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Name: _____ **Date:** _____

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

CONSENT TO BE A RESEARCH SUBJECT

Early diagnosis and longitudinal assessment of human prion diseases and other rapidly progressive neurological conditions

Michael Geschwind, M.D., Ph.D.

A. PURPOSE AND BACKGROUND

Michael Geschwind, M.D., Ph.D. from the Department of Neurology at the University of California, San Francisco, is conducting a study of rapidly progressive neurologic conditions, including "prion" disorders, autoimmune encephalitis syndromes, and other rapidly progressive neurologic conditions. This study is being sponsored by the Federal Government through the National Institute of Aging / National Institutes of Health, the American Academy of Neurology, and Quest (Athena Diagnostics).

Symptoms of rapidly progressive neurologic conditions may include forgetfulness, confusion, difficulty with movements, unsteady gait, muscle spasms, problems with vision, and difficulty speaking. Several diseases may present with these symptoms and sometimes can therefore be difficult to distinguish from one another.

Autoimmune Encephalopathies and related syndromes, such as anti-NMDA receptor, anti-voltage gated potassium channel complex (VGKC) are inflammatory disorders that are usually due to the body developing antibodies that attack proteins found in the nervous system. These syndromes usually are treated by suppressing the immune system. This study hopes to better understand these syndromes, including why some patients may respond better to specific treatments, why some patients have relapses whereas others do not, and what are the long-term consequences of having these disorders.

Another major form of rapidly progressive dementia is Creutzfeldt-Jakob Disease (CJD), a prion disease. Prion diseases are rare disorders of the brain that are caused by the prion protein (PrP). Disease results when an abnormal shaped form of PrP interacts with the normal form of PrP and converts it to the abnormal shaped form, leading to the accumulation of the abnormal form of PrP in the brain.

Although most prion diseases occur sporadically (spontaneously) and are due to unknown causes, a small number of cases (about 10-15%) are due to an abnormal gene, and are inherited. These inherited forms of CJD are caused by defects in the prion protein gene, *PRNP*. One goal of this study is to determine which parts of *PRNP* or other genes are relevant to prion diseases.

Currently, no test has been proven to accurately diagnose CJD without direct examination of brain tissue (after death, by autopsy or in life by biopsy). There is currently no treatment or cure for CJD, but researchers are actively working on treatments and potential cures

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Because these conditions are rapidly progressive, diagnosis of the disease often is made late in the illness. It is important that we learn how to make an accurate diagnosis earlier so that treatments (if and when available) can be given to patients as early as possible.

The primary goals of this study are to improve diagnosis and assess the progression of human prion diseases, autoimmune encephalopathies, and other rapidly progressive neurological conditions.

You are being asked to participate in this study because you are a patient, or a surrogate of a patient, with a rapidly progressive dementia/neurologic condition or you are a healthy control (a patient with another form of dementia or who is at risk for familial Creutzfeldt-Jakob disease).

B. PROCEDURES

Most of the procedures involved in this study typically would be done as standard medical care in diagnosing a rapidly progressive dementia or other neurologic condition. In some cases a procedure(s) may not have been done before your enrolling in this study and therefore will be ordered through this study. In some cases a procedure will have already been performed, but needs to be repeated for clinical purposes. In other cases, a procedure has been performed before enrolling in the study and does not need to be repeated for clinical purposes, but is only needed for research purposes. Before each procedure, you will be informed why it is being performed. You may be asked to participate in the discussed procedures one or multiple times over the course of a year. You may decide if you want to return for repeat visits. Each visit may last for up to 3 days.

If you agree to participate in this study one or more of the following procedures will occur:

1. A physical exam, including an abbreviated general physical exam and a standard neurologic exam, may be performed. For the neurologic exam, your primary senses (e.g., hearing, vision, etc…), your strength, your sensation (feeling on your skin), and your coordination will be tested. This will take approximately 30 minutes. You will be asked to consent to have the neurologic exam videotaped. The videotaping is to ensure accurate documentation of the examination and may also be used for teaching or educational purposes. Videotapes will be labeled with unique identify codes, secured in locked areas, and no footage shall contain audio or visual representations of your last name. You or your surrogate will sign a separate video consent form to indicate the specific authorized uses for the video usage and the timeframe for which any usage is authorized. You do not have to consent to be videotaped in order to participate in this research study.
2. Brain MRI scans may be performed. A brain MRI is a picture of brain tissue, which is taken without any radiation (x-ray) exposure. The MRI scanner is a tube surrounded by a giant circular magnet. During an MRI, you will lie on your back on a table positioned inside the tube. The scanner will make loud "knocking" sounds. If you are agitated or you cannot lie still for approximately one hour, you may be given a sedative (medication to calm you or help

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you sleep) for the MRI. In some cases, if you cannot lie still, you may need to be placed under general anesthesia (given medication to put you to sleep and make sure you are not moving). For this procedure, temporary endotracheal intubation may be necessary to help you breath while you are under anesthesia. Endotracheal intubation is a procedure by which a flexible tube is inserted through the mouth down into the trachea (the large airway from the mouth to the lungs). The tube serves as an open passage through the upper airway. The purpose of endotracheal intubation is to permit air to pass freely to and from your lungs. The endotracheal tubes may be connected to a machine to provide artificial respiration. You will be asked, but are not obligated, to undergo a second MRI during your initial visit and up to two follow-up MRIs at follow-up visits. Each brain MRI should take 1 hour to perform. If you require general anesthesia for the MRI, the MRI and anesthesia will take approximately 2 hours and you may require a few more hours to fully awaken after the anesthesia.

3. You may undergo autonomic testing, a study of your skin conductance and heart rate. This will take place during the "resting state" portion of your MRI. Set up should take no more than 5 minutes. To measure skin conductance, sensors will be attached to your index and middle fingers by Velcro straps. A gel will be applied between the small contact of the electrode and your skin. This electrode is cleaned with isopropyl alcohol after each use. The MRI machine has integrated recording equipment that will measure respiration, blood oxygenation, and EKG. Respectively, this involves placing a cushioned belt loosely around your chest, clipping a small device to your finger, and placing three adhesive patches with electrodes on the chest. It is also possible that pupil diameter will be measured. This will be done using a machine placed behind the MRI scanner and a small mirror placed above your eyes.
4. An electroencephalogram (EEG), a study of electrical current within your brain, may be performed. Electrodes will be attached to your scalp with removable adhesive (glue). Wires attach these electrodes to a machine that records the electrical impulses in your brain. The results are either printed out or displayed on a computer screen. Different patterns of electrical impulses can denote various problems within the brain and may help diagnose your condition. This procedure should take about one half hour. You may be asked, but are not obligated, to return to UCSF for follow-up EEGs. Repeat EEGS generally will be performed at least one week apart.
5. A lumbar puncture (LP; also called spinal tap), in which about 20 ml (~2 tablespoons) of spinal fluid is removed, may be performed. The LP may be performed at the initial and subsequent evaluations. The LP will be done by insertion of a needle into your lower back in order to reach the spinal canal. The procedure will be done by a neurologist and under sterile conditions using local anesthesia (numbing medicine) over the area where the needle is inserted. The procedure takes about 15 minutes to set up and 15 minutes to perform. You will need to lie flat and rest for a short period after completion of this test**.** Additional procedures, such as intubation, or medications, may be needed to do the lumbar puncture; intubation will only be done if the lumbar puncture is required for standard of medical care. Subjects or their legal guardian may be asked to sign additional procedure consents as necessary. With your permission, a sample of your spinal fluid may be stored at UCSF for future analysis. If you are on blood thinners, an LP will not be

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performed for the research study, but may be performed for standard medical care. In some cases, your CSF may be sent to another laboratory for research analysis.

6. A nerve conduction study (NCS) may be performed to detect possible nerve disorders (such as neuropathy). In this test, the nerve is electrically stimulated while a second electrode detects the electrical impulse 'down stream' from the first. This is done with small surface patch electrodes (similar to those used for an electrocardiogram or EKG) that are placed on the skin over the nerve at various locations. One electrode stimulates the nerve with a very mild electrical impulse. The resulting electrical activity is recorded by the downstream electrodes. For this research study, a NCS will only be performed once. If your NCS is not being done as part of research, but as part of standard medical care, an electromyogram (EMG) may be done at the same time as the NCS to exclude or detect muscle disorders.
7. A magnetoencephalogram (MEG) may be performed to evaluate your brain function and may help diagnose your condition. The MEG machine works like a very sensitive microphone to detect magnetic activity of brain cells and results of the test. For this test, your scalp will be scrubbed with a mildly abrasive electrode gel, and a number of small discs will be fastened with electrode paste, a sticky material that will be cleaned off at the end of the test. Alternatively, an electrode cap may be used; in this case, you will be asked to wear a cap, much like a swim cap, that has electrodes sewed into the fabric. The procedure should take about 1- 2 hours and may be performed at each visit. On average the procedure takes about one hour for our patients, and is divided up into 4 to 10 minute sessions. Between, each session there is a 2 minute break, although more time will be given if requested. If a patient is very agitated at the time of or before the procedure, he/she may be given a small oral dose of sedative, such as lorazepam.
8. You may be asked if you would agree to participate in force transducer-based motor testing. We are using these techniques to assess for subtle changes in motor function (movements).
    a. *Tongue protrusion force testing* might be done to assess your tongue movement. The testing will take less than 10 minutes to complete. During this time, you will be asked to rest your head on a height-adjustable chin-rest. A circular cushion with a disposable, non-reusable cover will be at mouth-level in front of your face. You will hear several cues to stick out your tongue and use it to apply force to the cushion. A machine connected to the cushion will measure the strength and consistency of your tongue force.
    b. You might be asked to perform *isometric grip force testing* to evaluate the degree of coordination and precision you have between your thumb and index finger. This testing involves holding a small device with these two fingers for up to 30 seconds at a time. During that time, you will be asked to keep your arm in a fixed position as weights are added to the device. This task will be repeated with both arms separately and with two different weight sizes. The total testing time will be less than 15 minutes.
    c. *Isometric grip force match testing* might be done to assess your ability to maintain a target grip. You will be asked to grasp a small device with your thumb and

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index finger and match the level of force shown on a monitor. Both hands will be tested individually. This test will take approximately 5 minutes to complete. .

d. You may be asked to perform *transducer-based tapping tasks* to measure the strength of your index fingers during various tapping activities. This test consists of tapping on a small padded device with the index finger of each hand. You will be instructed to tap at various speeds, including your fastest pace and at a cued pace. During this test, you will be provided a plate for wrist support and may rest your arm on the testing table. This test should talk less than five minutes to complete.

9. You may be asked if you would agree to undergo optical testing. We are using these techniques to assess for subtle changes in your retina.
    a. *Standard visual testing* might be done to evaluate your vision, ocular pressure, and ocular anatomy. You will be asked to bring your glasses or contact lenses to the examination. You will be asked to track moving objects with your eyes, read eye chart at various distances, and identify what you see in several pictures to check for color blindness. Your eyes will be examined with an ophthalmoscope—a non-invasive tool that will shine a light in your eyes to look at the front and back of your eyes. You will also be given eye drops which will dilate and numb your eyes. This will allow for the physician to measure the pressure of your eyes with a special machine. You will be asked to look straight ahead at a blue circular light. You will not feel any discomfort with this testing. This testing will take approximately 20 minutes to complete.
    b. *Optical coherence tomography (OCT)* with autofluorescence might be performed to count the nerve fibers in the back of your eye. A light will be shined in your eye for just a moment and, through a complex computer program, allowing for the evaluation of the health of your retina and optic nerve (loss of nerve fibers cause a thinning of the layers behind the eye). This testing will take approximately 30-45 minutes to complete and may include up to three of the following tests:
        i. *Full field visual-evoked potentials (VEP) testing* might be done to gather information about your optic nerve functioning. Painless, sticky electrodes will be placed on the back of your head and you will be asked to look at checkerboard lights that re shined on all different parts of the back of your eye. This takes about 20-30 minutes**.**
        ii. *Multifocal visual-evoked potentials testing* is used to gather information about optic nerve functioning within specific areas of the visual field. It is performed similarly to the full-field VEP with painless, sticky electrodes. This is the longest test and takes about 45 minutes to complete.
        iii. *Visual field testing* might be performed to assess your field of vision. You will be asked to look at a computer screen and keep your eyes focused on the center of the screen. Several visual cues will pop up on the surrounding areas of the screen. When you see these images in your periphery, you will press a hand-held button. This test will take approximately 30 minutes to complete.

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c. You may be asked to have *fundus photos* taken. Your pupils will be dilated with eye drops, and photographs of your retinas (the areas at the back of the eyes) may be taken. This will take about 15 minutes.

10. You may be asked to undergo neuropsychological and cognitive testing, which consists primarily of answering standardized questions, drawing and writing. If you agree to undertake any of these tests, you are under no obligation to finish them and can take breaks from testing whenever you wish. Although time taken to complete testing varies from individual to individual, we expect it may take approximately one hour to complete.
11. Blood draws may be done as part of standard medical care, for research purposes or as safety assessments prior to or as part of research. In some cases, your blood may be sent to another laboratory for additional research analysis. If you are having the lumbar puncture, analysis of your blood will be used to determine if completing the lumbar puncture will be safe and to compare with certain cerebrospinal fluid results. If you have a skin biopsy your blood will be analyzed for infectious diseases including syphilis, HIV, hepatitis B, hepatitis C, and some other viral diseases. These are the same tests that would be performed if you donated blood and they are done only for laboratory safety reasons. A separate consent for HIV testing is required. If these tests are abnormal, we will try to give you the test results in person with counseling about the meaning of these results. If you cannot return for these results, we will provide the results to your primary care provider for disclosure to you.
12. Additional blood may be drawn for generation of peripheral blood mononuclear cells (PBMCs) and subsequent development of cells, similar to what will be done with skin biopsies (described below). These samples may be sent to the National Cell Repository for Alzheimer's disease (NCRAD), the Institute for Neurodegenerative Diseases, or other collaborators for processing and/or storage. Outside researchers or institutions will not receive direct identifiers with these samples.
13. As a part of this study, a UCSF medical staff member may take two to three skin biopsies. A small area on the underside of your forearm or other part of your body (based on your preference), will be sterilized with an antiseptic solution and wiped with an alcohol swab. A small amount of local anesthetic will be injected just under your skin. After the skin is numb, a small piece of skin, less than one-third the size of a dime, will be removed. The area where the skin was removed will be left open to heal. An antibiotic ointment will then be put on the area, and a Band-Aid applied. The tissue from the biopsy will be grown in the laboratory so that we can obtain cells for this study. You will not receive any results from these tests. Usually two biopsies will be collected, but a third may be necessary if the person performing the biopsy thinks the previous samples are not viable or were damaged in the biopsy process. This process will take about 30 minutes.
14. Sleep studies may be done as a part of this study. In order to complete the sleep study, you will stay overnight into the Clinical Research Center. This will require you to be admitted and discharged through the hospital using standard clinical research protocols. Our sleep technician will place a series of sensors on your scalp, face, torso and limbs to measure your sleep, muscle movements and heart rate. In addition we will measure if you have any sleep apnea. This will be done using two bands around your torso, a pulse oximeter on your finger and a small tube at the base of your nose to measure your breathing. In addition, we will be recording you using both video and audio acquisition

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during the night. When you are ready to go to sleep, we will turn out the lights and return in the morning to remove all of the sensors. On rare occasions, you may be asked to do the sleep study in your own home or where you are staying instead of the Clinical Research Center. This will involve a study team member going to you and setting up the equipment, and then returning the next day to pick it up.

15. You may be asked to have other procedures performed as part of standard medical care that may help to diagnose your disease. These procedures will not necessarily be part of this research study.
16. If you are a subject with potential prion disease, Alzheimer's disease, other non-prion-related neurologic disease, or if you have a family history of any of these disorders, you may be asked to have a sample of your blood sent to the National Prion Disease Pathology Surveillance Center (NPDPSC) to determine whether you have a genetic mutation associated with prion disease. If this sample is sent, you agree to allow Dr. Geschwind to provide this testing center with your age, state of residence, first two initials of your first and last names, a brief clinical history (including a brief family medical history), any familial relationship to other study subjects, and the age of onset of any relevant neurological symptoms. The primary purpose of the NPDPSC is pathological surveillance of prion disease cases throughout the United States. Their funding is provided by the Center for Disease Control and Prevention (CDC). The NPDPSC prefers to have your full name associated with this sample in order to improve their surveillance efforts and more importantly to further decrease the chance of samples being mixed up. You may choose to provide the NPDPSC with your full name. The NPDPSC is a CDC appointed site, approved for the collection and data analysis designed to monitor the occurrence of prion diseases. Data collected by the NPDPSC will be stored in a secure data storage warehouse known as the Secure Research Environment (SRE), hosted in a professionally managed FISMA & HIPAA-compliant Tier III data center. Please indicate at the end of this consent form if you are willing to include your full name when sending a sample of your blood to the NPDPSC for genetic testing. You may be asked to stay in the UCSF CTSI Clinical Research Center (CCRC) for a period of approximately1-2 days, with your spouse or another family member, in order to undergo some of the tests listed above. In rare cases, a research participant staying in the CCRC will wander off the unit, or, in the case of outpatients, out of the office where evaluations are taking place. Every effort will be made to prevent this from happening; you will not be left unattended at any time. As part of the CCRC protocol, you may be asked to wear a GPS monitoring device while participating in this research project.
17. You will be asked to consider an autopsy to definitively establish your diagnosis in the event of your death. You may agree to have an autopsy and to provide tissues for research. You do not have to agree to autopsy to participate in this research study.
18. In the course of this study, the researchers will gather information about you either directly, by communicating with your caregivers, medical providers, or by reviewing your medical records. Your caregivers or medical providers may be asked to complete certain scales assessing your current condition or your symptoms. This information will be used to:
    - Determine if you are eligible for the study
    - Assist in confirming or determining your clinical diagnosis

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- Decide your research group placement (e.g., autoimmune disease, non-prion disease, symptomatic prion disease, presymptomatic genetic prion disease, etc...)
- Learn more about your illness

All of the information also will be stored in a password protected secure database, designed by the GCRC and the UCSF Memory and Aging Center. Research data that may identify individual subjects will be shared only among the investigators who are a part of this project, or as permission is given. You will be assigned a unique identification number that may be used to identify your data. The information to be gathered will include, but not be limited to: date of birth, race, ethnicity, date of onset of your symptoms, your medical history, your family's medical history, your social history (i.e., education, travel history, drug use, wild game consumption), results of all clinical evaluations, results of laboratory and diagnostic clinical tests (including actual MRI films), medical questionnaires, and contact information for yourself, as well as your family members, caregivers and doctors.

All research procedures for this study will be performed at UCSF Medical Center, the Memory and Aging Center at UCSF, or San Francisco General Hospital. The data accumulated from these procedures will be analyzed in conjunction with any medical information we receive from procedures performed at outside facilities for the purposes of our research.

Specimens may be shared with other researchers, institutions, and companies, but only for use in research protocols that have undergone scientific and ethical review. When blood or tissues are shared with other researchers or institutions, they might receive some of the following information: age, gender, diagnosis, symptoms, *PRNP* mutation status, *PRNP* codon129 polymorphism, and whether or not you are symptomatic.
Typically, outside researchers or institutions will not receive direct identifiers such as your name, birth date, social security number, or contact information. There are, however, exceptions. When sending CSF for testing as a part of this study, your name and date of birth may be included in the paperwork. This is because the tests are done clinically. The results from this testing do not go on to your medical record and are stored in a protected study database.

Some of your spinal fluid, blood, or cell lines created from your skin or other cells may be used now or in the future for research purposes. These samples may be used to learn more about how prion diseases or other diseases develop and/or may result in new products, tests or discoveries. In some instances, these may have potential commercial value. This tissue to be kept for research purposes will be obtained only at the same time as your regular procedures are performed; you will not have to undergo any special procedures for this purpose. There will be no additional charge, and you will not receive any payment or financial benefit from any products, tests or discoveries. You may also be asked in the future if you are willing to be in additional research studies. You will not be told the results of any future research. Participation in this extra research is voluntary, and if you choose not to allow the extra research it will in no way affect your care on the main study. You may at any time contact the researchers and request your samples be withdrawn from research use, and any identifiable original samples still in their possession will be destroyed. The cell lines created from your cells, however, will not be destroyed. Please

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indicate whether you are willing to allow this extra research by initialing one of the lines at the end of the form, after section L.

There is a possibility that an abnormality that was previously unknown will be discovered during one of the study tests or procedures. In the event that an abnormality is found, the researchers may ask you for permission to contact your physician regarding these results. In this case, your physician will review the results and decide if additional testing is recommended.

C. RISKS/DISCOMFORTS

1. ***Physical and Neurological Examination****:* The physical and neurological examination may be frustrating for subjects that have difficulty with or are unable to perform certain aspects of the exam. The videotaping can be stopped at any point if you are uncomfortable. Having you or your caregivers fill out certain scales and providing your medical history may be an inconvenience. You or your caregivers may refuse to answer certain questions.
2. ***Neuropsychological Testing:*** Neuropsychological testing may be fatiguing for patients, particularly for those with cognitive impairments. The duration of test sessions will made shorter or limited and will be left to the discretion of the test administrator. In the event that a subject appears to be under undue distress, testing for that patient will be terminated. You may ask to have a break or terminate the testing at any time.
3. ***Lumbar Puncture:*** This procedure may be associated with some mild discomfort and may be painful for some people. Local anesthesia (numbing medicine) will be applied to the skin with a small needle in the area of the lower back where the LP will be performed; this local anesthesia likely (>50%) will cause a brief (1-2 seconds) burning or stinging sensation. The LP is occasionally (about 10%) associated with a headache, which is usually relieved by lying down, but may last up to several days. Occasionally (<10%) a procedure called a blood patch is required to stop a severe headache after an LP. An anesthesiologist performs the blood patch. Very rarely (<1%) a spinal hemorrhage may occur from the vessels near the spinal cord, although this is much more common with patients on blood thinners (who are not allowed to participate in this study). An even more rare (<1%) potential complication is a bleed in or around the brain. Meningitis, or infection of the lining of the brain and spinal cord, is also a rare (<1%) but possible complication that is manifested by fever, confusion and stiff neck. If you experience persistent headache, weakness or numbness of one or both legs, or fever and confusion, you will notify the researcher who performed the lumbar puncture, or call Dr. Geschwind (clinic: 415-476-6880) or his research staff (415-476-2901 or 8791), or go to the nearest emergency room for advice or evaluation.
4. ***MRI:*** Patients who have any metallic materials within the body must notify their physician before the examination or inform the MRI staff. Metallic chips, materials, surgical clips or foreign material (artificial joints, metallic bone plates, or prosthetic devices, etc.) can significantly distort the images obtained by the MRI scanner. Patients who have heart pacemakers, metal implants, or metal chips or clips in or around the eyeballs cannot be scanned with an MRI because of the risk that the magnet may move the metal in these areas. Similarly, patients with artificial heart valves, metallic ear

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implants, bullet fragments, and chemotherapy or insulin pumps should not have MRI scanning. Because the risks to a fetus from MRI are unknown, pregnant women must not participate in this study. Even though the MRI is well lit, open at both ends, ventilated, and has an intercom, some people undergoing brain scans feel anxious being in the MRI scanner. You may request a mild sedative before the scan if you expect to be uncomfortable. The MRI scanner makes loud noises and some patients may experience temporary hearing loss after the MRI. There are risks from general anesthesia, if it is required. Some patients may react to the anesthesia and become ill or even die. This is extremely rare (<1%). You must let the researchers know if you or any family member has ever had a bad reaction to general anesthesia. Endotracheal intubation may result in damage to the mouth, teeth, throat, vocal cords or lungs, which may or may not be reversible; all measures will be taken to ensure this does not occur. If general anesthesia is required for patients who cannot stay still this will require intubation and sedation, both of which have additional risks.

5. ***Autonomic testing:*** There may be irritation to your skin from placement of the sensors. All equipment will be either MR-compatible or housed outside of the scanner room to avoid any accidental injury.
6. ***EEG:*** There may be irritation to the scalp from placement of electrodes. You must lie still during the test.
7. ***MEG:*** There may be some mild discomfort from holding still during the procedure and when the tape is removed.
8. ***Nerve Conduction Study:*** There are no known risks to nerve conduction studies. The electrical impulses may cause very brief discomfort with each impulse. Occasionally, individuals will describe this as painful; the procedure will be stopped immediately if the subject requests this.
9. ***Force transducer-based motor testing***: There are no known risks to grip force, tapping, or tongue force analysis testing. The muscles being tested may become fatigued during testing (i.e. your tongue, thumb, index finger, and other hand or wrist muscles).
10. ***Sleep Studies****:* There may be some discomfort due to wearing the sleep/waking/activity recording head or wrist bands, or overnight measurement of vitals device. The bands can emit a low radiofrequency signal to communicate with the docking station/recording device at the bed side. This radiofrequency is below the level measured by the FDA or that emitted during a cell phone conversation. Sleep disruption may occur while subjects are acclimating to the head or wrist bands. Further sleep disruption could occur during the measurement of overnight vitals and during the overnight stay for the PSG. Subjects may become frustrated and tired when they are prevented from sleeping between the assigned naps during the MSLT or again during the MWT. Subjects and their partners may find the video or audio recordings and monitoring to be uncomfortable or intrusive. If the sleep study is completed in the subject's home, he or she may feel uncomfortable having a study member(s) go to their home / where they are staying to set up the overnight PSG.
11. ***Blood Draw***: Drawing blood from a peripheral vein may be uncomfortable, may produce bruising or rarely cause an infection. Dizziness may accompany a loss of blood and the patient will be instructed to remain reclined for 15 minutes after blood draw.

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12. ***Infectious Disease Testing***: Being tested for HIV may cause anxiety regardless of the test results. A positive test indicates that you have been infected with the HIV virus, but no one knows for certain when, if ever, you will become sick with AIDS or a related condition. Receiving positive results may make you very upset. If other people learn about your positive test results, you may have trouble obtaining insurance or employment. If your test is negative, there is still the possibility that you could be infected with the HIV virus and test positive at some time in the future. Also, it is always possible that the test results could be wrong. California regulations also require laboratories to report new cases of HIV, hepatitis B, and hepatitis C infection to the county public health department. The reports include the patient's name, social security number, and other identifying information. Information about these new infections is used to track these diseases statewide and nationwide. Other than this required reporting, your results will be treated confidentially by the study staff. Personally identifying information will not be reported to other departments or agencies.
13. ***Skin Biopsies:*** This procedure may be associated with some mild pain or discomfort, most commonly experienced as a burning sensation from the numbing medicine. There will be minor bleeding at the skin biopsy site. It is possible that a small scar will result. There is a small risk of infection, which can be treated with antibiotics if needed. There is also a small risk of an allergy to local anesthetic.
14. ***Genetic Testing:*** Genetic information about you and your family may be uncovered during this research project. Prion diseases are currently incurable and therefore knowing what the result shows will not allow you to prevent the disease. This may cause undue stress, depression, hopelessness, fear of having children or fear that your current children will get the disease. Genetic testing may also disclose infidelity or unsuspected paternity. Because of this reason you may choose not to find out the results of your genetic testing. However if you are interested in the possibility of knowing the results of your genetic analysis of the prion gene for any reason, genetic counseling will be provided at UCSF without charge to assist with the decision of whether or not to learn the results.
15. As prion diseases are reportable diseases in the state of California, if we diagnosis you with prion disease, we will be required to report this to the state of California. The report may include sending your name, contact information, demographic information, and some medical records to the California Department of Health Services.

D. BENEFITS

You will not necessarily have a direct health benefit from being in this research study. Findings from this study may benefit you if your clinical diagnosis is in question, by helping to diagnosis your condition. It is possible, depending on several factors, that you may be able to have additional neurologic evaluation at UCSF without participating in this study. The study primarily may benefit future patients with rapidly progressive dementias or other neurologic conditions, through earlier and improved diagnostic methods and a better understanding of your disease or condition.

E. ALTERNATIVES

You do not have to participate in this study, and choosing not to participate will not affect your current and/or future medical care at UCSF.

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F. COSTS

There will be no costs to you for participating in this study. There will be no charges for scheduled visits or laboratory tests that are part of this study and are not standard of medical care. You remain responsible for other medical costs. Many of the procedures involved in this study would be done as standard medical care in diagnosing your illness. In certain cases, some procedures or tests (e.g., MRI, EEG, LP, blood tests) may not have been done before your enrolling in this study (or they have been performed but need to repeated) and therefore will be ordered as standard medical care. In this case you or your insurance company will be billed and you will be responsible for the costs of these procedures. In some cases, the study may be able to pay for these procedures, if not covered by insurance. If a procedure has already been performed before enrolling in the study and does not need to be repeated for clinical purposes, then the study will pay for the procedure and you or your insurance company will not be billed.

G. PAYMENT

Participants will be not be reimbursed for participating in this study. No other compensation will be provided.

H. RESEARCH-RELATED INJURIES

It is important that you tell your study doctor, Michael D. Geschwind, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him at 415-476-2900.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California or the study sponsor, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.

I. CONFIDENTIALITY

Confidentiality is a concern of this research study. Every possible effort will be made to keep the research information in the strictest confidence, but we cannot absolutely guarantee that accidental disclosure will not happen. There is a potential risk that unlawful actions will result in the loss of confidentiality. In order to minimize such risks, all test materials are kept in secured areas. Information on each subject will be entered into a password protected secure database, designed by the GCRC and the UCSF MAC. Research data that may identify individual subjects will be shared only among the investigators who are a part of this project. You will be assigned a unique identification number that may be used to identify your data. This subject number can be used to further protect patient confidentiality. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research test results will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of information added to your medical record as a result of your participation. Organizations that may look at and/or copy your medical records for

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research, quality assurance and data analysis include: The University of California, Quest (Athena Diagnostics), Washington University, Mayo Clinic, The NPDPSC at Case Western Reserve University, and the NIH (National Institutes of Health). For some patients, the local or state health departments or the US Center for Disease Control and Prevention (CDC) may need clinical records for public health concerns. We will provide these records to these authorities when requested.

J. QUESTIONS

You have talked to either Dr. Geschwind or the person who signed below about this study and have had your questions answered. If you have further questions, you may call Dr. Geschwind or the study coordinator at (415) 476-6880. If you have any comments or concerns about participation in this study, you should first talk with the researchers. If for some reason you do not wish to do this, you may contact the Committee on Human Research, which is concerned with the protection of volunteers in research projects. You may reach the committee office between 8:00 and 5:00, Monday through Friday, by calling (415) 476-1814, or by writing: Committee on Human Research, Box 0962, University of California, San Francisco/San Francisco, CA 94143.

K. CONSENT

PARTICIPATION IN RESEARCH IS VOLUNTARY. You are free to decline to be in this study, or to withdraw from it at any point. Your decision to participate or withdraw in this study will have no influence on your, your family member, or your significant other's present or future status as a patient at UCSF, Department of Neurology. You may be withdrawn from this research study if you do not follow the directions of the study.

If you are judged not to have capacity to consent to this research study, a surrogate may consent for you. If this occurs and during the course of, or after, participating in this study, you become competent, you will not be allowed to continue in the course of the study unless you choose to and sign a consent form accordingly.

You will be asked to sign a separate from authorizing access, use, creation, or disclosure of health information about you.

a. EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

You have been given a copy of this consent form and Experimental Subject's Bill of Rights to keep.

SAMPLES FOR FUTURE RESEARCH:

____ You do not want your extra spinal fluid, blood samples or tissue used for any research or tests other than those needed for the main research study.

____ The researchers may keep your extra spinal fluid, blood samples and tissue for future research.

GENETIC TESTING:

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____ You do NOT want your full name provided to the NPDPSC with your blood sample sent for PRNP genetic testing.

____ You are willing to have your full name provided to the NPDPSC with your blood sample sent for PRNP genetic testing.

YOU WISH TO PARTICIPATE IN THIS STUDY

_____	_____	_____
Signature of subject	Name (please print)	Date
_____	_____	_____
Person Obtaining Consent	Name (please print)	Date

AND/OR:

_____	_____	_____
Legally Authorized Representative	Name (please print)	Date

_____
Relationship to Subject

_____	_____	_____
Person Obtaining Consent	Name (please print)	Date

The person being considered for this study is unable to consent for himself / herself. You have been asked to give your permission to include this subject in this study. You know of no reason why he / she would refuse were it possible to do so now.

_____	_____	_____
Signature	Name (please print)	Date

_____
Relationship to Subject