Consent to be part of a Research Study
To be conducted at
The University of Texas Southwestern Medical Center

Key Information about this Study

You are invited to take part in a research study designed to understand the natural history of Essential Tremor (ET). Currently, we do not know what causes this movement disorder and our objective is to examine the environmental factors involved in the etiology of ET.

For this purpose, we are currently studying the relation between levels of Harmane, a dietary neurotoxin found in blood, and Essential Tremor and Parkinson's disease (PD), as well as the levels of neurofilament light chain (NfL), a protein linked to various neurological disorders. Two different groups of participants are being recruited to compare levels of this compound; subjects diagnosed with Essential Tremor (1), To determine if the results found are different from the general population, we are also including a group of healthy individuals 2).

The duration of the study is approximately 5 years. The study requires a phone interview, a screening packet to be completed at home, and one-time interview with the research staff where different research activities will be performed. These include dietary questionnaires, a blood draw, a smell test, cognitive testing, and a videotaped neurological examination. The visit will last approximately 3 hours and it will be scheduled according to your availability.

You will not receive any direct benefits from being in this study. However, your participation may result in knowledge that would help us understand modifiable risk factors in ET.

The risks associated with this study include the potential for loss of confidentiality, loss of balance, and discomfort due to the blood draw. Different measures are adopted during the research to minimize these risks; nonetheless, we want you to be fully aware of them.

This consent form gives you detailed information about the study. Research staff will walk you through every section and answer any questions you might have. Once you understand the study you will be able to decide if you wish to formally enroll and we'll ask for your signature in this document.

Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study.

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 UT Southwestern staff or doctors. 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 Medical Center, 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. Elan Louis, Chairman of the Department of Neurology and Neurotherapeutics.

Conflict of Interest
None of the researchers involved in this study has reported a Conflict of Interest.

Funding

National Institutes of Health, a federal agency that promotes scientific research, is funding this study. This organization is providing money to UTSW 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 role of environmental factors in Essential Tremor. Previous research have suggested a link between Harmane (HA), a dietary neurotoxin, and ET. A link has also been suggested between this toxin and PD, a related tremor disorder. Additionally, in recent years, neurofilament light chain has emerged as a biomarker of axonal loss and an indicator of disease activity in other related neurologic disorders, including multiple sclerosis, Alzheimer's disease, and stroke. The purpose of this research study is to assess blood levels of HA and NfL in patients who have ET and control participants who do not have ET or other neurological disorders. Our goal is twofold: (1) nail down the link between HA and ET. (2) Further explore NfL as a potential biomarker for ET.

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

You are being invited to be a participant in this study because you contacted us to volunteer to participate and meet the criteria for one of the four groups: a) People diagnosed with Essential Tremor, or 2) you want to participate as a Control, not diagnosed with any of the above mentioned conditions and meet the criteria for such group.

How many people are expected to take part in this study?

This study will enroll approximately 400 study participants.

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 participate in the activities mentioned below.

Screening during Research

Once you have expressed your interest in the study, the research team will contact you to administer a screening questionnaire. We will collect the following information:

- Brief medical history including current and previous medications taken
- History of brain surgery for the treatment of Essential Tremor
- Family history of movement disorders and features of your tremor (onset, severity, etc.)

We will also forward you a supplemental questionnaire and blank pieces of paper for you to draw some spirals.

The screening phase will take approximately 30 minutes. All the data collected at this stage will be used to verify if you meet the inclusion criteria. Once you send the spirals to our office we will present your information to the principal investigator, Dr. Elan Louis, and he will confirm your eligibility and determine your classification to one of the two study groups.

Groups that differ by criteria
According to the movement disorder diagnosis you have, you will be categorized as a participant in one of the following groups:

1. Essential Tremor
2. Healthy individuals

Please note that the research activities carried out for each group are the same.

Shortly after, you will be contacted to schedule an interview with a research assistant according to your availability.

Procedures and Evaluations during the Research

If you agree to take part in this study, you will be asked to undergo an in-person evaluation. The length of this evaluation will be three hours. You will have the option to choose between an in-home visit or meet the Research Assistant at Aston Clinic. Due to the COVID-19 pandemic, we will offer to conduct the interview remotely with your computer or tablet, via Zoom. If the evaluation is done remotely you will be sent an email to sign the consent electronically before the interview takes place. The research assistant will explain in the email what you need to do to and provide the link to the online consent.

The evaluation consists of the following:

1. General questionnaires and dietary questionnaires: You will be given several questionnaires that will ask you about your age, past medical history, any tremor you might have, and current medications. You will also be asked about your diet, and your smoking habits.

2. Cumulative Illness Rating Scale: We will ask you more details about your previous medical history.

3. Neurological videotaped examination: We will videotape a portion of the examination. This examination will be similar to a standard neurological examination in which your strength, coordination, and movements are tested. This examination will also include tasks such as pouring water from one cup into another and drawing spirals with pen and paper. The videotape will be identifiable, meaning facial features may be recorded in a way that would allow others to recognize you. However, you will NOT be identified by name, social security number, address, telephone number, etc. You may not participate in this study if you refuse to be videotaped. You will find a detailed explanation in the following section.

4.

5. Height and weight: You will be weighed, and your height will be measured.

6. Blood draw: You will be asked to provide a blood specimen (2 tablespoons of blood or one ounce). Blood will be tested for the chemicals Harmane and neurofilament light chain, which have been associated with tremor-related neurological disorders. Your blood samples will be stored indefinitely in a locked freezer at UTSW. You may not participate in this study if you refuse to have your blood drawn as it is an essential activity in our study. If the interview is done remotely, via Zoom, we will coordinate an appointment at the Clinical Research Unit facility in the Aston Clinic at your earliest convenience. Failure to provide the blood sample will result in removal from the study at no consequence to you.

7. Smell test: You will be asked to complete a brief smell identification test (SIT). This is a test of 40 odorants useful in determining olfactory function. Loss of smell can be an early sign of a number of neurological diseases. If the interview is not done in person, but by Zoom (remotely) this test will not be administered.

Activities after the in-person interview

Due to the length of the visit, the research assistant will leave you with an envelope that contains additional questionnaires. We do not wish to overwhelm you with a prolonged interview so that's why we have decided to distribute the tests this way. You will be able to complete them at your own pace and once they are ready, please forward the material to our office.

1. Sleeping questionnaires: You will be asked about your sleeping habits and routines in two different questionnaires.
2. Mood questionnaires: You will be asked in two separate questionnaires about your feelings and possible signs of anxiety and depression.

Once you mail back this information, your participation in the study will formally end.

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.

Your data/samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your data and/or samples.

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician.

Videotaped neurological examination consent

We are requesting your permission to obtain a videotaped neurological evaluation to confirm your diagnosis of Essential Tremor and further assess the progression of symptoms over the years as a critical procedure of this study.

If you agree to participate, we will keep the tapes in locked storage and the information will be only accessed by the research team involved in the study. To protect your confidentiality, the neurologist evaluating your video will NOT be informed of your name, social security number, address, telephone number or any other personal information that might lead to identifying you.

Your examination may be used for medical education purposes including publication in professional journals, medical books, and curriculum materials for medical students. If the videos are shared with the scientific community, no identifiable information will be published or made available with the publication. Take into account that your voice and face will be visible.
However, you may choose not to have your tapes used for these purposes, which would not impact your participation in the remainder of the study.
You have the right to choose how we use these videotaped evaluations. Please read carefully the following paragraph and check the options that match your wishes:

I give my consent for the videotaped neurological examination to be obtained for "Risk Factors Underlying Essential Tremor III-IV"

The films may be used for (Check if you agree)
A. - Use of the tapes:

- **a. _____ Medical education purposes including publication in professional journals, medical books, curriculum materials, and online materials.**
- **b. _____Research purposes only.**

B. - How long we may keep your tape:

- a **_____ My tapes may be kept permanently for research, educational or training purposes.**
- b **_____ My tapes must be destroyed after completion of study.**

I understand that my consent for the videotaped neurological examination to be used for ***educational purposes*** is **optional**, and I am free to refuse this request and still participate in the study. The research staff will honor my request promptly.

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

This study is of minimal risk for the participants. However, we want you to be aware of the following potential risks:

Risks Relate to Blood Draw
Having blood drawn is a safe procedure and our research assistants have been extensively trained in phlebotomy. You might feel a mild and brief discomfort in your arm when the needle is inserted. A bruise might develop where the needle is placed. A bruise will go away by itself and it might help if you wrap a warm towel around your arm.

Risks related to Neurological Assessment
You may experience a loss of balance while doing some activities. Every effort will be made to ensure your safety during the assessment. A research assistant will be close to you to minimize the possibility of falling.

Other Risks

There is the possible risk of loss of confidentiality. This means that identifiable information might be accessed by different parties than the research staff. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Are there Risks related to withdrawing from the study?

If you decide to withdraw from this study early, please discuss your decision with the Research Assistants. There is no risk to you if you choose not to participate in the study.

Are there risks if you also participate in other research studies?

You can take part in more than one study without approval from the researchers.

What if a research-related injury occurs?

The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section "Contact Information" for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

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 help to advance scientific knowledge about the risk factors present in certain types of tremors like ET and PD. Furthermore, this knowledge might benefit other people with similar conditions in the future.

Payments – Will there be any payments for participation?

You will be issued a UT Southwestern Greenphire ClinCard, which can be used as a credit or debit card. The one-time $40 compensation will be credited to the card after completion of the three-hour study visit. Your name, address, date of birth and social security number will be shared with a third-party solely for the purposes of compensation processing. All information will be stored in a secure fashion.

Please note that if you are on record as owing money to the State of Texas, such as for back child support or a delinquent student loan, the payment may be applied to that debt.

An IRS Form 1099 will be sent to you if your total payments are $600 or more in a calendar year unless it's a reimbursement.

Costs – Will taking part in this study cost anything?

There are no costs to you for participating in this research study.

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.

How will my information and/or 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. The processing of the blood samples is done with no identifiable information and no one will be able to link your identity to the levels of Harmane found. Similarly, lab personnel at the UT Southwestern Microarray Core Facility will be processing the blood samples for neurofilament light chain under the supervision of Dr. Quan-Zhen Li. Again, no identifiable information will be released and no one will be able to link your identity to the levels of neurofilament flight chain found. The key linking your information to samples will be locked in our offices where only research staff will have access to it.

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 samples to be used for future research studies without your consent, you should not participate in this study

HIPAA Section:
Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

What is Protected Health Information (PHI)?
Protected Health Information is information about a person's health that includes information that would make it possible to figure out whose it is. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to the investigators and the research study staff (individuals carrying out the study) to see and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include:

- Demographic information such as: your age, marital status, occupation and the years of education you have completed.
- Cognitive, clinical, and neurological data: information collected during your participation in the study through the neurological exam, interviews, questionnaires, and results from blood test. Sensitive information related to depression and anxiety may also be collected.
- Medical history: past and current medications taken, previous history of surgery/hospitalizations

- Research study records, including phone calls and other study visit information.

We will get this information by reviewing your medical records through EPIC for screening purposes, interviewing you or during research related study visits.

How will your PHI be shared?
Because this is a research study, we will be unable to keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- The Sponsor, the National Institutes of Health (NIH), funding the study. The sponsor includes any people, entities, groups or companies working for or with the sponsor or owned by the sponsor. The sponsor will receive written reports about your participation in the research. The sponsor may look at your health information to assure the quality of the information used in the research;
- Other institutions that are involved with the study, such as Columbia University Medical Center.
- The members of the local research team;
- The Institutional Review Board, Human Research Protection Program Office and the Compliance Office of the University of Texas Southwestern Medical Center, and other groups that oversee how research studies are carried out;
- The Research offices at the University Of Texas Southwestern Medical Center.

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to a central location or it may be transmitted electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

How will your PHI be protected?
In an effort to protect your privacy, the study staff will use code numbers instead of your name, to identify your health information. Initials and numbers will be used on any photocopies of your study records, and other study materials containing health information that are sent outside of the University of Texas Southwestern for review or testing. If the results of this study are reported in medical journals or at meetings, you will not be identified.

Do you have to allow the use of your health information?
You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties but you will not be allowed to participate in the study.
After you enroll in this study, you may ask the researchers to stop using your health information at any time. However, you need to say this in writing and send your letter to Dr. Elan Louis at UT Southwestern Medical Center, Department of Neurology & Neurotherapeutics, 5323 Harry Hines Blvd., Dallas, TX 75390-8813. If you tell the researchers to stop using your health information, your participation in the study will end and the study staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

Can you ask to see the PHI that is collected about you for this study?
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the study staff if you have a need to review your PHI collected for this study.

How long will your PHI be used?

By signing this form, you agree to let us use and disclose your health information until research analysist is complete.

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

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments or complaints later or you wish to report a problem which may be related to this study please contact:

The RULET Research Team
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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.

Research Consent & Authorization Signature Section

If you agree to participate in this research and agree to the use of your protected health information in this research, sign this section. You will be given a copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE FOLLOWING STATEMENTS ARE TRUE:

- You have read (or been read) the information provided above.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.
- You have freely decided to participate in this research or you are voluntarily giving your consent for another person to participate in this study because you believe this person would want to take part if able to make the decision and you believe it is in this person's best interest.
- You understand that a copy of this signed consent document, information about this study, and the results of any test or procedure that may affect your medical care, may be included in your medical record. Information in your medical record will be available to health care providers and authorized persons including your insurance company.
- You authorize the collection, use and sharing of your protected health information (another person's protected health information) as described in this form.

Adult Signature Section

			AM PM
Printed Name of Participant	Signature of Participant	Date	Time
			AM PM
Printed Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date	Time

Blind or Illiterate Signature Section *At the time of consent, also complete this section if consent is obtained from an individual who is unable to read and/or write but can otherwise communicate and/or comprehend English (e.g., blind, physically unable to write, etc.)*

Declaration of witness:
By signing below, I confirm I was present for the entire consent process. The method used for communication (e.g., verbal, written, etc.) with the subject was: _____ .

The specific means (e.g., verbal, written, etc.) by which the subject communicated agreement to participate was: _____.

			AM PM
Printed Name of Witness	Signature of Witness	Date	Time