Protocol 170957

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**UNIVERSITY OF CALIFORNIA - SAN DIEGO**
INFORMED CONSENT
**TO ACT AS A RESEARCH SUBJECT IN**

**Alzheimer's Disease Research Center (ADRC)**
**LONGITUDINAL STUDY**

Note: In this consent, the word "you" refers to the person being considered for enrollment in the study described. This may be you as the reader of this document, or a person for whom you are serving as the Legally Authorized Representative (LAR) or surrogate.

James Brewer, MD, PhD, Douglas Galasko, M.D., and their colleagues at the Alzheimer's Disease Research Center (ADRC) are conducting a research study to find out more about Alzheimer's disease (AD) and related dementias, a group of neurodegenerative diseases that eventually lead to loss of memory. The purpose of this research study is to collect information to help with the diagnosis of AD and other types of dementia, especially at the earliest stages. We will also follow the progression of these diseases with the purpose of discovering more about changes in the brain, risk factors, and causes of AD. We are inviting you to take part because:

- You have AD or a related disorder.
- You have symptoms suggesting that you may be at risk for developing Alzheimer's disease or a related disorder over time.
- You are a healthy adult without memory problems and are suitable to be part of a control or comparison group.
- You are an adult with Down Syndrome.

We will ask you to come with a study partner. Your study partner is someone who knows you well and will provide information we gather at your visits. We will speak with your study partner to gather information about your daily activities, mood, sleep and behavior. It is important that you and your study partner understand the description of the research study before you agree to participate. As you read this form, ask questions if something is not clear.

## DESCRIPTION OF STUDY PROCEDURES

About 4,000 participants will take part in the study. You will come to the ADRC for a detailed visit once per year. Components of this visit, which will happen over several days, are described below.

If you agree to participate in this study, the following will happen to you:

1) **Clinical and Cognitive Assessments:** We will review outside medical records as needed. You will be asked to complete a series of questionnaires about your general medical history, including any medications you are currently taking, your family history, your mood, sleep, behavior and daily activities. A neurological exam will be performed and will consist of an evaluation of your muscle reflexes, sensation to touch, posture and balance. Your blood pressure, pulse, height and weight will be taken. You will take several tests to evaluate your ability to think, concentrate and remember. This testing takes two to five hours to complete and will usually be done in one to two visits. This assessment process will be repeated once per year and continue until death, or until you withdraw from the study.

2) **Blood Pressure and Arterial Stiffness Assessment:** You will undergo a non-invasive assessment of central blood pressures and arterial stiffness using a blood pressure device (Pulse Wave Velocity (PWV)). This measurement will take approximately 20 minutes. During this time, blood pressure will be taken on both your arm and upper leg. While blood pressure is being taken on the upper leg, you will be lying down and a hand-held device will be used to measure the pulse in your neck.

3) **Blood Draw:** You will have a total of approximately 16 teaspoons (80mL) of blood drawn from a vein in your arm during your annual visit. This blood will be used for:

    a. **Clinical Laboratory Blood Tests:** About 2 teaspoons (10 mL) of your blood will be tested for glycohemoglobin (a blood test that measures the amount of sugar or glucose bound to hemoglobin and creatinine levels (a common blood test to assess kidney function). If any abnormalities are reported, we will notify you for follow-up with your treating physician**.**

    b. **Research Blood Tests:** The remainder of your blood sample will be used for research tests. **b1. Biomarkers**: Some of your blood sample will be used to measure proteins and other markers in your blood, and some blood will be stored in the ADRC laboratory indefinitely to allow future studies. See the ‘Data and Sample Sharing’ section below for further details. **b2. Genetic (DNA) testing**: Some of your blood will be used to extract DNA (the material in the cells of your body that contains genes and codes for the proteins that your body makes).

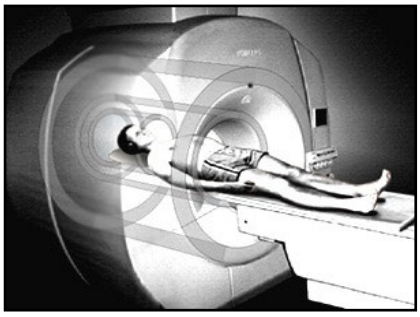
4) **Lumbar Puncture (LP):** You will be asked to undergo a research cerebrospinal fluid (CSF) draw (called a lumbar puncture or LP). Optional additional LP’s may be requested at future visits when appropriate but are not mandatory to participate in this study. This will allow ADRC

investigators to measure the levels of a number of different proteins (called biomarkers) in the CSF.

**LP involves inserting a small needle in the lower back below the end of the spinal cord. A small amount of fluid is collected.**

An LP is a procedure in which a small amount of CSF that surrounds the brain and spinal cord is removed by inserting a needle in the lower back. It is a routine neurodiagnostic procedure that we are using for research. You may come without eating, or having only a light meal before the LP. For this procedure, you will be positioned lying on your side and curled up in a ball, or sitting up and bent forward, whichever is easier for you. The lower part of your back will be cleaned with antiseptic. The doctor will inject local anesthetic (Lidocaine, 1%) into the skin of your lower back. When the area is numb, a very thin needle will be inserted into the spinal canal in the lower back, well below the level where the spinal cord ends. About 1 ½ teaspoons (20mL) of spinal fluid will be removed for analysis and storage. Undergoing the LP procedure takes approximately 10-30 minutes. Your body replaces this spinal fluid within 1-2 hours. Study staff will discuss certain conditions, such as a history of a bleeding disorder, use of Coumadin or blood thinners, or a local back problem, as they may prevent you from participating in the LP portion of this study.

After the lumbar puncture is completed, you will remain in the clinic for about 30 minutes. You will be given something to eat and drink before you leave. You will be allowed caffeine after completion of the procedure. A staff member will review after care instructions with you, which include avoiding any strenuous activity (lifting, bending, exercise, housework) for the next 24 hours. We will call you the day following your lumbar puncture to discuss how you are feeling.



**Sample MRI Machine**

**5) Magnetic Resonance Imaging (MRI) Scan:** You will be asked to have an MRI scan of your brain. Optional additional MRI scans may be requested when appropriate but are not mandatory to participate in this study. Study staff will ask you about implanted metal devices, as this may prevent you from participating in the MRI scan portion of the study. An MRI scan will provide a detailed picture of the structure of your brain, which will allow ADRC investigators to find out more about how this relates to people's abilities to form and retain memories, solve problems, and other skills. Each MRI scan will take approximately 30-45 minutes to complete. The magnetic resonance scanner is a long, narrow tube that is open on both ends. You will lie on your back and enter the MRI machine, during which you will hear loud knocking noises.

6) **Autopsy:** You will be asked to undergo an autopsy with removal of your brain after you die. This examination of your brain may provide conclusions about whether or not AD or related disorders were present. This contribution may provide valuable information that may further our understanding of memory changes and aging. In addition, we will store brain tissue to allow further research. There is a separate consent form for brain autopsy.

7) **Return of Results:** You may be provided with a research diagnosis based on your clinical and cognitive assessments. A research diagnosis is not the same as a clinical diagnosis provided by your doctor, but it can be helpful in understanding your brain health. If you choose to receive your research diagnosis, a diagnosis call will be scheduled with an ADRC clinician to disclose the diagnosis. A letter will be sent to you and you may choose to share the results with your primary care provider for further evaluation.

   After each annual visit, you will have the option to receive the results of certain biomarker tests. Each year, we will ask whether you would like to receive this information. If return of results is requested, an ADRC clinician may discuss biomarker procedures and the respective results with you and your study partner. Depending on the biomarker procedure, it may take several months for results to become available.

   We will not return results of any genetic testing performed on your blood samples. These tests are conducted in a research laboratory that is not Clinical Laboratory Improvement Amendments (CLIA) certified, meaning the results cannot be used for diagnostic purposes. If you are interested in learning about your genetic risk, we recommend seeking guidance from a genetic counselor or your health care provider.

   We will not return results of research analyses of your brain MRI. However, if our researchers identify an abnormal finding on your MRI scan, we will let you know. You will be given a disk with a copy of your MRI, but the scans will not be accompanied by a clinical read. Clinically significant findings will be incidental. If there is a clinical concern, an ADRC clinician will provide you with the scan and encourage you to bring the MRI disc to your health care provider for review.

   All families who wish to receive a brain autopsy and pathology report will receive a letter and copy of the neuropathology report. This report includes information about any changes observed in the brain, such as those associated with AD pathology or other disorders. The pathology report may take up to six months to one year to be completed and shared after the brain autopsy.

| ADRC Research Procedure | Information Disclosed | Method of Disclosure |
|---|---|---|
| Cognitive Assessments | No impairment or Impairment (and Level) in each Cognitive Domain | Annual Letter from Neuropsychologist |
| Clinical Evaluation | New Diagnosis or Change in Diagnosis | Phone/Zoom with Neurologist |

| | | |
|---|---|---|
| CSF Amyloid from Lumbar Puncture | Amyloid Positive or Negative | In-person Meeting or Phone/Zoom with Neurologist |
| MRI Scan | Incidentally Detected Abnormal Finding | Copy of Scan and In-Person Meeting or Phone/Zoom with Neurologist |
| Autopsy | Pathological Diagnosis | Letter from Pathologist |
| Plasma Amyloid from Blood Draw | Not Disclosed at This Time | |
| APOE Genotype | Not Disclosed at This Time | |

8) **Additional Research Studies.** You will be asked if you are interested in getting information about additional research studies. We will ask you now, and at each annual visit. If you are interested, we will contact you or your study partner with information about these studies, and you can decide whether to participate or not. These additional studies are separate from the longitudinal study and your decisions about them will not affect your ability to continue to participate in this study.

## RISKS

The most common risks or discomforts of this study are:

**1) Clinical and Cognitive Assessments:** Repeated evaluations of mood and mental status may be frustrating or produce fatigue and boredom. Frequent rest breaks are offered as needed.

**2) Blood Pressure and Arterial Stiffness Assessments**: No significant risks.

**3) Blood Draw:** Removal of blood with a needle and syringe poses a small risk of pain or bruising at the site of the needle stick, but this is temporary. Some people may experience fainting or dizziness, and there is also a slight risk of infection at the site of the needle stick. To minimize these risks, trained phlebotomists will handle all the blood drawing procedures.

**4) Lumbar Puncture (LP):** During the procedure, you may have temporary pain and discomfort in your back. Occasionally, a low-pressure headache may develop after a LP, presumably due to leakage of spinal fluid. If this headache persists it may require an additional treatment called a blood patch. A blood patch involves injecting some of your blood into the lumbar puncture site to seal the spinal fluid leak. This often relieves the headache immediately. Although very rare, it is possible that you may have an allergic reaction to the local anesthetic (Lidocaine, 1%) used for the lumbar puncture. This would cause swelling and a rash on your skin where the anesthetic was injected. Potential but rare risks of lumbar puncture include infection, damage to nerves in your back, and bleeding into the spinal fluid space. The risk of these is much less than 1%. To minimize these risks, the lumbar puncture procedure will be performed by Drs. Brewer or Galasko or a neurologist specifically trained in the procedure.

**5) Magnetic Resonance Imaging (MRI) Scan:** The MRI machine is a powerful magnet. This magnet may cause any metal in your body to move. If you know of any metal in your body, you will need to tell the researcher and MRI technician right away. Otherwise, there are no known risks for MRI. Some people with claustrophobia (fear of closed spaces) may find the MRI scanner too confining. In that case, you can ask to be removed from the scanner and this will be done immediately. The MRI scanner makes a loud beeping sound. We may ask you to wear protective earplugs during scanning**.**

**6) Autopsy:** No risks.

**7) Return of Results:** Some people may become distressed by the knowledge of their biomarker status. Others find knowing their results an empowering tool to plan for the future. To minimize the risks of undue emotional burden, education will be provided before and after the results are returned by a neurologist, and social work services will be made available to you if you need additional support.

**8) Additional Research Studies:** You will not be required to participate in additional research if you do not want to. If there are risks associated with additional research studies, they will be discussed with you at the time that your consent to take part in additional studies is discussed.

**Possible Unknown Risks:** Because this is a research study, there may be some unknown risks that are currently unforeseeable.

**Risks of Incidental DNA Findings:** Your samples will be used for research only and you will not receive specific results from these tests. However, in rare cases, researchers may discover a gene variant linked to a specific neurological or other disease. You will have the option to decide whether or not you want to be informed about such findings. The decision to have such information revealed is highly personal and can be stressful.

**Risk of Loss of Confidential Information:** Your samples and data will be labeled with a unique subject ID that contains no personal identifiers. When shared with the National Centralized Repository for Alzheimer's Disease and Related Dementias (NCRAD) or a secure government health research database, only de-identified data will be used. Both NCRAD and the government database use secure computer systems, and safeguards are in place to reduce this risk.

## DATA AND SAMPLE SHARING

Your samples and associated genetic and biomarkers tests will be stored in secure research repositories and in secure databases. All samples will be stored locally in the **UCSD ADRC Biorepository**. Some samples, such as blood or DNA for genetic studies, will be sent to the **National Centralized Repository for Alzheimer's Disease and Related Dementias (NCRAD)** at Indiana University. They will share it with the NIA-funded **Alzheimer's Disease Genetic Consortium** – AD Sequencing Project (ADSP). The ADRC and NCRAD biorepositories also collaborate with other academic institutions and companies in the biotechnology or pharmaceutical industries. The results of these experimental analyses will not be

shared with you, your caregiver or your heirs due to the exploratory nature.

All blood, DNA and CSF samples will be coded by number and no identifying information will be stored with the samples. Only your unique subject identifier will be used to identify your sample and research information about you. These de-identified samples are necessary for long-term research and will be stored indefinitely. Your biological samples, including your DNA, may be provided to researchers at academic institutions, hospitals, and biotechnology/pharmaceutical companies. De-identified clinical and genetic data may be provided to the researchers requesting biological samples. These researchers may perform analysis of the biological samples you have provided. Results from tests that are still in experimental development will not be returned. While your research results will not be added to your regular medical record, you may choose to receive certain biomarker results, if available. If you have concerns about genetic conditions, we recommend discussing them with your doctor, who can order separate clinical testing outside this research.

Your genetic material may be used in advanced research, including genetic modification and the development of new medicines, cell lines, or treatments. These efforts may one day have therapeutic or commercial value. In the future, your derived cells or cell products may be transplanted into humans or animals. Any cell lines or products created from your samples may be used in humans or animals. By consenting, you agree to allow this kind of future use without restriction on who may benefit.

Dr. Brewer or Dr. Galasko and the ADRC participate in the **National Alzheimer's Coordinating Center (NACC),** which is funded by the National Institute on Aging (NIA), and stores and combines data from over 35 research centers for broader scientific use. Both NACC and the UCSD ADRC are protected by a Certificate of Confidentiality, which helps safeguard your private information.

With approval of Dr. Brewer or Dr. Galasko, your biospecimen samples including blood, plasma, DNA, cells, autopsy brain tissue and clinical data, including data from imaging, CSF, and genetic samples, might be shared for scientific analysis with these organizations. When these samples, images, and data are shared, they will be identified with a coded number only that does not include personal identifiers.

All qualified scientific investigators may request samples and data from the ADRC. Decisions about sharing will be made by Dr. Brewer, Dr. Galasko and a resource-sharing committee responsible for overseeing use of stored specimens. These samples may be used by researchers at the University of California or other institutions and companies in the biotechnology or pharmaceutical industry. In the future, other companies may study your genes for similar or yet unidentified purposes related to AD.

If your samples are proposed for a <u>new research use not described</u> in this consent form, the project will first be reviewed by the UCSD Institutional Review Board (IRB). This Board protects the rights and welfare of research subjects like you, and will determine whether or not we should contact you for additional consent.

Results of the analysis of the biological samples and de-identified clinical data you have provided may be

submitted to a government health research database that will assist other researchers investigating various diseases, including AD and related dementias. This government health research database will have access limited to approved researchers. Your data may be removed at any time, upon your request. However, data that has already been distributed for approved research will not be retrieved.

By signing this consent, you give permission for your data and samples to be stored and used indefinitely. You may revoke this permission at any time by submitting a written request to Dr. Brewer or Dr. Galasko. If you withdraw from the study, you can also choose to stop any future use of your data and samples. However, any samples or data already shared may not be retrievable or destroyed.

You may request to review your participation records at any time. Because the information collected is complex and intended for research use, we ask that a clinician be present to help explain the results and answer your questions.

## DEVELOPMENT FOR COMMERCIAL GAIN

The information obtained from your biomarker samples may have significant therapeutic or commercial value and may be used to develop a commercial test for AD or to develop tests for other disorders. You will not receive any compensation or other benefits as a result of future studies from these samples. If these samples are shared with other researchers, they will be identified only by a code number and descriptive data (such as age and gender). The results of these analyses will not be shared with you, your caregiver or your heirs due to the exploratory nature. By signing this form, you are consenting to such uses. You do not give up any legal rights by signing this consent document.

## BENEFITS OF PARTICIPATING IN THIS STUDY

You will not benefit directly from this study. This study does not involve any treatment for the improvement or cure of AD or related dementias. However, by participating in this research study:

1. You will receive an annual exam at no cost to you. If you wish, we will share the results of the exam with you and anyone else you choose. This information may help clarify your diagnosis and the underlying cause of your symptoms. Our research clinicians will provide you with information about normal aging, AD, and other forms of dementia and discuss what you might expect in the future.

2. You will be able to meet with a licensed clinical social worker who can give you suggestions and advice about how to cope with problems associated with Alzheimer's disease and provide referrals to community resources.

3. You will also have the opportunity to learn about experimental drug studies which are taking place at our research center. These studies will be discussed with you to see if you are interested in participation.

4. You will be contributing to a body of knowledge about AD and related dementias and changes in the brain with age. This may help researchers learn more about the diagnosis, treatment, possible causes of AD and other dementias.

5. You will be contributing to the body of knowledge about arterial stiffness, which might predict cardiovascular risk and future cognitive impairment.

6. You will have the option to receive certain research results. An ADRC clinician will be available to discuss these results with you and answer any questions.

## COMPENSATION (MEDICAL/FINANCIAL) IN CASE OF ILLNESS OR INJURY

Procedures related to the study will be provided at no charge to you. There will be no costs to you for participation in this study. For your time and effort, you will receive $50 compensation for each in-person visit. If you undergo a lumbar puncture, you will be paid $100.

Assistance with transportation is available upon request. The study covers all ride costs, and our team assists with scheduling. To arrange transport, you will provide minimal information (first name, address, phone number) to be used for the transportation service. Drivers are not informed about research participation. Caregivers or study partners may ride for free alongside participants when their assistance is necessary due to impairment. Participants may opt out of transportation services at any time without affecting their participation in the study.

If you are injured as a direct result of participation in this research, the University of California will provide any medical care needed to treat those injuries. The University will not provide any other form of compensation to you if you are injured. You may call the UCSD Human Research Protections Program at (858) 246-4777 for more information about this, to inquire about your rights as a research subject, or to report research-related problems.

## CONFIDENTIALITY OF RECORDS

Research records will be kept confidential to the extent provided by law. All of the health information generated or collected about you during this study may be inspected by the Department of Health and Human Services (DHHS) agencies and/or the Institutional Review Board (IRB). Your identity and the information collected will not be disclosed even to your primary care provider without your written consent. Confidentiality applies to both the data we collect and the samples that we store. Information about you will be kept confidential by using coded numbers and a locked file in a computer with restricted access. You will not be identified in any reports or publications.

Biomarker samples, which include CSF and genetic samples, will be stored and maintained in a coded manner without any identifying information. This data coding protects your privacy. Data will not be

revealed to family members, insurance companies, employers, or other individuals or organizations. Any information gained from genetic research will be reported in anonymous summary form. No information will be entered into your regular medical record. Both the ADRC and the NACC carry Certificates of Confidentiality from the DHHS. See the 'Certificate of Confidentiality' section below for more information.

We will provide you with a copy of the UCSD Health Insurance Portability and Accountability Act (HIPAA) Notice that describes use of your Protected Healthcare Information and medical records in relation to this research study.

Federal and State laws generally protect your genetic information in the following ways: a) Health insurance companies and group health plans may not request your genetic information from this research. b) Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. c) Employers with 5 or more employees may not use your genetic information from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that these laws do not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

We will minimize the possibility of results from this research being linked to you, but there is always the remote possibility that information from the research may be disclosed. If your genetic risk for certain diseases is accidentally divulged to the wrong source, you may be discriminated against in obtaining life or health insurance, or employment.

## CERTIFICATE OF CONFIDENTIALITY

A Certificate of Confidentiality has been issued for this project from the U.S. Department of Health and Human Services (DHHS). This Certificate will protect the Investigator(s) from being 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.

This protection, however, is not absolute. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). It does not apply to any state requirement to report certain communicable diseases. In addition, researchers must report child or elder abuse to appropriate authorities.

You should understand that 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, then the researchers may not use the Certificate to withhold that information.

Drs. Brewer, Galasko or the other investigators will not voluntarily, without your consent, disclose information that would identify you as a participant in this research project.

## VOLUNTARY PARTICIPATION

This form explains the research so that you may make an informed decision about participating. Participation in this study is voluntary. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. You are free to discontinue participation at any time without prejudice to your subsequent care and are free to seek care from a health care provider of your choice at any time. You may refuse to participate or withdraw at any time by calling the ADRC at 858-822-4800. Drs. Brewer and Galasko will still be able to use the information collected about you prior to your withdrawal from the study. Information that has already been shared cannot be withdrawn. Your participation also may be stopped by the study doctors without your consent. If this happens, it might be due to your inability to participate in study-related activities. If you are experiencing any distress from a procedure you are undergoing, you may ask to stop the procedure at any time.

## CONTACT PERSONS

Dr. Brewer, Dr. Galasko or _____has explained this study to you and answered your questions. If you have other questions or research related problems, you may reach Dr. Brewer, Dr. Galasko or study personnel at 858-822-4800.

## STATEMENT OF CONSENT

You have read (or have had read to you) the above description of this research study. You have been informed of the risks and benefits involved, and all of your questions have been answered to your satisfaction.

You will receive a copy of this signed consent form, and a copy of the "Participant's Bill of Rights" to keep.

You agree to participate.

| | | |
|---|---|---|
| **Subject's Name** (Print) | **Signature** | **Date** |
| **Legally Authorized Representative** (Print) *(If applicable)* | **Signature** | **Date** |
| **Person Obtaining Consent's Name** (Print) | **Signature** | **Date** |

## STUDY PARTNER'S CONSENT TO PARTICIPATE

You have read this consent form and have been given a copy of it and "Participant's Bill of Rights" to keep. You have had the opportunity to ask questions, and your questions have been answered to your satisfaction. You agree to serve as a study partner for the above named individual and to confirm the information we gather at each visit.

| | | |
|---|---|---|
| **Study Partner's Name** (Print) | **Signature** | **Date** |