG-equipment** include those which are:

Likely

- Discomfort from wearing the electrodes
- Feel skin irritation caused by the electrode cream and skin exfoliating process

Risks and side effects related to the **procedures** include those which are:

Likely

- Discomfort from refraining from sleeping outside of the designated sleep periods during the experiment visits.
- Discomfort from refraining to consume caffeine of any kind 48 hours before your test day and until you are done with the testing procedure that day.

Placebo: During this study there is a 50% chance that you will receive a placebo. This could lengthen the amount of time before you receive a treatment that may be effective. During this time you may experience worsening of your condition. The researchers will carefully monitor your condition. If your symptoms worsen and make you uncomfortable, you can withdraw from the study.

Confidentiality: There may be a risk of breach of confidentiality during this study.
Psychological discomforts: Some of the procedures may cause embarrassment or anxiety, or the questions the researchers ask you may be upsetting or make you uncomfortable. If you do not wish to answer a question, you can skip it and go to the next question. If you do not wish to participate you can stop.

Unknown risks: There may be risks related to the research that we don't know about yet. However, you will be informed of any additional risks to which you may be exposed, and any changes that are made to the study, as a result of any newly-identified risks.

Reproductive Risks: You should not get pregnant while in this study as it is not known if the drug used in this study could harm an unborn baby. Check with the researchers about what types of birth control, or pregnancy prevention, to use while in this study. You should also not breastfeed a baby while in this study, for the same reason**.**

ARE THERE BENEFITS TO PARTICIPATING IN THIS STUDY?

Participant Benefits

You will not directly benefit from participation in this study.

Benefits to Others or Society

Other people may receive the following benefits from the information gathered from this study: The investigators may learn more about how sleep affects memory. This may prove important in leading to treatments in a wide range of disorders as well as enhancement of normal cognition.

WHAT OTHER CHOICES DO I HAVE IF I DON'T WANT TO PARTICIPATE?

There are no alternative treatments or procedures available. The only alternative is not to participate in this study.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

Compensation

You will receive $300 in the form of cash for your participation in this study. You will receive your compensation upon completion of the study. Compensation is broken down as follows: $100 for each of the two nap experimental visits, $50 for the adaptation nap, and a $50 bonus for completing the study. If you withdraw from the study before completion, the payment will be prorated based on the portion of the study you completed. You will not be compensated for only completing the initial interview or the medical examination.

Reimbursement

You will be reimbursed for costs of transportation.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There is no cost to you for participation in this study. However, there may be out-of-pocket expenses such as parking and transportation fees.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number listed at the top of this form.

If you are injured as a result of being in this study, UCI will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or the study sponsor, the National Institute of Health, or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation

for injury. For more information about this, you may call UCI Human Research Protections (949) 824-6068 or (949) 824-2125 or by e-mail at IRB@research.uci.edu

WHAT HAPPENS IF I WANT TO STOP TAKING PART IN THIS STUDY?
You are free to withdraw from this study at any time. **If you decide to withdraw from this study, you should notify the research team immediately**. The research team may also end your participation in this study if you do not follow instructions, miss scheduled visits, the study sponsor decides to stop the study or your safety and welfare are at risk.

If you experience any of the side effects listed above, if your health worsens, or if you are injured during the research, you may need to be withdrawn from the study, even if you would like to continue. The research team will make this decision and let you know if it is not possible for you to continue. The decision may be made to protect your safety and welfare, or because the research plan does not allow people who develop certain conditions to continue to participate.

If you withdraw or are removed from the study, the researcher may ask you to return all study-related equipment, such as the actigraph wrist monitor.

If you elect to withdraw or are withdrawn from this research study, you may choose to terminate the continued use or disclosure of your protected health information (PHI) for research purposes. The request to end the use or disclosure of your PHI should be made in writing.

HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT?
Subject Identifiable Data

No identifiable information will be collected about you except for your contact information if you agree to allow the investigators to retain this information.

Data Storage

Research data will be maintained in paper format in a secure location at UCI. Only authorized individuals will have access to it.

Research data will be stored electronically on a secure computer in an encrypted file with password protection.

Data Retention

Investigators will keep the study data for 6 years as required by for studies that include identifiable information per HIPAA regulations

WHO WILL HAVE ACCESS TO MY STUDY DATA?
The research team, authorized UCI personnel, the National Institute of Health, and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to your study records to protect your safety and welfare.

Any information derived from this research project that personally identifies you will not be released or disclosed by these entities without your separate written consent, except as specifically required by law. Research records provided to authorized, non-UCI entities will not contain identifiable information about you. Publications and/or presentations resulting from this study will not include identifiable information about you.

While the research team will make every effort to keep your personal information confidential, it is possible that an unauthorized person might see it. We cannot guarantee total privacy.

ClinicalTrials.gov is a Web site that provides information about clinical trials. 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.

Certificate of Confidentiality

To help us protect your privacy, we are in the process of obtaining a Certificate of Confidentiality. With this Certificate, researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The Certificate also prohibits the researcher from providing to any other person not connected with the research, your name or any information, document, or biospecimen that contains identifiable, sensitive information about you that was collected or created for the research. There are exceptions – and they are noted below.

The Certificate of Confidentiality does not prevent researchers from voluntarily disclosing information that would identify you as a participant in the research project as required by Federal, State or local laws, and with your consent, as necessary, for your medical treatment. This includes the disclosure of information that must be released to meet the requirements of the Food and Drug Administration (FDA). No voluntary disclosures will be made.

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, the researchers may not use the Certificate to withhold the information.

ARE THERE OTHER ISSUES TO CONSIDER IN DECIDING WHETHER TO PARTICIPATE IN THIS STUDY?

Use of Specimens
Any specimens (e.g., urine) obtained for routine labs will be discarded or destroyed once they have been used for the purposes described in this consent.

Investigator Financial Conflict of Interest

No one on the study team has a disclosable financial interest related to this research project.

UCI researchers may contact me in the future to ask me to take part in other research studies.

YES	NO

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?
If you have any comments, concerns, or questions regarding the conduct of this research, please contact the research team listed at the top of this form.

A 24-hour number is also listed on the top of this form to report any health concerns or unanticipated problems you may experience after normal hours or on weekends.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any suggestions, problems or concerns you may have about the study, please contact UCI's Office of Research by phone, (949) 824-6068 or (949) 824-2125, by e-mail at IRB@research.uci.edu or at 141 Innovation Drive, Suite 250, Irvine, CA 92697.

What is an IRB? An Institutional Review Board (IRB) is a committee made up of scientists and non-scientists. The IRB's role is to protect the rights and welfare of human subjects involved in research. The IRB also assures that the research complies with applicable regulations, laws, and institutional policies.

HOW DO I AGREE TO PARTICIPATE IN THIS STUDY?
You should not sign and date this consent form until all of your questions about this study have been answered by a member of the research team listed at the top of this form. You will be given a copy of this signed and dated consent form, and the attached "Experimental Subject's Bill of Rights" to keep.
Participation in this study is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your future relationship with UCI or your quality of care at the UCI Medical Center.

If, during the course of this study, significant new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the research team listed at the top of the form.

Your signature below indicates you have read the information in this consent form and have had a chance to ask any questions you have about this study.

Note: If the research described in this form involves your protected health information (PHI), you will be asked to sign separate UC HIPAA Research Authorization form for the use of your PHI.

I agree to participate in the study.

Subject Signature	**Date**
Printed Name of Subject	
Signature of Person Obtaining Informed Consent *(Individual must be listed on Page 1 of this consent)*	**Date**
Printed Name of Person Obtaining Informed Consent	

A witness signature is required on this consent form only if: (Researchers: check which one applies)

☐Consent is obtained from the subject via the Short Form process, as approved by the IRB.
☐The subject has decision-making capacity, but cannot read, write, talk or is blind.
☐The subject's guardian/legally authorized representative (LAR) cannot read, write, talk or is blind.
☐The IRB specifically mandated a witness signature for this study (e.g., high risk and/or invasive research procedures).

Note: The witness must be impartial (i.e. not a member of the subject's family, not a member of the study team).

For the witness:
I confirm that the information in this consent form was accurately explained to and understood by the subject or legally authorized representative and that informed consent was given freely.

_____ _____
Witness Signature **Date**

_____
Printed Name of Witness

UNIVERSITY OF CALIFORNIA, IRVINE
Experimental Subject's Bill of Rights

The rights listed below are the right of every individual asked to participate in a research study. You have the right:

1. To be told about the nature and purpose of the study.

2. To be told about the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. To receive a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. To be told of any benefits that you may reasonably expect from the participation in the study, if applicable.

5. To receive a description of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. To be told of what sort of medical treatment, if any, will be available if any complications should arise.

7. To be given a chance to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. To refuse to participate in the research study. Participation is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your right to receive the care you would receive if you were not in the experiment.

9. To receive a copy of the signed and dated written consent form and a copy of this form.

10. To be given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study you should contact the research team listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research subject, please contact the UCI's Human Research Protections unit in the Office of Research by calling (949) 824-6068 or (949) 824-2125 Monday – Friday, 8 am – 5 pm; or by e-mail at IRB@research.uci.edu; or by writing us at 141 Innovation Drive, Suite 250, Irvine, CA 92697.