**Project title:** Investigating how sex hormones in the combined-oral contraceptive affect the human female brain.

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It is important that you read this Participant Information Sheet thoroughly so that your decision about participating (or not) is an informed one.

We are a group of researchers at the University of Auckland in the School of Pharmacy, and Optometry and Vision Sciences at the University of Auckland. You are being invited by us to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with your friends and relatives if you wish, to help you decide whether or not you would like to take part. In this study you will be asked questions about your menstrual cycle and medications that you take. We encourage you to ask as many questions as you need to, so that you can feel comfortable about your understanding of your role in the study. There are no direct benefits to you in taking part in this study, and so you may or may not benefit from participation. To thank participants for their contribution to the research, each will receive $60 in vouchers. If you are unable to complete the study a kōhā of $20 will be provided for each complete (or incomplete) visit.

This study involves the collection of blood samples. If you are of Māori descent, you are encouraged to consult with your whānau, hapū or iwi regarding participation in this project. You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending or storing your tissue should be discussed with your family/whānau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose.

This study is funded by the Neurological Foundation.
What is the purpose of the study?

You are invited to participate in research that investigates the interactions between the sex hormones in your body and the brain’s natural inhibitory and excitatory systems. In particular, we wish to examine whether the inhibitory and excitatory systems of the brain change over the course of a month on the combined oral contraceptive pill. The results of this study will be used to inform planned future research into menstrual cycle related disorders and hormonal treatments.

To measure excitation and inhibition in your brain we will ask you to complete simple visual perception tasks in front of a computer that involve viewing patterns and making a button presses according to instructions. We will then record your electroencephalogram (EEG) patterns when you perform a series of further similar simple tasks.

Why have I been chosen?

You have been chosen because you are a healthy volunteer who has indicated they are taking the combined oral contraceptive pill. We need 25 volunteers to complete the study and you have requested further information. If you decide to take part you will be asked to sign a consent form and you will be given a copy of this to keep. We will ask you some medical questions to make sure that you meet the requirements for the study.

If you are a student of the researchers we give our assurance that your participation or non-participation in this study will have no effect on your grades or relationship with the University and that you may contact your academic head should you feel that this assurance has not been met.

Do I have to take part?

No, it is up to you if you take part 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 will I be asked to do if I take part in the research study?

If you decide that you would like to take part you need to attend for 3 visits in total to the University of Auckland, Faculty of Medical and Health Sciences, Grafton Campus. You will also be asked to complete a questionnaire every day for the month of participation to track any premenstrual symptoms.

Each of the 3 visits will take approximately 2 hours each. The study will take about 6 hours of your time.

Each visit requires:

- An EEG recording (see page 4 for more information on what an EEG involves)
- A blood sample
- Simple visual perception tasks

The exact days will depend on when it is convenient for you and on the answers you give us about your combined oral contraceptive pill timing. You will need to attend on day 3, day 21, and day 24 of your pill packet (counted as though day 1 is the first day of active hormone pills). There is a maximum
flexibility of each session occurring one day earlier than this. The day 3 and day 21 sessions must occur in the same month. The day 24 session may occur in a separate month.

On each study visit you will be asked about your health including in menstrual related mood or physical symptoms you may be experiencing, and any medications you may have taken in the last week.

Blood samples will be taken for us to measure your hormone levels (15 mL will be taken, which is equivalent to 3 teaspoons).

You will then take part in tests of your basic visual perception by looking at simple patterns (such as stripy circles) and making simple button presses according to instructions. These will take up to 30 minutes. Eye tracking may be used to follow where on the screen you are looking.

Next, we will then setup your EEG and perform some basic EEG tests with you that will take up to 60 minutes. These tests will also involve looking at simple patterns on a computer screen or listening to beeping tones.

The daily questionnaire can be completed on your phone or computer, it has 26 questions and only takes a few minutes. You will be provided with a link that is unique for you. The results are received into a secure University of Auckland managed Google Drive. You will not be asked to put your name in the questionnaire, and it will be stored with only your study identifier number on it to maintain your confidentiality. You will be sent a reminder by text every evening from the agreed start date to fill it in. If your day 24 session occurs on a separate month to your day 3 and day 21 session, you will complete the daily questionnaire for the hormone-free week separately on that month also.

The daily questionnaire asks you questions about your menstrual cycle and any pre-menstrual symptoms you may be experiencing. These include physical symptoms such as pain and bloating, and also questions about your mood such as feelings of worthlessness, hopelessness, or sadness you may experience.

**Exclusion Criteria**

You will not be eligible to take part in this experiment if you:

- Have taken the combined oral contraceptive pill for less than 3 months (e.g. Ava, Levlen ED, Microgynon ED, Brevinor)
  - NOT Ginet or pills containing cyproterone acetate
  - NOT Yasmin or Yaz or pills containing drospirenone
- Are older than 35, or under 18 years of age
- Are currently pregnant
- Have any previous or current psychiatric and/or neurological illnesses (for example: depression, epilepsy or current weekly or menstrual migraine)
- Current use of any psychotropic medication (for example: prescribed antidepressants, anxiety medication, antipsychotics)
- Current use of any hormonal medication (aside from oral contraceptive)
- Have ever undergone gender affirming surgical or hormone treatment procedures
- Are pregnant
- Suffer from premenstrual dysphoric disorder (severe menstrual cycle related depression, some PMS is fine)
- Report use of alcohol greater than 21 units per week
What are my responsibilities?

- You must attend for all the study days, or let us know if in plenty of time if you cannot be there.
- You must not take any recreational drugs during the whole study, and no alcohol on the day of and evening before each study day.
- To make the set-up easier please come to the study days with clean and dry hair with no hair-care products in your hair.

What are the risks of taking part?

There is no risk from any of the measurements we take, except for a slight risk of bruising from the blood tests.

Confidentiality

All our records on you are confidential and the measurements we collect are kept in files only identified by a study number.

Use of Data

Data will be stored electronically (on password-protected computers or University of Auckland servers) and/or in hardcopy format in a locked laboratory for at least 6 years. Your identity will be kept strictly confidential. Only your consent form will connect your name with your data, and only the investigators on the study will have access to your consent form.

Blood samples will be stored securely at the University of Auckland before being analysed. Samples will be destroyed after use. No samples will leave New Zealand. The samples will be labelled with a study identifier, not your name.

Withdrawal and Results

You may withdraw from participation without giving a reason at any time during the study and you may withdraw your data within three months of completing the study. We are happy to provide you with a summary of findings upon completion of this research project but please be aware that it can take up to three years for us to finalise the results.
The following page describes the EEG procedure in more detail

The electrical activity produced by your brain can be measured with electrodes that are attached to the scalp surface (example in figure below). Because the signal amplitudes are very small, a good signal transmission is reached by using an electrolyte gel to ensure good contact. The procedure of electrode attachment is painless (though it might occasionally give rise to a slight feeling of discomfort). However, after the recording session, the electrolyte gel may need to be removed 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 sit still throughout the recordings, we will ensure there are enough breaks you can use to move around.

The EEG recordings that we will perform here are without any diagnostic value nor health benefit. Should an abnormality exist in your brain this is unlikely to be seen in the data acquired in the context of this experiment and our research staff are not trained to spot any abnormalities should they exist.

The Auckland University EEG cap
If you would like to participate in this research project or if you have any questions about the project, please contact:

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For any queries regarding ethical concerns you may contact:

The Chair, The University of Auckland Human Participants Ethics Committee

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Approved by the University of Auckland Human Participants Ethics Committee on 20/02/2020 for three years. Reference Number 023544