Chronic Insomnia and CSF Markers of Dementia
NCT# NCT04024020
Document date: 11/15/2022

Continuing Review

Basic Info

Confirmation Number:	**dhbjifaj**
Protocol Number:	**829221**
Created By:	**GUNTER, PAUL**
Principal Investigator:	**GEHRMAN, PHILIP R**
Protocol Title:	**Chronic insomnia and CSF markers of dementia**
Short Title:	**Chronic insomnia and CSF markers of dementia**
Protocol Description:	**The goal of this project is to examine the relationship between chronic sleep disturbance (insomnia) and dementia biomarkers and orexin levels as assessed in cerebrospinal fluid (CSF). Fifteen adults age 30-50 with chronic insomnia and age- and gender-matched good sleepers will undergo overnight polysomnography and morning CSF sampling.**
Submission Type:	**Biomedical Research**
Application Type:	**FULL**

PennERA Protocol Status

Approved

Level of IRB Review Required

Convened Full Board Review

The following documents are currently attached to this item:

There are no documents attached for this item.

Summary of protocol modifications approved since last continuing review
Please provide a description of changes which have been reviewed and approved by the IRB since the last continuing review.

Subject Enrollment

Target subject enrollment at Penn

0

Target enrollment at other centers (multi-center study)

0

Number of subjects enrolled at Penn since the study was initiated

0

Actual enrollment at participating centers

0

Number of subjects enrolled at Penn since the last continuing review

Total number of subjects who provided consent

0

Number of subjects determined to be ineligible

0

Number of subjects currently active/on study

0

Number of subjects lost to follow-up

0

Number of subjects no longer participating for other reasons

0

Number of subjects who have completed the study

0

Number of subjects who have withdrawn from the study

0

Race:

American Indian or Alaskan Native

0

Asian

0

Black or African American

0

Native Hawaiian or Pacific Islander

0

White

0

Other

0

Unknown or Not Reported

0

Ethnicity:

Hispanic or Latino

0

Not Hispanic or Latino

0

Gender

Male

0

Female

0

Other

0

Unknown / Not Reported

0

Total

0

Vulnerable Populations

Has your study enrolled pregnant woman?*

No

Has your study enrolled prisoners?*

No

Has your study enrolled children?*

No

Subject Withdrawal

How many subject voluntarily withdrew from the study?

0

How many subjects were withdrawn from the study at the request of the PI/Co-PI?

0

Number of subjects withdrawn due to adverse events/unanticipated problems

0

Subject withdraw reason*
If subjects voluntarily withdrew or were withdrawn, please indicate the reasons.

Issues with recruitment/retention, informed consent, or other issues
If applicable, please provide a brief summary of any difficulty you experienced obtaining/retaining subjects or obtaining informed consent during the entire approval period. Additionally, please indicate if there have been any complaints about the research.

Informed Consent Process*
Recognizing that informed consent encompasses much more than a form or document there are a number of methods employed to educate a potential subject as to what is involved in a particular research project. The forms used are one method for documenting the informed consent process.Is written informed consent required for this project?
No

Is written HIPAA authorization required?*

No

New Findings

Significant preliminary observations/interim findings
Have there been any significant preliminary observations/interim findings during the past approval period. If yes, please describe below.

DMC or DSMB exists*
Does a data monitoring committee (DMC) or data and safety monitoring board (DSMB) exist?
No

DMC or DMB Report Status

The following documents are currently attached to this item:

There are no documents attached for this item.

Multi-site trial summary
If this study is a multi-site trial, provide a narrative summary of any relevant reports that have been received in the past year, regardless of whether the report has been previously submitted to the IRB.

Disclosure of Significant Financial Interests*
Investigators (persons responsible for the design, conduct or reporting of this research protocol) must disclose any of the following financial interests / relationships with any entity that sponsors, provides support, or otherwise has a financial interest in the conduct or outcome of this research protocol (Outside Organization): Payments received for the past 12 months from a publicly traded Outside Organization for personal services (e.g., consulting, lecturing / speaking, service on the Scientific Advisory Board) plus the value of any current equity that when aggregated exceeds $5,000Payments received for the past 12 months from a non-publicly traded Outside Organization for personal services that in total exceed $5,000, or having any equity interestMembership on the governing board of any Outside Organization, including service on its board of directors, or having a position of authority or responsibility to act in its best interests, including being an officer, manager, partner, or limited liability company member with management responsibilityInvestigators must also disclose any financial interest in a drug, device or other product or a competing product (IP rights), regardless of whether the IP has been patented, licensed, or assigned to the Penn, if such IP is being tested, evaluated, or developed in, or if its commercial value could be affected by, this protocol.Investigators are not required to disclose equity in mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles.Does any Investigator (or his or her spouse or dependent children) have a SIGNIFICANT FINANCIAL INTEREST, as defined above?
No

If "YES", was this Financial Interest previously reported to the Conflicts of Interest Standing Committee?
Not Applicable

If "YES", has there been a change regarding this Financial Interest from what was previously reported to the Conflicts of Interest Standing Committee?
Not Applicable

The following documents are currently attached to this item:

There are no documents attached for this item.

Penn Intellectual Property*
To the best of the Principal Investigator's knowledge, does this protocol involve the testing, development or evaluation of a drug, device, product, or other type of intellectual property (IP) that is owned by or assigned to the University of Pennsylvania? Please refer to the Patent and Tangible Research Property Policies and Procedures.
No

Certification
I have reviewed the Financial Disclosure and Presumptively Prohibited Conflicts for Faculty Participating in Clinical Trials and the Financial Disclosure Policy for Research and Sponsored Projects with all persons who are responsible for the design, conduct, or reporting of this research; and all required Disclosures have been attached to this application.
Yes

Study Completion / Expiration

Study Complete*
Is this study complete?
No

Study Complete - Explanation
If study is completePlease indicate why (eg., research related activities and data analysis are complete, required number of subjects reached, issues with protocol safety,etc.)

The following documents are currently attached to this item:

There are no documents attached for this item.

IRB Approval Expired*
Has IRB approval for this protocol expired or will it expire before the scheduled IRB review?
No

Research During IRB Approval Lapse
If the IRB approval for the protocol has expired or will expire before the scheduled IRB review, confirm that no research related activities occurred/will occur without approval from the IRB unless the PI contacted the Office of Regulatory Affairs and the IRB Executive Chair (or authorized designee) determined that it is in the best interest of subjects to continue during the lapse in IRB approval. For example, in a clinical trial there are (1) subjects who are enrolled but not on intervention, (2) subjects who are on intervention, and (3) subjects who have completed the intervention phase and are in follow up. The IRB Executive Chair must evaluate each of these groups separately regarding continuation of participation in the research after IRB approval has expired.Have any research activities occurred, or will any research activities need to occur, during the lapse in IRB approval?
No

Unanticipated Problems*
Since the last IRB Review, have there been any unanticipated study related events that have not been

previously reported to the IRB? If No, do not include these events with this submission. Refer to www.upenn.edu/regulatoryaffairs/index.php?option=com_content&task=view&id=16&Itemid=8
No

The following documents are currently attached to this item:

There are no documents attached for this item.

Adverse Events*
Since the last IRB review, has the profile of adverse events (in terms of frequency, severity, or specificity) changed from previous experience or as documented in the research protocol, informed consent document, or investigator's brochure?
No

The following documents are currently attached to this item:

There are no documents attached for this item.

Documents attached from the IRB protocol application.

The following documents are currently attached to this item:

Full sponsor's protocol (csfprotocol.pdf)

Informed consent form (consent_1sep2022.pdf)

Additional Document (csf_cr_coverletter_29sep2022.doc)

List of Documents Details
Please detail the rationale for why any of the above documents are not attached to the submission (i.e. No Investigator's Brochure, Protocol, or Consent Forms are utilized for this protocol).

Protocol Details

Resubmission*
Yes

Hospital Sites
Will any research activities and/or services be conducted at a Penn Medicine affiliated hospital site?
Yes

Active Hospital Sites

Hospital of the University of Pennsylvania (HUP) ***Primary***

Study Personnel

Principal Investigator

Name:	**GEHRMAN, PHILIP R**
Dept / School / Div:	**10261 - PS-Affective Disorders Program**
Campus Address Mail Code	**6021**
Address:	**U of PA Dept. of Psychiatry** **3535 Market Street, Suite 670**
City State Zip:	**PHILADELPHIA PA 19104-3309**
Phone:	**215-746-3578**
Fax:	**215-573-0759**
Pager:	
Email:	**philip.gehrman@pennmedicine.upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**05/17/2022**
Name of course completed :	**Good Clinical Practice: An Introduction to ICH (GCP) Guidelines**

Study Contacts

Name:	**BARILLA, HOLLY**
Dept / School / Div:	**10261 - PS-Affective Disorders Program**
Campus Address Mail Code	**3309**
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City State Zip:	**PHILADELPHIA PA 19104-3309**
Phone:	**215-746-4384**
Fax:	**-**
Pager:	
Email:	**hbarilla@upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**06/14/2024**
Name of course completed :	**Good Clinical Practice: An Introduction to ICH (GCP) Guidelines**

Name:	**KAUTZMANN, JEREMIE**
Dept / School / Div:	**2100 - Health System**
Campus Address Mail Code	
Address:	**Clinical Practices of University of Pennsylvania** **Psychiatry Admin**
City State Zip:	
Phone:	
Fax:	
Pager:	
Email:	**Jeremie.Kautzmann@Pennmedicine.upenn.edu**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed :	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**Yes**
Training Expiration Date:	**11/08/2024**
Name of course completed :	**Penn CR: Full Onboarding: Good Clinical Practice: An Introduction to ICH GCP Guidelines (2HRS)**

Other Investigator

None

Responsible Org (Department/School/Division):

10261 - PS-Affective Disorders Program

Key Study Personnel

Name:	**RAIZEN, DAVID M**
Department/School/Division:	**NE-Neurology**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Name:	**GOONERATNE, NALAKA**
Department/School/Division:	**DM-Geriatrics**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**POR Recertification Quiz - Full Board Review - SOM**
GCP Training Completed:	**Yes**
Training Expiration Date:	**01/21/2024**
Name of course completed:	**Good Clinical Practice (GCP) for the Experienced Investigator - OCR**

Name:	**FINDLEY, JAMES C**
Department/School/Division:	**DM-Sleep Medicine**
HS Training Completed:	**Yes**
Training Expiration Date:	
Name of course completed:	**CITI Protection of Human Subjects Research Training - ORA**
GCP Training Completed:	**No**
Training Expiration Date:	
Name of course completed:	

Disclosure of Significant Financial Interests*
Does any person who is responsible for the design, conduct, or reporting of this research protocol have a **FINANCIAL INTEREST**?
No

Penn Intellectual Property*
To the best of the Principal Investigator's knowledge, does this protocol involve the testing, development or evaluation of a drug, device, product, or other type of intellectual property (IP) that is owned by or assigned to the University of Pennsylvania? Please refer to the Patent and Tangible Research Property Policies and Procedures.
No

Certification
I have reviewed the *Financial Disclosure and Presumptively Prohibited Conflicts for Faculty Participating in Clinical Trials* and the *Financial Disclosure Policy for Research and Sponsored Projects* with all persons who are responsible for the design, conduct, or reporting of this research; and all required Disclosures have been attached to this application.
Yes

The following documents are currently attached to this item:

There are no documents attached for this item.

Biomedical Research

Clinical Trial*
Is this a clinical trial? Please note the following definition:Clinical trial is defined as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. See CFR 45.46.102(b)
No

Investigator Initiated Trial*
Is this an investigator initiated trial? Please select "Yes" if ALL the following conditions are met:The research is subject to FDA regulations for human subjects research.The individual PI both initiates (plans and designs) and conducts an investigation and under whose immediate direction the investigational agent is administered or dispensed. The individual investigator has absolute responsibility and accountability and designs, conducts, monitors, manages the data, prepares reports and oversees all regulatory and ethical matters. See 21 CFR 312.3
No

Drugs or Devices*
Does this research study involve Drugs or Devices?
No

IND Exemption

For studies that fall under an IND exemption, please provide the number below

For studies including IND or IDE's, please provide the number(s) below

IDE Review*
NOTE: For research involving investigational devices, you are required to review the guidance on Managing Research Device Inventory. Consult the Penn Manual for Clinical Research: https://www.med.upenn.edu/pennmanual/secure/investigational-product-management-at-sites-not-using-investigational-drug-services-(ids).html Please check the box Yes if you have reviewed the guidance.
Yes

Research Device Management*
Please indicate how research device(s) will be managed.
Not Applicable (no investigational devices)

Drug, Herbal Product or Other Chemical Element Management *
Please indicate how drugs, herbal products or other chemical entities will be managed.
Not Applicable (no drugs, herbal products or other chemical entities)

Radiation Exposure*
Are research subjects receiving any radiation exposure solely because they are enrolled in this protocol? (e.g. X-rays, CT, Fluoroscopy, DEXA, pQCT, FDG, Tc-99m, etc.)?IF YES, the protocol must be approved by the RRSC (Radiation Research Safety Committee). Consult EHRS web site: www.ehrs.upenn.edu/protocols/radiohuman.html for more information.If you have questions, email jjesik@ehrs.upenn.edu or kavyap@upenn.eduIf your protocol includes Nuclear Medicine Procedures, the protocol must be reviewed by the Nuclear Med Operations Committee: https://redcap.link/NMOPS
No

Human Gene Therapy, Human Gene Transfer, Human Gene Editing*
Does this research involve the administration of any of the following to human subjects? Please consult your investigator's brochure, as needed. Recombinant or synthetic DNA or RNA (r-s-NA); Genetically modified Biologics (e.g., CAR T Cells) or Biosimilars; Recombinant or genetically modified:infectious organisms (e.g., Listeria),established cell lines, viral vectors, agents/products; Non-biologic vectors/transfer agents delivering any of the above for a clinical trial; Use of novel gene editing approaches (e.g., CRISPR/Cas9, PRIME)IF YES, the study protocol and attendant materials must be registered in PIERS (Penn IBC Electronic Registration System) and reviewed by the Institutional Biosafety

Committee (IBC). Consult the EHRS website: https://ehrs.upenn.edu/health-safety/biosafety/institutional-biosafety-committee-ibc. If you have questions, contact the Penn Institutional Biosafety Committee at 215-898-4453 (number subject to change) or contact the Institutional Biosafety Officer (cell: 215-651-0546 or email: amaks@upenn.edu) The protocol may also require review by the Human Research Advisory Committee (HRAC). The IRB will notify the PI and study staff if this review is warranted. For new protocols requiring IBC registration and review, IRB approval cannot be granted until IBC approval is granted. Enrollment for a clinical trial cannot be initiated before obtaining IRB and IBC approvals.For new protocols requiring HRAC review, IRB approval cannot be granted until HRAC approval is granted.
No

Human Source Material*
Does this research include collection or use of human source material (i.e., human blood, blood products, tissues or body fluids)? IF YES, consult the EHRS web site: www.ehrs.upenn.edu/programs/bio/bbpathogens.html for information on OSHA Bloodborne Pathogens requirements (training, vaccination, work practices and Exposure Control Plan). If you have questions, call 215-898-4453.
Yes

Image Guided Biopsies*
Does the research involve imaging guided biopsy? IF YES, please contact the Clinical Imaging Core. See https://www.med.upenn.edu/cbi for more details. Any questions should be directed to the Director of Research Operations, Dept of Radiology, Kathleen Thomas.
No

Computerized Tomography (CT) Studies*
Does the protocol involve CT scans that are not considered standard of care and are being performed for research purposes?IF YES, complete the CACTIS Committee Application: https://is.gd/CACTIS and consult CACTIS website: http://www.uphs.upenn.edu/radiology/research/labs/cactis/ for application requirements.
No

CAMRIS and MRI Studies*
Is an MRI scan being performed for research only and NOT considered standard of care (example: specific scanner, parameters or solely for the purposes of research)?NOTE: Research/non-standard use of MRI may include but is not limited to any of the following: Situations in which MRI results may impact subjects current clinical care plan or treatment decisions, such as:The study requires a customized report with specifics regarding the study protocol (i.e., specific measurements or details); Introduction of a device of any kind during the MRI that is not used during a 'standard of care' type scan.Your MRI is not consistent with standard care time points for MRI imaging.Your MRI is not paid for by insurance.IF YES, consult CAMRIS website: https://www.med.upenn.edu/camris/application-and-faq.html for application requirements and required institutional consent form language.
No

Investigational Agent or Device within the Operating Room*
Does the research project involve the use of an investigational agent or device within the Operating Room?
No

Cancer Related research not being conducted by an NCI cooperative group*
Does this protocol involve cancer-related studies in any of the following categories? Therapeutic, Prevention, Supportive Care, Screening, Early Detection, or Diagnostic, Epidemiologic, Observational, Outcome, Ancillary or Correlative. For a description of these categories, see http://www.ctsrmc.org/submitting_a_protocol.php NCI Cooperative Groups are as follows:Alliance for Clinical Trials in OncologyNCI Clinical Trials Group (Canadian Cancer Society) (NCCTG)Children's Oncology Group (COG)NRG Oncology GroupECOG-ACRIN Cancer Research GroupSouthwest Oncology Group (SWOG) IF YES, the protocol must be submitted to the Cancer Center's Clinical Trials Scientific Review Committee for scientific review and approval prior to obtaining IRB approval. Consult the CTSRMC website: www.ctsrmc.org for application requirements
No

Processing of Materials*
Will the research involve processing (such as over encapsulating, or compounding)?
No

In-House Manufacturing of Materials*
Will the research involve processing (such as over encapsulating, or compounding)?
No

HIPAA / Protected Health Information
Does the research proposal involve accessing (viewing / using), collecting, or disclosing of protected health information (PHI) directly from participants or their medical or dental record for research purposes?
Yes

Indicate which item is provided with this submission:

Modified research informed consent document that incorporates HIPAA requirements

Cohort/data analysis tools used

Remote Study Visits
Does the research proposal involve conducting research visits remotely via any type of video conferencing software?
No

Remote Study Visits
Does the research proposal involve conducting research visits remotely via any type of video conferencing software?
No

CHPS Resources*
Does the research involve CHPS resources?
Yes

HUP Inpatient Nursing Resources
Does this research include an inpatient admission at HUP?
No

Pathology and Laboratory Medicine Resources*
Will samples be collected by hospital phlebotomy and/or processed or analyzed by any of the clinical laboratories of the University of Pennsylvania Health System?
No

Research Involves Apheresis, Cell Collection, and/or Blood Product Collection*
Does this research involve collection of blood products in the Penn Donor Center and/or the use of apheresis for treatment or collection of cells or other blood components?
No

Research involving blood transfusion or drug infusions*
Will your research involve blood transfusion or infusion of study drug in 3 Ravdin Apheresis Unit for research purposes?
No

HUP Perioperative and Procedural Services *
Does the research require the following: The collection of tissue, fluid, or blood in HUP Perioperative and Procedural Services ORThe administration of medications in HUP Perioperative and Procedural Services?This is inclusive to all phases of Perioperative care: pre-operative, intraoperative, and postoperative periods in all HUP Perioperative Procedure locations.If you have questions, please contact: HUPPeriopClinicalResearch@PennMedicine.upenn.edu
N/A

Trial in Radiation Oncology
Is this research a prospective trial being done in Radiation Oncology, and if so, has this protocol been approved by the Radiation Oncology Protocol committee?
N/A

Study in Radiation Oncology
Is this research a retrospective study being done in Radiation Oncology, and if so, has this project been reviewed by the Radiation Oncology Clinical Research Group?
N/A

Use of UPHS services*
Does your study require the use of University of Pennsylvania Health System (UPHS) services, tests or procedures , whether considered routine care or strictly for research purposes? (UPHS includes all Penn hospitals and clinical practices, including the Clinical Care Associates network of community practices). Examples of UPHS services/tests/procedures includes the Clinical Translational Research Center (CTRC), laboratory tests, use of the pathology lab, cardiovascular imaging tests or radiology imaging tests (whether being billed via the Service Center or through UPHS), other diagnostic tests & procedures and associated professional services, etc.
No

Veteran's Affairs (VA) Patients or Subjects
Does your study involve data from Veteran's Affairs (VA) patients or subjects?
No

If yes, was this approved by the Philadelphia VA?

No

Out of State Research
Will any Penn personnel conduct any research activities outside of the State of Pennsylvania?
No

Research involving Virtua Health
Will any Penn personnel conduct any research activities at a Virtua Health site location, OR in collaboration with Virtua Health System personnel, OR using any Virtua Health System resources (e.g., medical records)?
No

Artificial Intelligence Technology*
No

Human Stem Cells*
No

Primary Focus*
Mechanistic or physiologic study in human subjects (T1 Translational research in humans or Phase I drug research)

Protocol Interventions

x	**Sociobehavioral (i.e. cognitive or behavioral therapy)**
	Drug
	Device - therapeutic
	Device - diagnostic (assessing a device for sensitivity or specificity in disease diagnosis)
	Surgical
x	**Diagnostic test/procedure (research-related diagnostic test or procedure)**
x	**Obtaining human tissue for basic research or biospecimen bank**
x	**Survey instrument**
	None of the above

The following documents are currently attached to this item:

There are no documents attached for this item.

Sponsors

Business Administrator

Name:	**CASTELLANO, DANIEL**
Dept / School / Div:	**4412 - PS-Psychiatry**
Phone:	**215-573-5833**
Fax:	**215-573-6410**
Pager:	
Email:	**dcastel2@pennmedicine.upenn.edu**

Department budget code

000 - 000 - 0 - 000000 - 0000 - 0000 - 0000

Funding Sponsors

Name:	**MERCK & CO., INC.**
Type:	**UPENN Commercial/Industrial**

Funding sponsors billing address
If you have selected a commercial or industry sponsor, please provide the appropriate address and contact information for the Sponsor for the purposes of billing for IRB review fees (initial review, continuing review and convened modification fees apply here). If the Sponsor is not industry/ commercial, this information is not necessary to provide with your application.

Funding sponsors gift
Is this research being funded by a philanthropic gift?
No

Regulatory Sponsor

IND/IDE Sponsor

none

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Industry Sponsor

None

Project Funding*
Is this project funded by or associated with a grant or contract?
Yes

Selected Proposals

Proposal No	**Title**
10063203	**Chronic Insomnia and CSF Markers of Dementia**

Sponsor Funding
Is this study funded by an industry sponsor?
Yes

Status of contract

Complete

The following documents are currently attached to this item:

There are no documents attached for this item.

Multi-Center Research

Penn as lead
1. Is this a multi-center study where Penn is serving as the Lead Site or the Penn PI is serving as the Lead Investigator?
No

Management of Information for Multi-Center Research

Penn irb of record
2. Is this a multi-center study where the Penn IRB will be asked to serve as the IRB of Record for other external study sites?
No

Other Sites

No other sites

Protocol

Abstract
The longstanding view has been that insomnia, and other forms of sleep disturbance, emerge as a consequence of dementia and are the result of progressive neuronal damage. However, there is growing evidence that the direction of causation may go both ways, with sleep disturbance potentially increasing vulnerability to dementia. Longitudinal studies have found that sleep disturbance often precedes and increases risk for dementia by several years.The purpose of this study is to examine the relationship

between chronic insomnia and dementia biomarkers and orexin levels found in cerebrospinal fluid (CSF). Fifteen adults age 30-50 with chronic insomnia and age- and gender-matched good sleepers will undergo overnight polysomnography and CSF sampling in the morning.

Objectives

Overall objectives
Patients with dementia very frequently have disturbed sleep that is thought to be caused, in part, by the dementing illness. There is growing evidence of the reverse direction of causation, with sleep disturbance increasing vulnerability to dementia. The recently-discovered glymphatic system, by which waste from neural metabolism is cleared from the brain, may be a mechanism for the sleep-dementia link. The goal of this project is to examine the relationship between chronic sleep disturbance (insomnia) and dementia biomarkers and orexin levels as assessed in cerebrospinal fluid (CSF). Fifteen adults age 30-50 with chronic insomnia and age- and gender-matched good sleepers will undergo overnight polysomnography and morning CSF sampling. These data will be used to address the following specific aims: Specific Aim 1: To examine the association between chronic insomnia and CSF markers of dementia. Hypothesis 1: Chronic insomnia will be associated with higher levels of CSF AB markers compared to good sleepers. Specific Aim 2 (exploratory): To examine the role of orexin in mediating the relationship between chronic insomnia and CSF markers of dementia. Hypothesis 2: Higher CSF orexin levels will mediate the relationship between chronic insomnia and A markers.

Primary outcome variable(s)
Dementia biomarkers in cerebrospinal fluid

Secondary outcome variable(s)
CSF orexin levels

Background
Patients with Alzheimers dementia frequently experience sleep disturbance that gradual worsens with increasing severity of the disorder. For caregivers, having a patient with dementia awake during the night is one of the primary reasons cited for nursing home placement. The longstanding view has been that insomnia, and other forms of sleep disturbance, emerge as a consequence of dementia and are the result of progressive neuronal damage. For example, Alzheimers dementia has been shown to target the suprachiasmatic nucleus, the master clock of the body. There is growing evidence that the direction of causation may go both ways, with sleep disturbance potentially increasing vulnerability to dementia. Longitudinal studies have found that sleep disturbance often precedes and increases risk for dementia by several years. In older adults without cognitive impairment, self-reported insomnia has been found to be associated with greater beta amyloid burden as assessed with PET imaging. One mechanism that could explain this relationship is the recently-discovered glymphatic system, through which potentially toxic byproducts of neural metabolism, such as A, are cleared from the nervous system. Metabolic solutes are excreted into the interstitial fluid, which then flow through interstitial space and pass into cerebrospinal fluid (CSF) for clearance. During sleep, the interstitial space increases by 60%, allowing greater transport of metabolites. Acute sleep deprivation in mice leads to an increase in A levels in CSF. These studies demonstrate that disturbed sleep increases markers of Alzheimers disease and may increase vulnerability to the disorder. While the mechanisms underlying the glymphatic system are still under investigation, there is increasing evidence that the peptide orexin plays a crucial role. In humans, high CSF concentration of orexin-A was associated with increased phosphorylated tau. In an animal model of Alzheimers disease, genetic deletion of orexin led to only moderate increases in sleep duration but strongly suppressed the formation of amyloid plaques. In a second study of this mouse model, delivery of an orexin antagonist significantly inhibited amyloid plaque formation. There is a need to better understand the role that orexin plays in the link between insomnia and Alzheimers disease. Much of the literature in this area utilizes models of acute sleep disturbance, usually total sleep deprivation. Less is known about the impact of chronic sleep disturbance as it occurs in the general population, most notably in the form of chronic insomnia. Given that AB levels accumulate for up to years prior to the onset of dementia, improved understanding of the mechanisms through which deposition occurs could dramatically shift the landscape from treatment of dementia to one of prevention in two ways. First, promotion of good sleep throughout the lifespan may decrease vulnerability to dementia. Second, sleep research may provide a window into the physiology of the glymphatic system and lead to novel insights for non-sleep approaches for prevention and treatment. Given the commercial availability of an FDA-approved orexin antagonist, there may be tremendous opportunity to decrease risk for dementia through

the treatment of chronic insomnia.

Study Design

Phase*
Not applicable

Design
Laboratory Observational study

Study duration
The total duration of the study will be 24 months, each participants duration in the study will be approximately 4 weeks.

Resources necessary for human research protection
Describe research staff and justify that the staff are adequate in number and qualifications to conduct the research. Describe how you will ensure that all staff assisting with the research are adequately informed about the protocol and their research related duties. Please allow adequate time for the researchers to conduct and complete the research. Please confirm that there are adequate facilities for the research.
The principal investigator involved in this project has extensive experience in sleep research, including having a history of success in conducting studies with CSF sampling. A study coordinator will be hired for this study and they will be trained in all designated duties and responsibilities of the study. Philip Gehrman will provide oversight of the study coordinator. The study will be conducted at the CTRC, where there are sufficient facilities and resources available.

Characteristics of the Study Population

Target population
Fifteen adults age 30-60 with chronic insomnia and fifteen age- and gender-matched good sleepers.

Subjects enrolled by Penn Researchers
30

Subjects enrolled by Collaborating Researchers
0

Accrual
Participants will be recruited through targeted advertisements in the Philadelphia area community. We have a track record of success in recruitment through these approaches. To estimate the appropriate sample sizes, statistical calculations were carried out using pilot data obtained from OxA and ABO measurements from N=6 individuals. Specifically, two-sided two-sample t-test was utilized for a two-group parallel design study which compared chronic insomniacs with good sleepers. For OxA, sample sizes needed to detect intended effect sizes (differences of 30%, 40%, and 50) were estimated at 80% power. For ABO, sample sizes were calculated to significantly detect the differences between two groups of 50%, 100%, and 150% at 80% power. Power calculations were performed on OxA and ABO in raw and natural log scales, respectively, after examining the normality of data with residual plots. Variability estimates at each time point were obtained as averages of sample standard deviations of two treatment groups per time point. As such, N=15/group would be sufficient to identify changes in the 8 AM samples considering effect sizes equal or greater than 30% and 100% for OxA and ABO, respectively.

Key inclusion criteria
All subjects must meet the following criteria: -Age 30-60 -Men and women To be included in the insomnia group, subjects must meet the following DSM5 Diagnostic Criteria for insomnia disorder: -dissatisfaction with sleep quantity or quality (difficulty initiating or maintaining sleep, or waking up too early) despite adequate opportunity for sleep -sleep disturbance causes clinical significant distress or impairment in functioning -present at least 3 times per week for at least 3 months -sleep disturbance is

not better explained by a medical or psychiatric condition or based on the effects of a substance - Insomnia Severity Index (ISI) score 14 or greater.

Key exclusion criteria
-Diagnosis or evidence of sleep disorders other than insomnia as determined by the screening questionnaires and clinical history -Women who have been pregnant or lactating within the past six months -Non-fluency in spoken or written English -Current or past month shiftwork defined as working during the evening or night shift -Current use of medications or OTC products that impact sleep - Evidence of neurological abnormalities that could include the risks associated with lumbar puncture (e.g.papilledema, mass lesion, Chiari malformation).

Vulnerable Populations

	Children Form
	Pregnant women (if the study procedures may affect the condition of the pregnant woman or fetus) Form
	Fetuses and/or Neonates Form
	Prisoners Form
	Other
x	**None of the above populations are included in the research study**

The following documents are currently attached to this item:

There are no documents attached for this item.

Populations vulnerable to undue influence or coercion
It is possible that a Penn employee could respond to a recruitment advertisement. They will be told that their participation or non-participation in the study will not in any way affect their employment with Penn.

Participant recruitment
Please describe the plan to equitably identify and recruit a diverse group of participants that is reflective of the population under study. If this is a multicenter protocol, the recruitment plan should describe the local (Penn) site's plan. Describe:how potential participants may be identified (review of medical records, Slicer Dicer, DAC reports including referrals from physician offices and clinics);who may approach potential participants;methods to achieve sample diversity and inclusiveness;what information may be presented to or discussed with them; andthe context and setting in which recruitment will happen.
Study advertising: Advertising will consist of newspaper advertisements, Penn Almanac, flyers and brochures, iConnect, Craigslist, Reddit, data pull from PennChart and ResearchMatch. We only use University of Pennsylvania approved methods and materials that have current UPenn IRB approval. We plan to use our IRB approved shared pre-screen (IRB Protocol # 849262) as a method of recruitment.

Recruitment Materials
Is the research team using any recruitment materials? These may include but are not limited to: phone call scripts, radio/video scripts, flyers/brochures, internet postings, email, letters to potential participants, letters to patient physicians, My Penn Medicine (MPM), other direct messaging, etc. For guidance regarding recruitment materials, please review the IRB's guidance on Participant Recruitment Materials online:https://irb.upenn.edu/recruitment
No

Use of Penn Media & Social Media Services
Will the recruitment plan propose to use any Penn media services (communications, marketing, etc.) for outreach via social media avenues (examples include: Facebook, Twitter, blogging, texting, etc.) or does the study team plan to directly use social media to recruit for the research?
No

The following documents are currently attached to this item:

There are no documents attached for this item.

Subject compensation*
Will subjects be financially compensated for their participation?
Yes

The following documents are currently attached to this item:

There are no documents attached for this item.

If there is subject compensation, provide the schedule for compensation per study visit or session and total amount for entire participation, either as text or separate document

There will be compensation provided. Subjects will be compensated $25 for the screening visit, $50 for the home monitoring and $250 for the 22 hours spent in the lab. The total compensation for completing the study is $325. Payments will be made through the Clincard system.

Study Procedures

Suicidal Ideation and Behavior
Does this research qualify as a clinical investigation that will utilize a test article (ie- drug or biological) which may carry a potential for central nervous system (CNS) effect(s)? Centeral nervous system(CNS) effect: the ability of a test article to enter into and potentially interact with the central nervoous system (brain and spinal cord). Clinical Investigation: Any experiment that involves a test article and one or more human subjects that either is subject to requirements for prior submission to the Food and Drug Adminstration (FDA) under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or is not subject to the requirements for prior submission to the FDA under these sections of the act, but, the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit.
No

Procedures
At an initial visit, participants will provide informed consent; complete standard questionnaires on sleep, cognitive functioning, and demographics this visit, which will be completed remotely. All information will be collected via RedCAP. Participants will then complete an ambulatory sleep study at home to screen for the presence of sleep disordered breathing and to characterize their sleep architecture. There is the potential for the data from the ambulatory sleep study to reflect reactivity to the recording equipment (i.e. a first night effect) this will be minimized by conducting the studies at home. Individuals who have evidence of sleep disorders based on the first night recording will be excluded from further participation in the study. The criteria for defining sleep disorders will be an apnea-hypopnea index greater than 15 events per hour for sleep apnea or a periodic limb movement index greater than 15 events per hour for PLMS. They will wear a wrist actigraph for one week and these data will be used to objectively assess sleep/wake patterns to determine eligibility based on habitual sleep duration.The actigraphy is a wrist-worn device that measures body movements. It is lightweight (17.5 g) and is worn like a wristwatch. Data are downloaded onto a personal computer and customized software uses the movement values to infer when the individual was awake or asleep. The methodology is commonly used to record sleep/wake patterns over several days. These data will be used to determine the individuals habitual sleep duration. In past studies, insomnia has most consistently associated with negative health outcomes when it is associated with objective evidence of short sleep duration (6 hours). As such, participants with insomnia who do not demonstrate average sleep duration 6 hours on actigraphy will not be eligible for further participation in the study. Participants who continue to be eligible following home sleep monitoring will then be studied in the Sleep Center on 11 Gates at the Hospital of the University of Pennsylvania for an overnight study. They will be arrive to the Sleep Center at 7:00 pm and will sleep overnight, following their habitual bedtime and wakeup time determined from the home actigraphy. Sleep will be monitored overnight using polysomnography. Standard polysomnographic procedures will be used to record the EEG, EOG, EMG, and EKG using an ambulatory system. Electrode placements of FpZ, CZ, OZ will be placed according to the International 10/20 system. Two EOG electrodes will be placed, positioned 1 cm below and

lateral to the outer canthus of the left eye and 1 cm above and lateral to the outer canthus of the right eye. Two surface EMG electrodes will be taped onto the chin 2 cm apart. Additional leads will be used to measure leg movements and breathing in order to rule out the presence of occult sleep disorders. Two electrodes will be taped over the anterior tibialis muscle of each leg to detect leg movements during the night. Flexible Resp-EZ belts will be placed around the abdomen and chest to measure breathing-related movements during the night. A nasal cannula will be used to detect pressure and an oximeter probe will be placed on the finger to measure blood oxygen saturation. Records will be scored in 30-second epochs according to standard criteria. PSG data will be used to compute standard sleep architecture variables of the amount of each stage of sleep in terms of minutes and percentage of total sleep time. In addition the following sleep continuity variables will be computed: sleep latency (SL; time from lights out to the first epoch of stage 2 or higher), total sleep time (TST), wake after sleep onset (WASO; number of minutes spent awake between lights out and lights on), and sleep efficiency (SE; total sleep time divided by the total recording period). Additionally, our technicians will attached two sensors to the chest area of the subjects in order to measure respiration and test the sensors to see the accuracy of detecting sleep apnea. TatchSleep is a flexible, thin, and wireless adhesive patch designed to collect physiological parameters related to sleep disorders in patients. Each patch consists of a wearable sensor and a bottom layer of double coat medical-grade adhesive. This adhesive is safe for patient use and enables the patch to stay affixed to the body throughout the night. The sensor also connects directly to a battery which is hidden within the patch. During the study, patients will be asked to wear three patches. Data from the patches are transmitted wirelessly throughout the night to a companion mobile application, which stores the data for clinicians to upload to a sleep analysis platform. Upon waking, wires will be removed and the subjects will be allowed to shower. Those in the insomnia group who choose to participate in the optional second part of the protocol will have a fasted blood draw at this visit. Study staff will walk the subjects over to CHPS outpatient. Around 8:00 AM a lumbar puncture will be performed by a neurology fellow to collect 25 mL of CSF. Prior to the lumbar puncture the neurology fellow will conduct a neurological exam including fundoscopic exam, in order to rule out any contraindications to the procedure such as a coagulopathy or central mass lesion. If contraindications are found, the lumbar puncture will not be performed and the subject will be withdrawn from all further study procedures. If no contraindications are found, a small, specialized needle called a sprotte needle will introduced through an introducer. This type of needle has been demonstrated to reduce risk of headache. 25 mL of CSF will be collected and stored in polypropylene transfer tubes. In addition, bedrest for one or more hours immediately after the procedure will be recommended to the participant. Oral hydration will be encouraged to help reduce risk of headache. After final samples are taken participants will have completed the protocol and will be free to leave. CSF Analysis: Analysis 1: Endogenous ABO levels in human CSF will be measured in a blind fashion in a flow-based ABO-specific sandwich ELISA using the Erenna immunoassay system (Millipore, Temecula, CA), described in Savage et al 2014 JN. In brief, Mercks proprietary 19.3 antibody coupled to paramagnetic microparticles will be used to capture ABO, repeatedly washed with assay-specific proprietary buffers, and detected using a fluor-labeled detection antibody, 82E1 (IBL, Minneapolis, MN). Human CSF samples (100 uL/well) will be loaded in a blinded fashion in triplicate. The standards (ADDL), prepared in-house, will be run alongside CSF samples in triplicate using a 12-point ½ serial dilution between 42 pg/mL and 0.04 pg/mL. Statistical analysis of the data, including limit of detection (LOD) for the assay (defined as 2 x SD Bkg/slope with percent coefficient of variance 20%) and unknown ABO concentrations will be calculated using Singulex Sgx link and GraphPad Prism (GraphPad Software, Inc., San Diego, CA) software. Analysis 2: OxA concentrations in CSF will be quantified by an in-house ELISA developed using Meso Scale Discovery (MSD) electrochemiluminescence detection technology platform (Gaithersburg, MD, USA). Purified polyclonal IgG (G-003-36, Phoenix Peptide, Burlingame, CA, USA), raised in rabbit against OxA (amino acids 16-33), will be used as a capture antibody. Goat anti-human polyclonal antibody against OxA (N-18) (sc-26491, Santa Cruz Biotechnology Inc., Santa Cruz, CA, USA) will be used as a primary detection antibody. Sulfo-Tag labeled anti-goat antibody, raised in donkey, will be used as a secondary detection antibody and will be provided by MSD (R32AG-5). Blinded CSF samples will be run in triplicate alongside OxA standard (run as a 10-point 1/3 serial dilution between 30,000 and 4.57 pg/mL). Statistical analysis of the data, including lowest detection limit (LDL) for the assay (defined as 2 x SD Bkg/slope with percent coefficient of variance 20%) and unknown OxA concentrations will be calculated by extrapolating a nonlinear regression curve (sigmoidal, 4PL, X is log (Concentration)) and will be corrected for weight by 1/Y^2 using GraphPad Prism (GraphPad Software, Inc., San Diego, CA) software.

The following documents are currently attached to this item:

There are no documents attached for this item.

Deception
Does your project use deception? Deception could be considered any direct misinformation presented to the subject or omission of key information pertaining to the design or nature of the project.
No

International Research
Are you conducting research outside of the United States?
No

Analysis Plan
Paired-samples t-tests will be conducted to compare each of the CSF analytes between patients with chronic insomnia and matched good sleepers. Multiple regression analyses will be used to examine whether CSF orexin levels mediate the relationship between chronic insomnia and AB markers. Mediation analyses will be conducted using a series of linear regression models in which group (insomnia or control) and orexin levels will be treated as independent variables and AB markers will be treated as the dependent variables.

The following documents are currently attached to this item:

There are no documents attached for this item.

Data confidentiality

- x **Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.**
- x **Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.**
- x **Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.**
- x **Wherever feasible, identifiers will be removed from study-related information.**

A Certificate of Confidentiality will be obtained, because the research could place the subject at risk of criminal or civil liability or cause damage to the subject's financial standing, employability, or liability.

A waiver of documentation of consent is being requested, because the only link between the subject and the study would be the consent document and the primary risk is a breach of confidentiality. (This is not an option for FDA-regulated research.)

Precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys.

Audio and/or video recordings will be transcribed and then destroyed to eliminate audible identification of subjects.

Subject Confidentiality
Each participant will be assigned a study ID #. All study-related paperwork and computer files will only utilize the ID #. All study files will be stored behind a double lock system at 3535 Market Street, Suite 670, Room 698. Only study staff will be able to access the data. All study records will be maintained in locked file cabinets for paper records and electronic files will be stored on an institutionally secured & managed network drive. The master file linking subjects with their ID #s will be kept in a separate locked file cabinet. Following completion of the study and all manuscripts are written, paper records will be archived and stored in accordance with regulations for retention of research records. PHI will be removed from electronic files at that point as well.

Sensitive Research Information*
Does this research involve collection of sensitive information about the subjects that should be excluded from the electronic medical record? [NOTE: This does not apply to: 1) research information that would not normally be included in the electronic medical record or 2) information that is in the electronic medical record as part of clinical care.]

No

Subject Privacy
Privacy refers to the person's desire to control access of others to themselves. Privacy concerns people, whereas confidentiality concerns data. Describe the strategies to protect privacy giving consideration to the following: The degree to which privacy can be expected in the proposed research and the safeguards that will be put into place to respect those boundaries. The methods used to identify and contact potential participants. The settings in which an individual will be interacting with an investigator. The privacy guidelines developed by relevant professions, professional associations and scholarly disciplines (e.g., psychiatry, genetic counseling, oral history, anthropology, psychology).
Participants records will only utilize a study ID # in order to avoid violation of privacy. Names of participants will not be shared outside of the study staff, except to the extent required by law. Participants will be asked to indicate their preferred means of contact (phone, email, etc). All study visits will take place in a private room and the door will be closed to maintain privacy.

Disclosures
Will any data or specimens from Penn participants OR other research generated work product (e.g., intellectual property) be disclosed to any individuals, entities, or vendors, etc. outside of Penn?
No

*Data Protection**

- x **Name**
- x **Street address, city, county, precinct, zip code, and equivalent geocodes**
- x **All elements of dates (except year) for dates directly related to an individual and all ages over 89**
- x **Telephone and fax number**
- x **Electronic mail addresses**
- x **Social security numbers**
- x **Medical record numbers**
- **Health plan ID numbers**
- **Account numbers**
- **Certificate/license numbers**
- **Vehicle identifiers and serial numbers, including license plate numbers**
- **Device identifiers/serial numbers**
- **Web addresses (URLs)**
- **Internet IP addresses**
- **Biometric identifiers, incl. finger and voice prints**
- **Full face photographic images and any comparable images**
- **Any other unique identifying number, characteristic, or code**
- **None**

Does your research request both a waiver of HIPAA authorization for collection of patient information and involve providing Protected Health Information ("PHI") that is classified as a "limited data set" (city/town/state/zip code, dates except year, ages less than 90 or aggregate report for over 90) to a recipient outside of the University of Pennsylvania covered entity?
No

Tissue Specimens Obtained as Part of Research*
Are Tissue Specimens being obtained for research?
Yes

Tissue Specimens - Collected during regular care*
Will tissue specimens be collected during regulator clinical care (for treatment or diagnosis)?
No

Tissue Specimens - otherwise discarded*
Would specimens otherwise be discarded?
No

Tissue Specimens - publicly available*
Will tissue specimens be publicly available?
No

Tissue Specimens - Collected as part of research protocol*
Will tissue specimens be collected as part of the research protocol?
Yes

Tissue Specimens - Banking of blood, tissue etc. for future use*
Does research involve banking of blood, tissue, etc. for future use?
Yes

Genetic testing
If genetic testing is involved, describe the nature of the tests, including if the testing is predicative or exploratory in nature. If predictive, please describe plan for disclosing results to subjects and provision of genetic counseling. Describe how subject confidentiality will be protected Note: If no genetic testing is to be obtained, write: "Not applicable."
Not Applicable

Consent

1. Consent Process

Overview
Study personnel will meet with each individual virtually and describe the study in detail. Individuals will be provided with the combined consent / HIPAA form to read. They will have the opportunity to ask questions and discuss participation with other family members. Individuals will be asked to sign a consent form on RedCAP. Individuals who continue participation will provide written informed consent will be given a copy of the consent form for their records at their overnight sleep study.

Children and Adolescents
Not Applicable.

Adult Subjects Not Competent to Give Consent
Not Applicable.

2. Waiver of Consent

Waiver or Alteration of Informed Consent*
No Waiver Requested

Minimal Risk*

Impact on Subject Rights and Welfare*

Waiver Essential to Research*

Additional Information to Subjects

Written Statement of Research*
No

If no written statement will be provided, please provide justificiation

The following documents are currently attached to this item:

There are no documents attached for this item.

Risk / Benefit

Potential Study Risks
There is no substantial risk associated with the completion of the initial evaluation, though the subject will be asked to respond honestly to personal questions. Risks associated with polysomnography: There are few risks associated with the sleep study procedure. However, some people do experience minor discomfort (dry skin, rash) from having the skin cleansed and sensors placed on the skin over the course of the in laboratory studies. Risk of Lumbar Puncture: There is the risk of brain swelling or herniation if the subject has particular neurological abnormalities (e.g. papilledema, mass lesion, Chiari malformation). The neurology fellow performing the LP will conduct a neurological exam with fundoscopic exam to rule out these contraindications and will only proceed if there is no evidence of these risks. The lumbar puncture may cause pain at the site where the needle goes in and the spinal fluid is taken. There is a small risk of infection or bleeding. After the lumbar puncture, there is a risk of headache. To minimize the risk of a headache, the doctor will use a small, specialized needle, a sprotte needle introduced through an introducer. This type of needle has been demonstrated to reduce risk of headache. In addition, bedrest for one or more hours immediately after the procedure will be recommended to the participant. Finally, oral hydration will be encouraged to help reduce risk of headache. If headache does occur, it is usually mild and can be controlled with bedrest, hydration (with oral fluids), and acetaminophen or NSAIDS. Rarely, the headache is severe and may require additional treatment with a blood patch. In this procedure, a small amount of the patient's own blood is injected into the lumbar puncture site. This procedure is generally effective in stopping the headache. Although very rare, it is possible to have an allergic reaction to the local anesthetic used for the lumbar puncture. Signs of an allergic reaction include swelling and/or a rash on the skin where the anesthetic was injected. The patient will be asked about prior allergies to lidocaine and will be monitored for evidence of this reaction. There is a small risk of hemorrhage related to lumbar puncture. This risk will be minimized by checking a platelet count and coagulation studies (PT/PTT) prior to the lumbar puncture. To further minimize any possible risk, the lumbar puncture will be done by a neurology resident who is specifically trained in the procedure. Potential sources of research risk of this proposed investigation include the burden to participants cause by the amount of time asked of them, performance of the actigraphy and sleep study, and the confidentiality of data obtained. We do not consider the time demands on participants a serious risk and they can withdraw at any time. In addition, study staff will be trained to minimizr the burden on research involving human participants, breach of confidentiality of personal data obtained as part of this study is a potential risk to participants.

Potential Study Benefits
It is possible that the sleep study could identify sleep disorders that participants are unaware of, enabling them to seek treatment. There are no other benefits to the individual for participation. The knowledge we expect to gain from this study will be used to better understand the relationship between chronic insomnia and dementia.

Alternatives to Participation (optional)
The subject can choose to not participate.

Data and Safety Monitoring
Principal Investigator

The following documents are currently attached to this item:

There are no documents attached for this item.

Risk / Benefit Assessment
The procedures in this study are greater than ordinarily encountered in daily life, but they are commonly used without problems in the context of biomedical research. As such this study is moderate

risk.

General Attachments

The following documents are currently attached to this item:

There are no documents attached for this item.