CONSENT FORM

GENESIS –Generating evidence about transient, stereotypical and non-epileptic symptoms in the context of chronic subdural hematoma

September 2020

INFORMATION AND CONSENT FORM FOR RESEARCH

Project title :	GENESIS – Generating evidence about transient, stereotypical and non-epileptic symptoms in the context of chronic subdural hematoma
Project number :	MP-31-2021-3687
Project funding :	Neurosurgery and neurology departments, Université de Sherbrooke
Principal investigator :	… - Department of Neurosurgery
Associate researchers :	… - Department of Neurology. … - Department of Neurology. … - Department of Neurology.

Contact information

…

We are asking for your participation in a research project because you have a diagnosis of chronic subdural hematoma with neurological symptoms. However, before agreeing to participate in this project, please take the time to read, understand and carefully consider the following information. If you agree to participate in the research project, you will need to sign the consent form at the end of this document and we will provide you with a copy for your records.

This information and consent form explains the purpose, procedures, risks and disadvantages as well as the advantages of this research project. It may contain words that you don't understand. We invite you to ask all necessary questions.

NATURE AND OBJECTIVES OF THE RESEARCH PROJECT

Transient neurological symptoms are often associated with epilepsy, even when tests are negative. We already know that patients diagnosed with chronic subdural hematoma and transient neurological symptoms do not respond as well to standard treatments for epilepsy (antiepileptics). We believe that many of these patients would rather have a cause other than epilepsy to explain these neurological symptoms. These patients may respond better to Topiramate (a less commonly used epilepsy drug). The objective of this study is therefore to compare the efficacy of Topiramate versus Levetiracetam in resolving transient neurological symptoms.

For this study, we calculated that it would be necessary to recruit a total of 56 patients. Most will be recruited at the CHUS. Depending on the speed of recruitment, other centers may be included in order to complete the entire recruitment.

PROGRESS OF THE RESEARCH PROJECT

The total duration of the participant's involvement is 6 months. If you agree to participate in the project, you will have to attend a selection visit and two medical follow-ups (at 2 months and 4 months), one in neurology and one in neurosurgery. It should be noted that these follow-ups would be necessary, even without participation in the research project. In addition, two telephone follow-ups (at 2 weeks and 6 months) should be carried out with a member of the research team (doctor or resident). These can be done at a time chosen by the participant.

During hospitalization

1) Selection visit :

During this visit, which lasts approximately 1 hour, we will complete a detailed questionnaire of your medical history which will determine whether you are eligible for the project. The person responsible for the research project will collect basic medical data regarding your medical history as well as the current episode for which you are hospitalized. You will not receive any study medication during this time.

2) Beginning of treatment :

If the completed questionnaire indicates that you are still eligible, you will be assigned at random (like tossing a coin) to one of the following groups:

Group 1 : Usual treatment (Levetiracetam)

Group 2 : Treatment less often used (Topiramate)

3) Rest of hospitalization :

During the remainder of your current hospitalization, your symptoms will be monitored. In addition to the diagnostic EEG (electroencephalogram - recording of your brain activity), two other EEGs will be performed, spaced 24 hours apart, unless one shows epilepsy, in which case a second EEG is no longer necessary. Also, if needed, depending on your doctor, if the EEGs are all negative, an MRI (magnetic reasoning imaging) of your brain may be done to rule out a cause for your neurological symptoms other than your intracranial bleeding.

After hospitalization :

1) Visites de suivi :

There will therefore be two clinic visits (one with a neurologist and the other with a neurosurgeon), which will be carried out at 2 months and 4 months following your hospitalization. There will also be two telephone follow-ups at 2 weeks and 6 months following your hospitalization.

The reason for these visits is to ensure the effectiveness of the treatment used, and if this is not the case, to adjust the medication. It will also make sure that there are no side effects with the drug, and if they are found, the dose of the drug may be reduced or stopped. The study will be completed after 6 months. Subsequently, if you wish to continue the medication (being effective and well tolerated), this can be done and usual follow-up will follow. The medication may also be changed or stopped.

Tests and procedures :

Here is the description of the different tests and procedures that will be carried out during your participation in the project.

- Medical history
- Weight and size
- Measurement of your blood pressure
- Blood test
- Questionnaires: average duration of 30 minutes (during the initial visit and clinical and telephone follow-ups)
    - These include questions regarding recurrence of neurological symptoms as well as their descriptions. They also include questions about the tolerability of the treatment, as well as the appearance of possible side effects.
- Electrocorticography: suggested assessment for patients requiring surgery. This optional participation is explained in the appendix
- EEG: two more brain recordings will be made. These aim to improve the ability to diagnose epilepsy. They will be carried out during your hospitalization. They will be separated by 24 hours and will last 20 minutes each.
- MRI: If relevant, according to the attending physician, a magnetic reasonance imaging of the head could be performed if all previous examinations are normal, in order to rule out a cause other than your bleeding for the neurological symptoms. This examination could lead to a diagnosis which could exclude you from the research project. Indeed, if an additional cause (such as a tumor) ultimately explains the neurological symptoms, a different treatment should then be instituted and the study would no longer be justified.

Your medical file will be consulted throughout the research project by the researcher and his research team.

PARTICIPANT'S COLLABORATION

- Avoid participating in several projects simultaneously.
- Keep medicines out of the reach of children.
- Carry the identification card we gave you at all times.
- Observe the warnings regarding co-medication and declare all drugs or natural products used.
- Discuss with a member of the research team before the change or addition of another antiepileptic by a physician not collaborating on the project.

RISKS THAT MAY ARISE FROM YOUR PARTICIPATION IN THE RESEARCH PROJECT

Possible side effects of both treatments. Note that they are all reversible upon discontinuation of the relevant treatment except for glaucoma.

- Dizziness (4-29%)
- Anxiety (9-18%)
- Fatigue (9-16%)

- Weight loss or decreased appetite (4-20%)
- Headache (15%)
- Sinus infection (7-13%)
- Abdominal pain (6-10%)
- Nausea and vomiting (6-10%)
- Increased blood pressure (10%, usually more in children)
- Diarrhea (6%)
- Rash (1-4%)
- Joint pain (3%)
- Gait disorder, loss of balance (3%)
- Behavior changes (2-3%, irritability, aggression, agitation, emotional lability)
- Numbness (2%)
- Confusion (2%)
- Psychosis or depression (2%, more severe: drug discontinuation required)
- Gastroesophageal reflux disease (1-2%)
- Urinary tract infection (1%)
- Fever (1%)
- Memory problem (1%)
- Hair loss (1%, during long term treatment)
- Glaucoma (<1%, condition causing vision loss which may be irreversible, found when taking long-term treatment)
- Kidney stones (<1%, more serious: discontinuation of the treatment in question)

RISKS RELATED TO PROCEDURES

Blood samples :

The risks associated with taking blood samples are: slight pain, dizziness, fainting, bruising, bleeding, and in rare cases, blood clots and infection.

EEG (Electroencelography) :

The risks associated with this examination are as follows: discomfort, slight pain when installing the electrodes.

MRI (brain magnetic reasonance) :

The risks associated with this examination are as follows: discomfort during the examination (related to immobilization, confined space, noise), fear and associated symptoms if claustrophobia (fear of small places).

RISKS ASSOCIATED WITH PREGNANCY

Your participation in this research project may involve risks, known or not, for pregnant women, embryos, fetuses or breast-fed infants. This is why pregnant or breastfeeding women cannot participate in this project. Women of childbearing age (under 50) will therefore need to take a pregnancy test.

CASUAL DISCOVERIES

It is important to note that the images and data collected during the study are not subjected to clinical analysis or examined for abnormalities. Therefore, you must not consent to participate in this research project in order to have a screening test.

However, there is always the possibility that the images show a discovery with the potential for clinical impact. In this case, we will refer you to a specialist doctor who will order the necessary diagnostic test and meet with you to discuss the results. These results will appear in your medical file. The medical file can be viewed with your permission by an insurer when applying for insurance.

DISADVANTAGES THAT MAY RESULT FROM YOUR PARTICIPATION IN THE RESEARCH PROJECT

There may be some disadvantages to taking anti-epileptics. It is still necessary to understand that even without participation in the study, a treatment with similar side effects would be considered. However, Topiramate remains a less well tolerated drug, hence its limited clinical use. Its main side effects are not serious, although bothersome, and are reversible when stopped.

There will be no additional travel to be made.

There will be two telephone follow-ups which will be carried out and which will require the participant to devote time to this exchange with the research team. In order to limit the impact, the follow-ups will be carried out at the times chosen by the participant. In addition, there will be a participant diary to fill out at home for neurological symptoms or side effects. This will be simplified as much as possible in order to limit the time to devote to it. It could reduce the time required for follow-ups.

ADVANTAGES THAT MAY ARISE FROM YOUR PARTICIPATION IN THE RESEARCH PROJECT

There may be personal benefit to you from participating in this research project, but we cannot guarantee this. Moreover, the information resulting from this research project could contribute to the advancement of knowledge in the field of neurology and neurosurgery.

ALTERNATIVE TO PARTICIPATION IN THE RESEARCH PROJECT

You do not have to participate in this research project to be treated for your disease. There are other anti-epileptic drugs available and your doctor can discuss them with you.

VOLUNTARY PARTICIPATION AND POSSIBILITY OF WITHDRAWAL

Your participation in this research project is voluntary. You are therefore free to refuse to participate. You can also withdraw from this project at any time, without having to give any reasons, by informing the research team.

Your decision not to participate in or to withdraw from this research project will have no

impact on the quality of care and services you receive.

The doctor responsible for this research project, the research ethics committee can terminate your participation without your consent. This can happen if new findings or information indicate that your participation in the project is no longer in your best interest, if you do not follow the instructions of the research project or if there are administrative reasons for abandoning the project.

If you opt out of the project or are withdrawn from the project, the information and material already collected as part of this project will nonetheless be retained, analyzed or used to ensure the scientific integrity of the project.

Any new knowledge acquired during the course of the project that could have an impact on your decision to continue to participate in this project will be communicated to you promptly.

CONFIDENTIALITY

Collection - Purposes for which personal information is requested

During your participation in this research project, the doctor in charge of this project as well as his staff will collect, in a research file, the necessary information to meet the scientific objectives of this research project.

Collection - What personal information is requested

This information may include information contained in your medical file concerning your past and present state of health, your lifestyle as well as the results of all tests, examinations and procedures that will be performed. Your record may also include other information such as your gender and date of birth.

Retention of information/data – Protection

All information collected will remain confidential within the limits provided by law. You will only be identified by a code number. The key to the code linking your name to your research file will be kept by the doctor responsible for this research project. It will be kept under lock and the key will be separated from the document containing the data collection.

To ensure your safety, a mention of your participation in this research project will be added to your medical file. Consequently, any person or company to whom you give access to your medical file will have access to this information.

The duration of the conversation

These research data will be kept for 25 years by the doctor responsible for this research project.

Dissemination of results

Research results may be published or be the subject of scientific discussion, but it will not be possible to identify you.

Right of access for control and security purposes

For surveillance, control, protection and security purposes, your research file as well as your medical files may be consulted by representatives of the institution or of the research ethics board. These people and organizations adhere to a confidentiality policy.

You have the right to consult your research file to verify the information collected and have it corrected if necessary.

COMPENSATION

You will not receive financial compensation for your participation in this research project.

IN CASE OF PREJUDICE

If you suffer any prejudice whatsoever as a result of any procedure related to this research project, you will receive all the care and services required by your state of health.

By agreeing to participate in this research project, you do not waive any of your rights and you do not release the doctor responsible for this research project and the establishment of their civil and professional responsibilities.

CONTACTS

If you have any questions or experience problems related to the research project or if you wish to withdraw from it, you can contact the doctor or resident in charge or a member of the research team. Please refer to the box on page 1.

If you have any questions regarding your rights as a participant in this research project or if you have any complaints to make, you can contact the Complaints and Service Quality Office of the CIUSSS de l'Estrie-CHUS via complaints.ciussse-chus@ssss.gouv.qc.ca or at the following number: 1-866-917-7903.

MONITORING ETHICAL ASPECTS

The CIUSSS de l'Estrie -CHUS Research Ethics Committee approved the project and will monitor the project for participating establishments in the Quebec health and social services network.

If you wish to join one of the members of this committee, you can contact the CIUSSS de l'Estrie - CHUS Research Project Authorization Office via ethique.recherche.ciussse-chus@ssss.gouv.qc.ca or at 819-346-1110, extension 12856.

SUBSEQUENT STUDIES

In the event that research projects similar to this one take place in the next 5 years, do you agree to a member of the research team contacting you to suggest you a new participation? Of course, during this call, you would be completely free to accept or

decline to participate.

☐ **YES**	☐ **NO**

CONSENT OF THE REPRESENTATIVE OF THE SUDDENLY UNFIT PERSON (For cases of sudden incapacity)

Due to the fact that Mr. / Mrs. _____ was suddenly rendered incapable of consenting for the reason identified below, the Civil Code of Quebec authorizes you, as _____ (your link with the participant) to consent for him (her) to participate in this research project.

As soon as Mr./Mrs. _____ has recovered sufficiently, we will invite him (her) to sign the consent form so that he (she) can indicate his / her desire to continue, or not, his / her participation in the study.

REASON WHY THE PARTICIPANT CANNOT CONSENT:

_____

By signing this page, I declare that I have read this information and consent form. I admit that I was explained the project, that all my questions were answered and that I was given time to make a decision. I voluntarily give my consent for _____ to participate in this study.

I authorize the research team to have access to his medical file.

_____

Name of representative	Signature du représentant	Date

I explained to the representative the research project and this information and consent form and answered the questions he asked me.

_____

Name of the person obtaining the consent	Signature of the person obtaining the consent	Date

CONSENT OF THE LEGAL REPRESENTATIVE OR CAREGIVER TO PARTICIPATION OF THE INCAPACITY
(For cases of permanent incapacity)

I have read this information and consent form. I admit that I was explained the project, that my questions were answered and that I was given time to make a decision.

I consent to _____ participating in this research project under the conditions stated therein. A signed and dated copy of this information and consent form will be given to me.

I authorize the research team to have access to his medical file.

If the incapacitated person is represented:

Name and signature of the legal representative (curator, tutor or agent) Date

If the incapacitated person is not represented as follows:

Name and signature of spouse
In the absence of a spouse, a close relative or
a person who shows a particular interest Date

I explained to the representative the research project and this information and consent form and answered the questions he asked me.

Name of the person obtaining the consent | Signature of the person obtaining the consent | Date

PARTICIPANT'S CONSENT

I have read the information and consent form. The research project and this information and consent form were explained to me. My questions were answered and I was given time to make a decision. After reflection, I agree to participate in this research project under the conditions set out therein.

I authorize the research team to have access to my medical file.

Participant name	Participant signature	Date

Signature of witness:

Required if language or reading barrier. If not applicable, write "N/A" on the signature line so as not to leave it blank.

Witness name	Witness signature	Date

I explained the research project and this information and consent form to the participant and answered the questions they asked me.

Name of the person obtaining the consent	Signature of the person obtaining the consent	Date

APPENDIX: OPTIONAL PARTICIPATION FOR PATIENTS NEEDING SURGERY

ELECTROCORTICOGRAPHY

Eligible patient :

☐ **YES** ☐ **NO**

Definition

Optional additional procedure during drainage surgery for subdural hematoma. This involves the insertion of two electrodes before the surgical wound is closed in the operating room. Recording will be performed through these electrodes for 72 hours, or until recording for 5 episodes of transient neurological symptoms. After recording, the electrodes can be pulled out at the bedside by traction and a single stitch will be made to the skin under local anesthesia.

Purpose of the intervention

The purpose of this recording is to increase the chances of diagnosing either epilepsy or cortical depolarizations. This will make it easier for follow-up, in addition to giving information on the prognosis. This procedure is entirely voluntary; refusal does not prevent participation in the study, nor adequate follow-up.

Risks associated with the procedure

This is accompanied by a minimal, but greater risk of perioperative infection (1%).
High possibility of slight wound discomfort during recording, as well as when removing electrodes and stitches.
In addition, following the insertion of the electrodes, there will be a 72 hour recording. This will not lengthen the length of hospital stay, but could prevent free mobilization out of the room due to the connected wires.

ELECTROCORTICOGRAPHY CONSENT

I have read the additional part about electrocorticography. I was told what electrocorticography is and the risks associated with it. My questions were answered and I was given time to make a decision. After some thought, I consented to have electrocorticography electrodes fitted following my drainage surgery.

CONSENT OF THE REPRESENTATIVE OF THE SUDDENLY UNFIT PERSON (For cases of sudden incapacity)

Due to the fact that Mr. / Mrs. _____ was suddenly rendered incapable of consenting for the reason identified below, the Civil Code of Quebec authorizes you, as _____ (your link with the participant) to consent for him (her) to participate in this research project.

As soon as Mr./Mrs. _____ has recovered sufficiently, we will invite him (her) to sign the consent form so that he (she) can indicate his / her desire to continue, or not, his / her participation in the study.

REASON WHY THE PARTICIPANT CANNOT CONSENT:

_____

By signing this page, I declare that I have read this information and consent form. I agree that I have been explained what electrocorticography is, that all of my questions have been answered and that I have been given time to make a decision. I voluntarily give my consent for _____ to have electrocorticography electrodes affixed.

Name of representative	Signature du représentant	Date

I explained to the representative the research project and this information and consent form and answered the questions he asked me.

Name of the person obtaining the consent	Signature of the person obtaining the consent	Date

CONSENT OF THE LEGAL REPRESENTATIVE OR CAREGIVER TO PARTICIPATION OF THE INCAPACITY
(For cases of permanent incapacity)

I have read this information and consent form. I admit that I was explained the project, that my questions were answered and that I was given time to make a decision.

I consent to _____ having electrodes for electrocorticography recording under the conditions set forth therein. A signed and dated copy of this information and consent form will be given to me.

If the incapacitated person is represented:

Name and signature of the legal representative (curator, tutor or agent)	Date

If the incapacitated person is not represented as follows:

Name and signature of spouse In the absence of a spouse, a close relative or a person who shows a particular interest	Date

I explained to the representative what the electrocorticography and this information and consent form represent and answered the questions he asked me.

Name of the person obtaining the consent	Signature of the person obtaining the consent	Date

PARTICIPANT'S CONSENT

I have read the information and consent form. My questions were answered and I was given time to make a decision. After reflection, I agree having electrodes for electrocorticography recording under the conditions set forth therein

Participant name	Participant signature	Date

Signature of witness:

Required if language or reading barrier. If not applicable, write "N/A" on the signature line so as not to leave it blank.

Witness name	Witness signature	Date

I explained the research project and this information and consent form to the participant and answered the questions they asked me.

Name of the person obtaining the consent	Signature of the person obtaining the consent	Date