

Participant Information Sheet

Investigating the role of the menstrual cycle in epilepsy

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Ethics committee ref.: 21/CEN/201

You are invited to take part in a study on the menstrual cycle and epilepsy. This Participant Information Sheet will help you decide if you'd like to take part or not. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have in a screening visit. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of the Participant Information Sheet, the Data and Tissue Management Information Guide, and the Consent Form to keep. Your guardian or caregiver will also need to read this form as they will also have the opportunity to provide consent. Both of you have to sign the Consent/Assent Form in order for you to be able to participate in the study.

This document is 14 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

VOLUNTARY PARTICIPATION AND WITHDRAWAL FROM THIS STUDY

It is up to you if you take part in this study or not. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you don't want to take part you don't have to give a reason. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive from us or your participation in future studies.

WHAT IS THE PURPOSE OF THE STUDY?

Some women with epilepsy experience an increased number of seizures at specific times of their menstrual cycle. These are called **catamenial seizures**. The purpose of this study is to improve our understanding of why catamenial seizures occur.

To do this we are using a type of brain recording equipment called EEG (the common term for electroencephalography). We are also taking blood samples to look at hormones and other blood components.

We hope to use this knowledge to conduct future studies into possible treatments. Right now, a lot of women do not have a working treatment for catamenial seizures. We will also share the findings from this study in scientific articles and in public talks.

HOW IS THE STUDY DESIGNED?

We will be recruiting three groups of people in this study. One group will be people without epilepsy. One group will be people who have epilepsy but not catamenial seizures. One group will have catamenial seizures. Each group will have 25 people in it. **You are reading this information sheet because you and/or your neurologist believe you have catamenial seizures.**

There are three main parts to this study:

- **Attending a screening with your parent/guardian to discuss the study with us:**

If you decide you would like to take part in the study, we will schedule a screening to determine if you are eligible for the next part of the study. We will go through this information sheet with you again and answer any questions you may have.

- **Making a record of your menstrual cycle and seizures:**

After the screening, we will ask you to begin recording when your period starts each month in a diary, and how many seizures you have each day.

We need you to record this for at least 3 months before your first study visit to confirm whether you are eligible for the main part of the study. If you are already collecting a menstrual cycle and/or seizure diary, we can use this, and it may mean we can schedule your study visits sooner.

We may determine from your seizure diaries that you do not fit into our strictly defined threshold for having catamenial epilepsy. In this case we would either not continue your participation into the study, or we may consider your eligibility for the other group in the study who do not have catamenial epilepsy instead.

In between the study visits we will ask you continue to record your menstrual cycle and seizure information. We will also ask you to do urine ovulation testing (we will give you the

same at-home tests people buy from the pharmacy when trying to time their cycle for having a baby). This will tell us when the second phase of your menstrual cycle begins, and we can use that to make sure we time your visits right. You do not have to do this part if you don't want to (it's optional).

- **Attending three main study visits to the university:**

The three study visits will be timed to specific points of your menstrual cycle. At each study visit we will take a blood sample. We will ask you some questions about your health, including medications you take, your epilepsy, and menstrual cycle. You will also have an EEG recorded while completing some simple tasks on a computer. More information on these procedures are provided in a later section.

WHO CAN TAKE PART IN THE STUDY?

You are reading this sheet because you or your healthcare provider thought that you might be eligible and/or you have contacted us after seeing an advertisement.

You may be eligible to participate in the study if you:

- Are 14 years or above and less than 45
- Have a diagnosis of epilepsy, and received this diagnosis from a neurologist
- Experience an increase in your seizures when your period is about to begin, and/or in the first few days of your period
- Have been stable on any epilepsy or other medications (such as antidepressants) for at least 8 weeks prior to the first Study Day
- Are able and willing to comply with all study requirements, in the research team's opinion
- Are willing and able to give informed consent for participation in the trial

You will not be eligible to participate in the study if you:

- Have been diagnosed with contrast sensitive seizures
- Have had an MRI confirm damage or lesions on the visual cortex of your brain
- Take the oral contraceptive pill
- Are on depo-provera or other hormonal medications that stop you from having a period every month.
- Have undergone gender affirming surgical or hormone treatment procedures
- Are experiencing highly irregular periods
- Have polycystic ovarian syndrome
- Are unable to speak or write English
- Are planning any major changes to epilepsy medication you're currently taking
- Have been regularly using any other medication the research team considers may be a problem for the study measures (to be considered on a case by case basis)
- Have any other condition judged by the research team as likely to impact on your ability to complete the study

If you change your medication for epilepsy or another neurological or psychiatric condition during the study, you may have to stop participating. You may start again when you have stabilized (after 8 weeks) if you wish.

To be allocated to the catamenial epilepsy group you must **EITHER**:

- Only have seizures in the week around your period starting.
- OR**
- Have twice as many (or more) seizures in the week around your period starting when compared to every other week of the month.

This must occur for at least 2 out of the 3 the months we collect seizure and menstrual cycle diary information. We will calculate this for you.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

How much time will the study take and where will it be?

If you decide that you would like to take part you need to first attend a screening visit that will take 1 hour or more. The visit may be at the University of Auckland, Faculty of Medical and Health Sciences, Grafton Campus or it can be online via Zoom. You will then make 3 visits to the university that will take approximately 2 hours each – 6 hours in total to complete the study. These sessions can't be completed at home/online.

You will also have to spend a few minutes up to every day completing a seizure diary (counting seizures per day) and recording when your period starts each month. This will be for more than 3 months in total, and is unlikely to be for more than 6 months. We will discuss how long this will be for you at the screening as it will depend on your particular circumstances.

Completing the menstrual cycle and seizure diaries:

The menstrual cycle and seizure diary is to record whether you had any seizures that day and whether your period started. If you don't already complete a seizure and menstrual cycle diary, then we will need to complete one for 3 months before your first visit. You can use any pen or paper, app or other method you currently use, and send us a copy every week. Otherwise, we can provide you with a daily reminder text/email and a short survey to fill in. For this option, you will be provided with a secure link that is unique for you.

Main study visits:

Where and when?

When we have confirmed your eligibility and allocated you to the catamenial epilepsy group using a seizure and menstrual cycle diary, you will be invited to attend 3 visits in total at the University of Auckland Grafton Campus Clinical Research Centre.

For an average menstrual cycle this will be around:

- Day 5-8 after your period starts
- Day 19-23 after your period starts
- Day 25-2 after your period starts (day 2 being of the following period).

This is to capture the different hormone changes that happen during your menstrual cycle. We will discuss scheduling these dates with you and if you have a longer or shorter cycle than 28 days, we will tailor the visits to your individual cycle length. We will reschedule any session within 24 hours of a tonic-clonic seizure.

What type of tests will I do during visits?

Blood samples

- A blood sample (20 mL will be taken, which is equivalent to 4 teaspoons)
- Blood samples will be taken for us to measure your hormone levels and other components like mRNA.

Questions

- On each study visit you will be asked about your health, and any medications you may have taken in the last week.

Simple visual perception tasks

- You will then take part in tests of your basic visual perception by looking at simple patterns (such as stripy circles) and pressing the arrow keys on a keyboard according to instructions. These will take up to 10 minutes.

An EEG recording

- Last, we will setup your EEG and perform some basic EEG tests with you that will take **up to 50 minutes**.
- These tests will also involve looking at simple patterns on a computer screen. The patterns will flash on and off the screen, so it is important that you don't have contrast sensitive seizures. If you are concerned about these tests please ask for more information from the study team.

The following describes the EEG procedure in more detail:

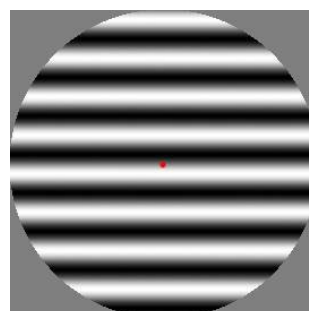
The electrical activity produced by your brain can be measured with electrodes that are placed on the scalp surface (example in pictures on the next page). A good signal is reached by using an electrolyte gel between the electrode and your head to ensure good contact with your skin. After the recording session you will be given the opportunity to clean the electrolyte gel from the hair, which is easily done by a hair wash.

There are no known or foreseeable risks or side effects associated with conventional EEG recordings. However, to avoid you feeling uncomfortable through needing to focus on a screen for the recordings, we will ensure there are enough breaks you can use to rest your eyes.

We will not be looking for seizures using EEG, instead we will be looking at how the visual processing part of your brain is functioning. This is because the visual processing part in your brain can tell us a lot about how your brain is responding to hormones more generally.



The Auckland University EEG cap



The types of pictures that will flash on the screen

Optional ovulation testing between visits:

To help us to schedule the dates for you to attend we will offer to send you home with ovulation testing kits (or courier these out to you). Ovulation testing involves urinating on a testing strip first thing in the morning for about 10 days of the month and then texting or emailing us the result (whether you are ovulating or not). We will explain to you how these tests work and also tell you which days to do this on. It will take a couple of minutes each day. It will greatly help us accurately time your visits so we will prefer that you do the testing. However, we recognise the potential inconvenience and so it is optional.



WHAT WILL HAPPEN TO MY BLOOD SAMPLES?

Our study requires participants to provide blood samples to look at hormone levels and also some other components like mRNA. We will not conduct any genetic testing on these samples that could lead to you being identified. All samples will be labelled with a study identifier, not your name. No blood samples will leave Aotearoa.

CULTURAL CONSIDERATIONS FOR MĀORI

The cultural issues associated with sending and storing your tissue should be discussed with your family/whanau as you feel appropriate. We acknowledge that personal and health information is a tāonga and will be treated accordingly.

We have identified that the study involves the taking of blood samples and touching of your head, which are tapu. We will ask for your consent and describe these procedures before touching you. Options for disposal of the blood samples with karakia and returning samples

can be discussed during the screening visit. If there are additional things that we can do to meet your needs, please feel free to discuss these with the study team.

WHAT ARE THE POSSIBLE RISKS OF THIS STUDY?

There is no direct risk of your participation causing or worsening seizures, however, at the screening visit we will discuss and make a plan for your visits to the university clinic. We will discuss potential triggers for seizures and how we may be able to help to avoid these. For example, we can reschedule a session if you have a very bad night's sleep the night before.

The plan will also detail what to do if you have a seizure while you are visiting the university. Developing a plan personal to you will help us to make sure our procedures are safe for you, and consider your individual preferences and needs during and immediately after a seizure.

If you have a seizure that lasts more than 5 minutes we will call 111 and paramedics will take you to the Auckland Hospital emergency department which is across the road from the university clinic. We will accompany you and arrange a next of kin to join you. Once you are in the care of a next of kin we will leave, and make a plan to call you the next day. Your GP and other care provider such as a neurologist will be notified.

There is a slight risk of bruising from the blood tests.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

You may benefit from the ability to have conversations about your menstrual cycle and epilepsy, and receive information of interest from the research staff and students about the relevant science.

We will be able to provide a summary report of your seizure and menstrual cycle diary, as well as the results of the hormone blood tests if you wish after your final study visit. These can be passed on to your doctor and may be useful in discussions about your menstrual cycle and epilepsy.

If you happen to have a seizure while we are recording the EEG we are able to make this available to your neurologist if you or they request it, however this is for their information only. Medical use of the recorded research data e.g. for diagnosis, treatment of disease or other such purposes is strictly forbidden by the manufacturer of the EEG equipment we use.

While there are neurologists involved in the study, there is not the capacity for a neurologist to provide a clinical review or meet with you as part of your participation. You will likely only have contact with research staff and students who cannot provide medical advice.

WILL ANY COSTS BE REIMBURSED?

We will pay for any costs that you incur taking part in the study. If you require a taxi to get to and from the study then we can arrange and pay for this. We recognise that taking part in the study will take around eight hours of your time and several months of contact with us and will provide you with \$150 of vouchers at the end of the study, or \$50 at the end of each of the three main study visits, in recognition of this generosity.

WHAT IF SOMETHING GOES WRONG?

If you were injured in this study, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

You may withdraw your consent for the collection of your information at any time, by informing a member of the study team. If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you.

If you agree, information collected up until your withdrawal from the study will continue to be used and included in the study. You may ask for it to be deleted when you withdraw, unless you withdraw after the study analyses have been undertaken or it has been made available for future use on online repositories. See the **Data and Tissue Management Guide** section 1.6 below for more information on the online repository.

CAN I FIND OUT THE RESULTS OF THE STUDY?

It can take quite a long time for us to analyse data from these kinds of studies. We hope to be able to tell you the final results one to two years after completion of the study. We plan to publish the results in scientific journals. Please let a member of the study team know if you would like a summary of the results in an easy to read format.

WHO IS FUNDING THE STUDY?

The Neurological Foundation

WHO HAS APPROVED THE STUDY?

This study has been approved by an independent group of people called a Health and Disability Ethics Committee (HDEC), who check that studies meet established ethical standards. The Central HDEC has approved this study.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Dr Rachael Sumner, Research Fellow

Phone: +64 022 4610242 or +64 923 1914

Email: r.sumner@auckland.ac.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz
Website : <https://www.advocacy.org.nz/>

For Māori health support please contact :
He Kamaka Waiora (Māori Health Team)
Phone: +64 9 486 8324 ext. 42324
Email: hkw@adhb.govt.nz

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS
Email: hdecs@health.govt.nz

Data and Tissue Management Guide

This Data and Tissue Management Guide outlines how data and tissue (blood) samples collected from you will be handled during the study and after its completion. It will cover:

1. Who will have access to and use the data you provide in this study?
2. How will we store your data and destroy it when the study is finished?
3. How can you request and correct your data?

Information about regulations, data and privacy can be challenging to read. If you would like clarification please contact the study team. We can arrange a phone call or meeting to explain things clearly, in a way that you understand even before any screening visit.

WHAT WILL HAPPEN TO MY INFORMATION?

During this study the study doctors/researchers, and other University of Auckland staff will record information about you and your study participation. This includes the results of any study assessments.

Information from your hospital records and your GP may also be collected as part of determining your eligibility for the study. You cannot take part in this study if you do not consent to the collection of this information.

1 Who will have access to and use the data you provide in this study?

1.1 IDENTIFIABLE DATA AND TISSUE (BLOOD)

Identifiable information is any data that could identify you (e.g. your name, date of birth, or address).

Identifiable data and/or tissue may be accessed by the following groups:

- The Investigator and designated study staff, to complete study assessments.
- Study monitor(s), to make sure the study is being run properly and that the data collected is accurate.
- The sponsor, ethics committees (specifically the Health and Disability Ethics Committees), or government agencies from New Zealand or overseas, if the study or site is audited. Audits are done to make sure that participants are protected, the study is run properly, and the data collected is correct.
- The participant's GP or appropriate specialist, to acquire required medical information for participation. Or if a study test gives an unexpected result that could be important for your health. This allows appropriate follow-up to be arranged.
- Rarely, it may be necessary for the Investigator to share identifiable data with people or groups not listed above – for example, in the event of a serious threat to public health or safety, or to the life or health of the participant or another person; or if the data is required for certain legal situations.

1.2 DE-IDENTIFIED DATA AND TISSUE (BLOOD)

To make sure your personal information is kept confidential, information that identifies you will not be included in any report generated by the study team or any study information sent to the sponsor. Instead, you will be identified by a code. The study team will keep a list linking your code with your name, so that you can be identified by your coded data if needed.

The following groups may have access to your coded information

- The Investigator and suitably trained and experienced study staff, to conduct the study.
- The LabPlus laboratory, for sample processing, analysis, and reporting purposes.
- The Health and Disability Ethics Committee, to comply with legal and regulatory duties.
- Health, regulatory, or government authorities, to comply with legal and regulatory duties.
- The LabPlus laboratory will not be authorised to share data and/or tissue with third parties.

De-identified data may be included in published study results including, but not limited to, peer-reviewed publications, scientific meetings, and regulatory / marketing submissions.

De-identified data may be included in databanks (refer to Section 1.6).

1.3 ANONYMISED DATA

The study team may remove the code from your de-identified information – this is called ‘anonymisation’. This makes it very difficult (but not impossible) to identify the information that belongs to you.

Anonymised data may be accessed and used by the same groups described above in Section 1.2.

Anonymised data may also be made available to other researchers, as described in Section 1.5 and 1.8.

1.4 FUTURE RESEARCH USING YOUR INFORMATION

De-identified data may be made available to other researchers on request for future research as and may be added to data from other sources to form larger datasets (see Section 1.6 Databank for how).

In all cases, the Sponsor must be satisfied that appropriate Data Management Plans are in place and that ethical approval for use has been obtained in accordance with local laws and regulations.

There will be no future use of blood samples.

1.5 COMMERCIAL USE OF DATA

Study data may lead to discoveries and inventions or development of a commercial product or producers. The rights to these will belong to the Sponsor. Participants will not receive any financial benefits or compensation from, nor have any rights to, any developments, inventions, or other discoveries arising from this analysis.

1.6 DATABANK AND DATABASE

Database: Identifiable medical information will be added to the EpiNet database <http://www.epinet.co.nz/index.cfm?PageID=1>. EpiNet is a platform that is used to record information about people with epilepsy, and it is being used simultaneously for both clinical purposes and for research. Patient's records can only be accessed by the New Zealand based investigators undertaking this research, neurologists and other health providers, who must log-on to a secure website, which is password protected.

Databank: De-identified data collected in the study will be submitted to the University of Auckland's Figshare Open Data Research Repository: <https://auckland.figshare.com/>

The purpose for the uploading of this data is to ensure reproducibility, transparency, integrity and fidelity of our study design and analysis methods. Due to the nature of the data collected, re-identification is highly improbable. The greatest risk of re-identification lies with the amount of demographic details tied to the data. As such, to protect the participants' privacy and to avoid re-identification, the only publicly available demographic details will be limited to sex and age-band where the age-band will be very broad: 14-18, 18-25, 25-35, 35-40. Other de-identified demographic data (e.g. ethnicity, education, handedness) will not be publicly shared and will remain with the research team.

Future unspecified research, may be conducted on the uploaded data. Given the nature of EEG data, it is possible the re-analysis of such data in novel processing methods may also be conducted. As this data will be considered public domain, it will not be possible for you to withdraw consent once the data is uploaded onto the online repository.

1.7 SENDING OF DATA AND TISSUE (BLOOD) OVERSEAS

De-identified data may be accessed from the databank described in Section 1.6 by people who are overseas, where there may be no New Zealand representation on overseas governance committees for how the data is used. See Section 1.6 for what type of data this encompasses and how we will protect participant privacy.

Identifiable and de-identified data (such as that on EpiNet) will not be accessible to overseas users as part of this study.

No tissue (blood samples) will be sent overseas for analysis or storage.

2 How will we store your data and destroy it when the study is finished?

2.1 IDENTIFIABLE DATA AND SOURCE DOCUMENTS

During the study, study-specific source documents will be maintained in locked file cabinets in locked rooms and password protected databases via password protected computers/servers/storage media for ten years. Documents will be shredded after this time.

Post-study, study-specific source documents will be archived in password protected databases via password protected computers/servers.

2.2 DE-IDENTIFIED DATA

Identifiable data will be converted to a de-identified form at the study site, at which point it is entered into case reports files. De-identified data will carry a unique study specific number. The Investigator will retain a log linking participant code with identifiers. The de-identified database will remain on University of Auckland servers for up to approximately ten years.

3 How can you request and correct your data?

You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected.

Please ask if you would like to access the results of your screening and safety tests during the study.

If you have any questions about the collection and use of information about you, you should ask the Lead Researcher Dr Rachael Sumner.

Consent Form

Investigating the role of the menstrual cycle in epilepsy

Please tick to indicate you consent to the following

I have read the Participant Information Sheet, or had it read to me, and I understand it.	Yes <input type="radio"/>
I have been given enough time to consider whether or not to participate in this study.	Yes <input type="radio"/>
I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.	Yes <input type="radio"/>
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.	Yes <input type="radio"/>
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.	Yes <input type="radio"/>
I consent to the research staff collecting and processing my information, including information about my health.	Yes <input type="radio"/>
I consent to my data being used in the University of Auckland's Figshare Open Data Research Repository and that once uploaded, I cannot withdraw consent to its use.	Yes <input type="radio"/>
If I decide to withdraw from the study before it is uploaded to the Open Data Repository, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	Yes <input type="radio"/> No <input type="radio"/>
I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.	Yes <input type="radio"/>
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethics Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.	Yes <input type="radio"/>
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.	Yes <input type="radio"/>
I understand the compensation provisions in case of injury during the study.	Yes <input type="radio"/>

I know who to contact if I have any questions about the study in general.	Yes <input type="radio"/>	
I understand my responsibilities as a study participant.		
I wish to receive a summary of the results from the study.	Yes <input type="radio"/>	No <input type="radio"/>
I wish to be contacted for further opportunities to participate in studies on epilepsy.	Yes <input type="radio"/>	No <input type="radio"/>

Declaration by participant and guardian:

I hereby assent to take part in this study.

Participant's name: _____

Signature: _____ Date: _____

I hereby consent to the participant taking part in this study:

Participant guardian's name: _____

Relationship to the participant: _____

Signature: _____ Date: _____

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name: _____

Signature: _____ Date: _____