Henry Wellcome Laboratories for Integrative Neuroscience & Endocrinology
Dorothy Hodgkin Building
Whitson Street
Bristol BS1 3NY, U.K.

Comparison of tissue and blood concentrations of hormones in healthy volunteers

Dynamic hormone diagnostics (ULTRADIAN)

Why have I been contacted?

You have been given this information sheet because you have responded to an advertisement or poster about our study.

You are invited 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 friends, relatives or your GP if you wish.

Please ask us if there is anything that is not clear or if you would like more information.

Take time to decide whether or not you wish to take part and remember that your participation is voluntary.

What is the purpose of this research study?

Hormones regulate the body's metabolism, growth, and function. Pulses of hormones are released into the blood in rhythmic patterns. When diseases disturb these rhythms it causes illness and suffering. Sometimes these conditions can be life-threatening.

We are investigating a new way of diagnosing hormone conditions called microdialysis. We hope that this will eventually make it easier to care for people with endocrine diseases.

In this study we will compare microdialysis with blood sampling to measure normal rhythms of hormones in healthy people.

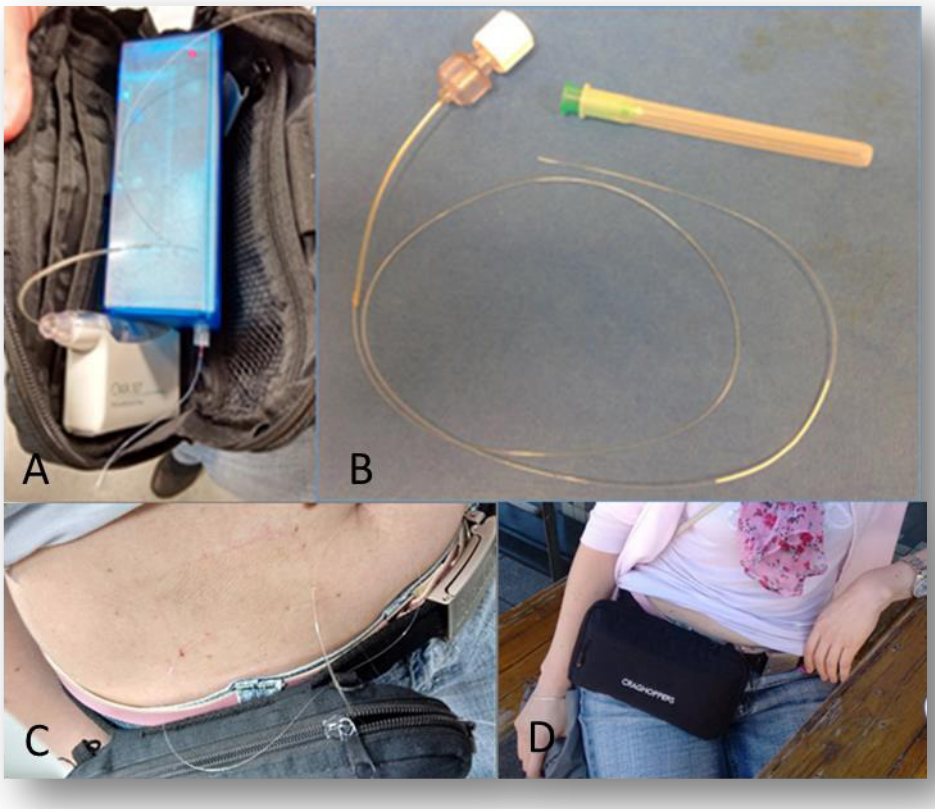
What is microdialysis?

The microdialysis probe is a very narrow tube (less than the width of a pin head) with tiny holes ("pores") through which certain molecules can pass. In this study the probe is placed just beneath the skin after making the area numb with local anaesthetic.

Once the probe is under the skin, it is connected to a small pump and a sample collector. These are both kept in a small bag, which is worn around the waist. Together, everything weighs less than a tin of baked beans. You can see a picture of the device on the next page.

The probe and pump are fully approved for use in humans (CE marked). The sample collector is a research device developed by our team. It does not have CE marking. However

it has already been successfully used in several trials of healthy volunteers and patients with no problems reported. The device stores samples of fluid only – safety valves prevent any flow of liquid back toward the body.



The microdialysis system. The sample collector (oblong box) and pump (smaller box) and are carried in a small bag around the waist (A). The probe (B) is a very small plastic tube placed just below the skin, usually on the lower part of the abdomen (stomach) (C). A volunteer wearing the connected microdialysis system (D).

What does the blood collection system involve?

An intravenous cannula (small plastic tube) will be inserted in a vein in your arm. This is then connected to a computerised pump which enables us to automatically draw very small amounts of blood painlessly from your vein every 10-20 minutes so that we can characterise hormonal pulsing in your blood.

Do I have to take part?

Taking part is voluntary – it is up to you to decide whether or not to take part. If you do decide to take part we will ask you to sign a consent form and give you a copy of this information sheet and the consent form to keep. If you change your mind, you can withdraw at any time. If you decide not to take part you do not have to give a reason, nobody will be upset.

Where do I come for the study visits?

The study will be carried out at the Joint Clinical Research Unit (JCRU), UHBristol NHS Foundation Trust, Marlborough St, Bristol, BS2 8HY.

What will happen to me?

We will talk to you by phone and/or email with some general questions about whether you can participate. If we think you are eligible, and you decide to take part, you will be invited to discuss the study further and provide written consent.

Screening visit

At the screening visit, the researcher will take your medical history to make sure that you are fit enough to take part in the study. Other information including your date of birth, smoking status, height and weight will also be recorded, as these may affect the way your body produces hormones. We will discuss with you all aspects of the study and show you the microdialysis system. If you would still like to be involved informed consent will be taken.

After you have given informed consent we will take a fasting blood sample from a vein in your arm to check routine tests (kidney, liver, thyroid, blood count). After the blood sample, you will be supplied with breakfast (let us know if you have any specific dietary requirements).

Before the study starts

For 2 days before the study starts, and throughout the testing session, you will be asked not to drink any alcohol, take any medications, or to exercise vigorously. You will be given an activity diary to fill in the day before and during sampling so that we can understand your daily routine (what time you go to bed, wake up etc.).

On the study day

You will arrive at the research unit at a pre-arranged convenient time. You will be asked to complete a brief quality of life and health care use survey. Women of child-bearing age may urine sample to test for drugs of abuse (e.g. marijuana, opiates) as hormone levels can be affected by different types of drugs and medications. We will take a fasting blood sample from a vein in your arm to check baseline hormone levels and then we will give you breakfast.

The probe will be inserted in a numbed area of skin and connected to the collection system. This whole procedure will take about one hour. The device will then sample automatically without you having to do anything. This whole process will take about 1 hour.

You will then have a break for 60-90 minutes. You may leave our department for some fresh air or stay with us over this break period. You will then need to come back to the research unit. At this time, an intravenous cannula (plastic tube) will be inserted into a vein in your arm. Out of this very small blood samples will be collected painlessly every 10 minutes using a computerised pump. These samples will be used to measure levels of different hormones.

Blood sampling runs over 24 hours so your last blood sample will be on the following day at the same time that blood sampling initially started on. We will provide meals (lunch, hot

dinner and breakfast) and refreshments. Lights will be switched off at 23.00 and switched on again at 06.30. Feel free to bring things to entertain yourself with such as a laptop or tablet.

If during the study, there appears to be a problem with the flow of blood through the cannula (the plastic tube in your vein), then you may receive a small amount of heparin (blood thinning agent) in order to improve the blood sampling.

You will not be able to have a shower/bath whilst wearing the device.

At the end of the study

The study will end 27 hours after the microdialysis sampler was switched on. At this time the device will be disconnected and removed from your skin and the venous cannula will be removed from your arm.

Saliva collection

During the sampling time we will ask you to collect three saliva samples. Instructions for saliva sample collection will be provided separately.

Support

At least one study researcher will be present throughout the duration of the study.

What are the potential side effects and risks of taking part?

Blood tests and the microdialysis sampling system

The microdialysis system is safe and we do not think there will be any significant side effects or risks to you as a participant. Minor bruising at the site of the microdialysis probe insertion or around the vein where you have your blood test might occur. Very occasionally people can faint while having a blood test – we will ask you if you have ever had any problems with fainting or blood tests before we start the study.

Like any other procedure there is a small risk of discomfort during insertion or at the site of the probe. There is theoretically a small risk of infection and localized allergic reaction at the site of the probe or blood sampling. This risk is considered to be extremely low as we use an aseptic (clean) method and the probe is made from low allergy material. If infection or allergy is suspected we will immediately remove the probe and stop the study.

The automated blood sampling system

A very small amount of blood is taken every 10 minutes and this amount is replaced by infusion fluid - therefore you should not feel faint or unwell. The total amount of blood we take over the 24 hour period is slightly less than the amount you give at a blood donation.

Unexpected abnormal blood test results

If during the study your blood results reveal any abnormality we will arrange a meeting with you to explain these results. We will ask you if you wish for this information to be sent to your GP and if appropriate we may recommend an appointment with your GP.

If you have any questions regarding this you can either discuss with a researcher or take this information sheet to your GP to discuss matters of concern. If, at any time during the study, new information becomes available, the researchers will talk to you about this and discuss whether you want to continue in the study.

Will I receive any reimbursement for my time?

Yes. You will receive £200 to cover all expenses related to the study. There is the option in taking part in other related studies within the ULTRADIAN project, if you decide to do this the maximum reimbursement you can receive is £300.

What will happen to my samples?

Some baseline blood tests will be analysed at the UH Bristol NHS laboratory. The rest of the microdialysis, blood and saliva samples will first be stored in a freezer within the University of Bristol and then sent away to the University of Bergen, Norway and a partner biotechnology company called OLINK, in Sweden. All samples will be totally anonymous and cannot be linked to you in any way. After initial analysis the samples taken for the research will be stored at a biobank at the University of Bergen for up to 5 years after the last person is recruited. Samples are kept in case analyses need to be repeated or if additional results are required to successfully complete the study. After this date your samples will be destroyed at the University of Bergen.

Results will be entered in to the protected project database with access limited to project investigators at the University of Bergen and Bristol.

If you decide to withdraw from the study, you can ask for your samples to be destroyed even if they have not already been analysed, or for any information obtained from analysing your samples to be destroyed.

What are my responsibilities?

We would like you to let us know of any changes in your health or any medication you may take. You will need to attend your appointments as per the agreed time.

How will I benefit from participating?

You will not benefit directly from taking part in this research study and your participation is voluntary. However, understanding of hormones rhythm will improve future management of endocrine disorders.

How will the results of this research be used?

The results of this study will be published in scientific journals and presented at medical meetings. A meeting of all research participants may be arranged to discuss our findings.

Who is organising and funding the research?

The Henry Wellcome Laboratories for Integrative Neuroscience (part of the University of Bristol) is carrying out the research in collaboration with the University of Bergen (Norway). The research is sponsored by the University of Bristol and is being funded by Horizon 2020, an EU Research and Innovation program.

It has full approval from the NHS Research Ethics Board and the Research and Innovation Department of UHBristol NHS Foundation Trust. Funding pays the salaries of some of the research staff and other direct costs of doing the research. Researchers are not receiving any payments other than their usual salaries.

Confidentiality

Any medical and research information from this study will remain confidential. Any information about you will be made anonymous so that you cannot be recognised from it. It will only be available to research staff, and to government bodies which regulate medical studies such as this one and make sure they are performed in a proper manner.

What do I do now?

Thank you for considering taking part in this study. If, after reading this information, you would like more information or decide that you would like to take part, please contact one of the study researchers.

Contact details

Email

ultradian-study@bristol.ac.uk

Call and speak to one of the study researchers

Dr. Georgie Russell	0117 331 3121
Dr. Thomas Upton	0117 331 3121
Prof. Stafford Lightman	0117 331 3167

If you would like more information

If you would like to discuss the science behind the study with an independent person, please phone Prof. Lightman's secretary on 0117 331 3167.

You can also visit the ULTRADIAN study website www.ultradian.net

If you have concerns

You should first speak with the researchers who will do their best to answer your questions. Otherwise you can contact Dr Tom Creed, head of the Joint Clinical Research Unit, UH Bristol (0117 342 4001).

If you wish to make a formal complaint, please write to:

Research Governance Team
Research and Enterprise Development
University of Bristol
Senate House
Tyndalls Ave
Bristol BS8 1TH

The University of Bristol, as the study Sponsor, operates a Clinical Trial protection scheme, which operates in respect of the University's legal liabilities for any injury arising specifically as a consequence of your participation in the study. Additionally, the standard provision of the NHS Indemnity Scheme will operate in respect of the provision of clinical treatment.