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Document: Informed Consent Form: ICF Part 1

Official Title of Study: Subcortical-cortical network dynamics of anesthesia and consciousness

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Consent and Authorization to be part of a Research Study
To be conducted at
The University of Texas Southwestern Medical Center
The University of California, Los Angeles

Part 1

Key Information about this Study

The purpose of this research study is to understand the effects of anesthesia on the human brain. The study involves participants who are undergoing one of the two following procedures: Deep Brain Stimulation (DBS) Implantation or DBS pulse generator implantation or replacement. Participants will be asked to complete one, 40-minute intraoperative research visit. This one-time study visit will involve administration of the general anesthetic propofol during your relevant operation under the care of an anesthesiologist. Participants will be asked to respond to visual, auditory, and/or verbal stimuli during the administration of propofol. Blood will be drawn, and the brain's electrical activity will be recorded during this time.

The greatest risks of this study involve placement of the electrode grid to record brain activity and the administration of propofol as an anesthetic. There is also a risk of loss of confidentiality and discomfort associated with increased surgery time.

If you are interested in learning more about this study, please continue to read below.

Information about this form

You may be eligible to take part in a research study. This is a multi-site study, meaning it will take place at several locations. Because this is a multi-site study the informed consent form will includes two parts. This form is Part 1 and includes information that applies to all study sites, like the purpose of the study and the research procedures to be conducted.

Part 2 of the consent form will include information specific to the study site where you are being asked to enroll. This could include any research procedures specific to a study site or local contact information for the study team. Please take time to review this information carefully. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

Please tell the researchers or study staff if you are taking part in another research study.

Voluntary Participation - You do not have to participate if you don't want to. You may also leave the study at any time. If you decide to stop taking part in this research study, it will not affect your relationship with the staff or doctors at your local institution. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the local institution, your status will not be affected in any way.

General Information – "Who is conducting this research?"

Principal Investigator
The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety and welfare as a participant in the research. The PI for this study is Dr. Nader Pouratian, MD, PhD, Department of Neurological Surgery at The University of Texas Southwestern Medical Center.

Funding
The National Institute of Health General Medical Sciences, a federal agency that promotes scientific research, is funding this study. This organization is providing money to The University of Texas Southwestern Medical Center and the University of California, Los Angeles so that the researchers can conduct the study.

Purpose – "Why is this study being done?"

You are asked to participate in this research study of the effect of anesthesia on the human brain. General anesthesia is a medically induced state of unconsciousness experienced by millions of people every year. While the behavioral characteristics of anesthesia are well defined, our understanding of how the brain changes under anesthesia is incomplete. A complete understanding of these changes is important for developing, optimizing, and monitoring anesthetics.

The researchers hope to use the neurosurgical opportunities presented during DBS surgery to gain an understanding of how the brain regulates and controls consciousness. Ultimately, the research will shed light on and provide a path towards developing therapies for disorders of consciousness.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Information about Study Participants – "Who is participating in this research?"

You are being asked to be a participant in this study because you are undergoing surgery for (1) implantation of deep brain stimulation (DBS) leads or (2) implantation of DBS pulse generator and have a diagnosis of Parkinson's disease or Essential Tremor.

How many people are expected to take part in this study?
This study will enroll approximately 144 study participants across all study sites.

Information about Study Procedures – "What will be done if you decide to be in the research?"

While you are taking part in this study, you will be asked to attend one visit with the researchers or study staff. This research visit will occur in conjunction with your scheduled procedure

It will not be necessary for you to return to the hospital/clinic for research purposes.

Assignment to Study Groups –
Groups that differ by stimulation
When it is determined you are eligible for the study, you will be assigned to one of two groups: "DBS on" or "DBS off". The Principal Investigator and neurosurgeon will determine your group. Participants in the "DBS on" group will receive stimulation from clinically implanted DBS leads at a therapeutic level while completing study tasks. Alternatively, participants in the "DBS off" group will have their stimulation turned off before surgery (if undergoing a

battery placement) or receive no stimulation after implantation (if undergoing initial DBS surgery) during the study tasks. You will be aware of your assignment prior to participating in the study.

Study Procedures - as a participant, you will undergo the following procedures:
DBS Implantation Study Procedures –
Before you begin the study, you will undergo the normal procedure for implantation of your leads or device, as discussed with your neurosurgeon and neurologist and as recommended to you based on your symptoms.

An anesthesiologist will administer the general anesthetic propofol via IV in intervals. Both the anesthesiologist and the study team measure loss or recovery of spontaneous movement, loss or recovery of movement in response to stimuli, and loss or recovery of movement to command. The research staff will place sticky electrodes around the participant's eye to monitor blinking during anesthesia administration. These will be removed after research. The anesthesiologist will also perform a blood draw at the end of every interval. Anesthesia will be administered in an incremented fashion until the participant stops responding to the behavioral task, or study time has exceeded 30 minutes.

During this time, signals will be recorded from within your brain from the deep brain stimulation leads that were already implanted in your brain for clinical purposes. Some participants might also receive stimulation at therapeutic frequencies during propofol administration. In addition, researchers will record from the surface of your brain using electrode grids placed on the surface of your brain. These electrode grids are for research purposes only and will be removed at the conclusion of the study prior to closing the skin.

During these studies, you may be videotaped or your voice may be recorded to document exactly when you did or said. If you are undergoing either type of surgery, your medical record (i.e., intraoperative fluoroscopy results) may be reviewed to collection information about the positioning of the electrodes on your brain during surgery.

DBS Pulse Generator implantation or replacement Study Procedures –
Prior to the surgery, an anesthesiologist will administer the general anesthetic propofol via IV in intervals. Both the anesthesiologist and the study team measure loss or recovery of spontaneous movement, loss or recovery of movement in response to stimuli, and loss or recovery of movement to command. The research staff will place sticky electrodes around the participant's eye to monitor blinking during anesthesia administration. These will be removed after research. The anesthesiologist will also perform a blood draw at the end of every interval. Anesthesia will be administered in an incremented fashion until the participant stops responding to the behavioral task, or study time has exceeded 30 minutes. At this time, the anesthesiologist will perform standard of care procedures to finish anesthesia administration needed for the pulse generator surgery.

These study procedures might occur with the deep brain stimulator device on, or off. Some participants might receive deep brain stimulation at therapeutic frequencies during propofol administration.

During these studies, you may be videotaped or your voice may be recorded to document exactly when you did or said.

Could your participation end early? There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:
- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is stopped.

Risks – "What are the risks of participation in the research?"

Risks from the research
This study will last up to an additional 40 minutes while you are in the operating room. Additional time during surgery can be associated with discomfort. The intraoperative environment is not always the most comfortable environment during surgery, and this may present a source of discomfort for you. Moreover, there is a theoretical risk of increased risk of infection with a prolonged surgery. Although studied many times, the increased risk of infection has never been proven in the type of surgery you will be undergoing.

Risks from the specific research procedures (drug(s), interventions, or procedures)
There are risks to taking part in this research study. One risk is that you may have side effects while on the study. There is risk / discomfort associated with placement of the electrode grid and administration of propofol as an anesthetic. In some cases, side effects associated with placing the electrode grid and anesthesia can be long lasting or may never go away.

Everyone taking part in the study will be watched carefully for any side effects. However, the study doctors don't know all the side effects that may happen. Be sure to tell your study doctor immediately, about any side effect that you have while taking part in the study.

The following section will describe the risks related to each your participation in this research study. You should talk to your study doctor about any side effects or other problems that you have while taking part in the study.

Side effects can range from mild to serious. Serious side effects are those that may require hospitalization, are life threatening or fatal (could cause death). The frequency that people experience a certain side effect can range from many (likely), few (less likely) or only one or two (rarely).

Placement of the electrode grid:
Although such grids are placed safely for clinical purposes on a regular basis and is generally considered safe, the placement of this grid is not without risk.

Risks and side effects related to the placement of the electrode grid include those which are:

Rare and Serious
In 100 people, approximately 1 or less may have:

- Bleeding on top of or into the brain or stroke, resulting in permanent neurological deficit and / or infection

Administration of anesthetic (propofol):
Propofol is an anesthetic used routinely in millions of procedures every year. Propofol is used to cause sedation and, at higher doses, general anesthesia. However, its use is not without risk. As with all general anesthetics, as doses increase, propofol can lead you to stop breathing and lead to a drop in your blood pressure. Both of these effects could be dangerous if not counteracted, so propofol should only be administered by individuals, like those in your anesthesia care team, trained in advanced airway management and cardiopulmonary resuscitation. The initial dose of propofol may feel hot in the vein, some people find this painful for a moment.

Risks and side effects related to the administration of anesthesia include those which are:

Rare and Serious
In 100 people, approximately 1 or less may have:

- Venous irritation

- Sudden jerking of muscles

For more information about risks and side effects, ask one of the researchers or study staff.

We will tell you about any significant new findings which develop during the course of this research which may relate to your willingness to continue taking part.

Are there Risks related to withdrawing from the study?
If you decide to withdraw from this study early, please discuss your decision with the principal investigator. There will be no additional visit to complete study withdrawal procedures.

Are there risks if you also participate in other research studies?
Being in more than one research study at the same time may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers.

Benefits – "How could you or others benefit from your taking part in this study?"

You may not receive any personal benefits from being in this study.
We hope the information learned from this study will benefit other people with similar conditions in the future.

Payments – Will there be any payments for participation?

You will be compensated $50 for your participation. Compensation will be provided to the participant upon signing the consent form. Please refer to the "Part 2 Consent" document for further details.

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

Certificate of Confidentiality:
To help us further protect your information, the investigators will obtain a Certificate of Confidentiality from the U.S. Department of Health and Human Services (DHHS). This Certificate adds special protections for research information that identifies you and will help researchers protect your privacy.

With this Certificate of Confidentiality, the researchers cannot be forced to disclose information that may identify you in any judicial, administrative, legislative, or other proceeding, whether at the federal, state, or local level. There are situations, however, where we will voluntarily disclose information consistent with state or other laws, such as:

- to DHHS for audit or program evaluation purposes;
- information regarding test results for certain communicable diseases to the Texas Department of State Health Services, including, but not limited to HIV, Hepatitis, Anthrax, and Smallpox;
- if you pose imminent physical harm to yourself or others;
- if you pose immediate mental or emotional injury to yourself;
- if the researchers learn that a child has been, or may be, abused or neglected; or
- if the researchers learn that an elderly or disabled person has been, or is being, abused, neglected or exploited.

The Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about your involvement in this research study. In addition, the researchers may not use the Certificate to withhold information about your participation in this research study if you have provided written consent to anyone allowing the researchers to release such information (including your employer or an insurance company). This means that you or your family must also actively protect your privacy.

A Certificate of Confidentiality does not represent an endorsement of this research project by the Department of Health & Human Services or any other Federal government agency.

How will my information and/or tissue samples be used?
With appropriate permissions, your samples and collected information may also be shared with other researchers here, around the world, and with companies.

By agreeing to participate in this study, your information or tissue samples could be used for future research studies or sent to other investigators for future research studies without additional consent from you. The information that identifies you will first be removed from your information or tissue samples. If you do not want your information or tissue samples to be used for future research studies without your consent, you should not participate in this study.

Contact Information – Who can you contact if you have questions, concerns, comments or complaints?

The University of Texas Southwestern Medical Center Human Research Protection Program (HRPP) oversees research on human subjects. HRPP and Institutional Review Board (IRB) representatives will answer any questions about your rights as a research subject, and take any concerns, comments or complaints you may wish to offer. You can contact the HRPP by calling the office at 214-648-3060.