PARTICIPANT INFORMATION SHEET

Study Title: (NESPRED-study 1)
Neurocognitive signatures predicting risk of recurrent depression

Chief Investigator:
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We would like to invite you to become a participant in a research study on risk factors for depression. This sheet explains what the study is about and what it would involve. Please take time to read the contents carefully and feel free to ask us if there is anything you do not understand or if you would like more information.

Why are we doing this research?
During everyday dealings with other people, we automatically think about their behaviour and our own and this affects how we feel about ourselves and other people. We have previously shown that brain MRI scans and computer tests whilst thinking about these things can predict risk of recurring depression. Here, we would like to see whether we can confirm this in a larger group of people and whether we might be able to replace brain scans with cheaper measures.

Why have you been invited to take part in this study?
You have been asked to participate in this study because you have recovered from depression. We will ask you to participate in follow-up interviews over 14 months to see whether our measures can predict whether you remain stable or develop another episode of depression over this period.

Do I have to take part?
No. There is no obligation at all to take part in the study and this will not affect treatment.

What would you have to do?
1. You will have contacted us after reading our adverts. We will have done a pre-screening online or via the phone to see whether it is likely that we are able to include you in the study. After this screening we will have sent this information sheet to you and asked you to consent to the study, you can sign the consent form on the first day of the study. For this study we can only include people who are currently not taking antidepressant medication. However, we do not want people to stop their medication just in order to participate in this study. Therefore, if you are currently taking antidepressant medication, but would otherwise fit our study criteria, we will ask you to get in touch again should you and your

doctor have come to the joint decision to stop it anyway and independently of your participation in this study.

2. If you are interested in taking part in the study and the information we have collected at the screening indicates that we can include you in the study, we would then make an appointment for the first visit of the study to take place either online or in-person. During this first session, you will be asked to take part in an evaluation of your mental health, a series of diagnostic interviews and some cognitive function tests some of which will involve the use of a computer, this part of the study will last about 3 hours. We may also carry out a urine drug screening test to rule out current drug use, we will tell you the result of this test, but will not share this with your GP/referring doctors. Positive screening for drugs will be an exclusion criterion.
3. If the evaluation of your mental health confirms that we are able to include you in the study, we will invite you to participate in an MRI brain scan (visit 2) of the study and you will receive samples to collect your saliva (about one teaspoon full, 6 times per day) on the day before the scan and a Virtual Reality Headset to use at home for a 10-15 minute task to assess how you respond to self-blame-evoking situations. We will ask you to bring back the Virtual Reality Headset and saliva samples on the MRI scan day. The samples will be safely stored, so that we can measure levels of important chemicals such as stress hormones and link them to your brain scan.
4. On the day of MRI-scanning, we will give you questionnaires about mood and cognition and you will perform computerised tasks prior to the MRI which takes up to 1 hour. After this we will take a series of images of your brain, which will take about 1 hour. However, the actual time you are in the scanner may be longer than this if there are any technical difficulties, it may then take up to 90 minutes. In the scanner you will see short statements prompting you to think about imagined social behaviour (e.g. "You are stingy towards your friend"). After the scanning you would perform computerised tests which could also take place online. Depending on social distancing rules, we will also measure the electrical activity of the skin of your palm whilst listening to sounds for 15 minutes, and use a blood pressure cuff on your arm to measure the time it takes you to sense this as painful, which you can stop at any time if it is too uncomfortable. We will ask you to collect another saliva sample and to recall emotional memories for 10 minutes, and if you agree, save an audio recording/transcript of your responses for further analysis. All of this testing takes about 1-1.5 h.
5. On the next day we ask you to complete a computerised questionnaire in which you have to make further ratings on the statements you saw in the scanner at home which we will send as an e-mail to you (you could also come in for another appointment to do the test if you wish or we could do it online in a video session with you). This will take about 1 hour to complete. We will ask you to send the questionnaire back to us.

This will complete the assessments we will mainly use to predict whether you will develop another depressive episode or remain without major depression.

6. Every month, we will send a brief electronic questionnaire that takes about 5-10 minutes to complete to stay in touch. In case you have developed symptoms of depression again, the questionnaire would suggest to bring forward your appointment and get in touch with us.

In an optional part of our study, we want to see whether disruptions in your sleep rhythms precede recurrence of depression as suggested by some literature. If you agree, we would give a commercially available sleep monitoring device to you. The device consists of a plastic ring, which we would ask you to wear every night for the duration of the study. The ring sends data about your sleep quality to an app which you would have to install on your smartphone. As part of our monthly follow-up questionnaire we would then ask you to upload a document with your monthly sleep quality data, that you can generate with your smartphone app. At the end of the study we would ask you to return the sleep monitoring device. If you do not own a smartphone, we would be able to lend you one.

7. After around 6 months and 14 months we would see you for an appointment (either at our Denmark Hill campus or via a video/phone conference). The full appointments would be similar to what we do on visit 1 of the study.
8. We would ask you to get in touch during the 14 months follow-up period should your contact details change or should you feel that depressive symptoms re-occur. In this case, we may invite you for an additional phone interview/appointment or shift one of the planned appointments.

Your participation in the study ends after the 14 months follow-up period or earlier in case you have developed another episode.

In addition, we will ask whether you are interested in participating in an additional part of the study. This would consist of computerised tasks which you may be able to do at home within 2 hours and which we would send to you by e-mail or online. Participation in this part is optional.

If you agree, we may want to take a video or audio recording of the assessment on the first day of the study which will only be looked at by members of our research team or experts on the use of some of the study instruments whose strictly confidential advice we may seek to check the quality of our interviews. If you do not agree to that, we do not have to do this. All recordings during the study will use technology to encrypt in transit and storage, such as Microsoft Teams/Stream or encrypted laptop or audio devices. Once recorded, we will use additional encryption to protect recordings from unauthorised access.

What expenses or payments will you receive?

You will receive compensation to participate in the study. This will be paid on a pro-rata basis as outlined below.

For example, we will pay in shopping vouchers:

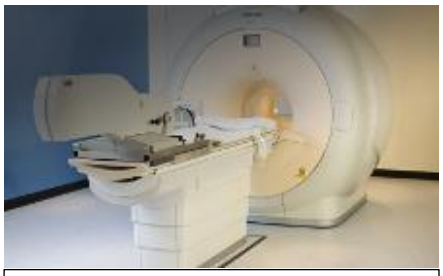
- £15 for the clinical assessment session (Visit 1)
- £10 for the saliva sample collection (at home)
- £40 for the MRI session (Visit 2)
- £10 for participation in the optional computer testing part of the study (at home)
- £30 for participation in the follow-up visit after 6 months (£20 if remotely)
- £30 for participation in the follow-up visit after 14 months (£20 if remotely)

(£135 in total if you took part in all of these)

What are the possible risks of taking part?

Risks/Discomforts of MRI

The imaging is done on a standard clinical scanning machine called a Magnetic Resonance Imaging (MRI) Scanner (3 Tesla). There is no ionising radiation (x-rays) involved in this type of scan and if all precautions are taken, there are no known risks.



Picture shows an MRI scanner

You will be asked to fill in a Safety Questionnaire that asks about the presence of any metal in or on the body before you enter the MRI scanning room. If you are a woman of childbearing age, you need to be sure that you are not pregnant as those who are pregnant cannot undergo a research MRI scan. Magnetic Resonance Imaging uses a strong magnetic field to obtain images of body organs and tissues. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will be asked to lie on a table that can slide in and out of the cylinder. While in the scanner you will hear loud knocking noises, and you will wear earplugs to muffle the sound. You will be able to communicate with the MRI scanning staff at all times during the scan. We will move you out of the machine anytime that you wish.

You will be at risk of injury from the MRI magnet if you have a pacemaker or other implanted electrical devices fitted, or if you have a brain stimulator, dental implant, aneurysm clip(s) (metal clip(s) on the wall of a large artery), metallic prostheses (including metal pins and rods, heart valves, and cochlear [ear] implants), implanted delivery pump, or shrapnel fragments. Welders and metal workers are also at risk of injury because of the potential for small metal fragments to be embedded in the eye of which you may be unaware. For this reason, if you have any of these conditions, you will not receive an MRI scan. If you have a question about any metal objects being present in the body, you should inform the researcher. In addition, all magnetic objects (for example, watches, coins, jewellery, and credit cards) must be removed before entering the MRI scan room. Individuals with fear of confined spaces may become anxious during an MRI and will not be suitable. There are no known long-term risks or consequences of MRI scans.

Risks of Virtual Reality (VR) assessment

VR headsets will be given to you whilst ensuring at least 72 hours between your and the last user's use to minimise COVID-19 transmission risk, in addition, we will use 70% alcohol solution to disinfect the facial masks which are fitted to the VR device which also meets general safety guidelines in the UK. The immersive nature of Virtual Reality might induce anxiety after wearing a headset for more than a few minutes. In order to avoid this, we have made our task as short as possible (around 10-15 minutes in total). In addition, some people who use Virtual Reality might complain of dizziness and nausea. This is because simulated movements can affect a person's perception of space. If you develop any of those symptoms, you can stop at any time.

Risks/Discomforts of blood pressure cuff

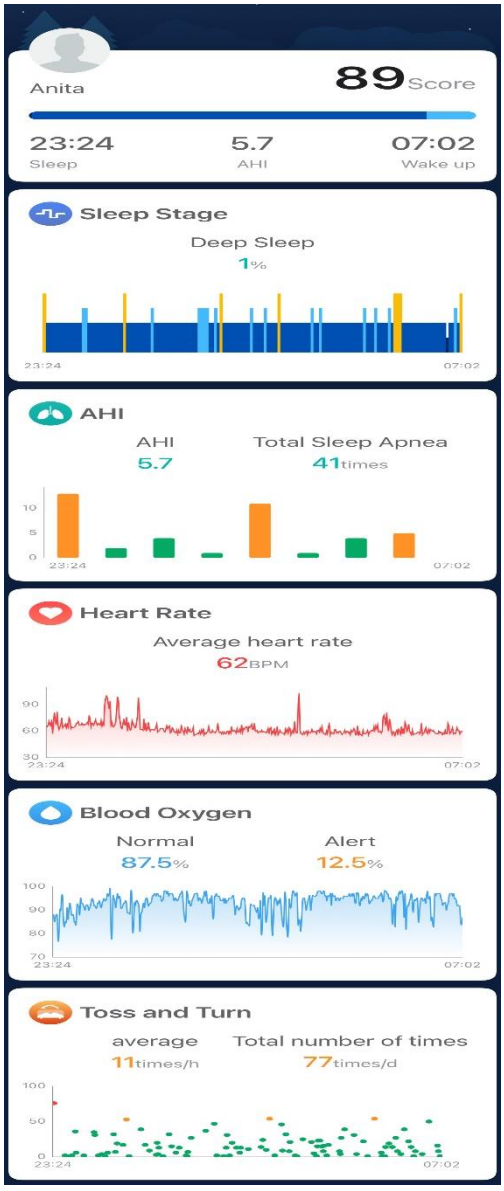
Once COVID-19 is under control, for measuring your pain sensitivity we will use a standard blood pressure cuff and inflate it to 200 mmHG which is often done in routine clinical settings, although this is uncomfortable, we will deflate the pressure as soon as you tell us to and after a maximum of 5 minutes.

Risks/Discomforts of electrical activity measure of your skin

Picture of EDOR device

Once COVID-19 is under control, there are no known risks of the EDOR device which will use in collaboration with a company (EMOTRA) who have registered this to see whether it can be useful in predicting relevant outcomes for depression. You will get a headset to listen to tones to measure how your nervous system responds. This is based on sweat produced in your skin which leads to changes in electrical activity.

Risks/Discomforts of Sleep-Monitoring Ring



The Go2Sleep sleep monitoring device is commercially available and tested, you are asked to only wear it on your finger at night and so risks of a rash are minimal. On the left you see an example report, which you can create on an the accompanying mobile app. The device sends data to your mobile phone app via your home wireless network about your heart rate and the depth of your sleep, as well as your oxygen levels at night and your breathing rhythms.

It may flag up information about your sleep such as signs of "sleep apnoea syndrome" – i.e. if you have pauses in your breathing at night which may increase your risk of cardiovascular diseases and make you feel less refreshed in the morning. This could be worrying but also helpful. We would recommend sharing such information with your GP directly as you normally would if you had bought the device yourself. The app allows you to share your sleep report with your doctors and us via an email attachment. If you feel that monitoring your sleep makes you worried, we advise that you stop using it and return it to us. SLEEPON, the US company who developed the device, will ask you to create an account with your name, email and date of birth. The company will store your sleep data linked to your account. We would recommend that you remain opted out of location-based data collection.

What if there is a problem?

Dr Zahn can be contacted with any problems, complaints or questions regarding the study. You can also contact the South London & Maudsley NHS Foundation Trust (SLaM)'s Patient and Liaison Service (Freephone: 0800 731 2864, Option 2 or pals@slam.nhs.uk). For complaints you could also write to Dr Gill Dale. Director of Research Quality; Head, Joint Research & Development office SLaM and Institute of Psychiatry, Psychology & Neuroscience (IoPPN), P005, King's College London, De Crespigny Park, London SE5 8AF. In the event that something does go wrong and you are harmed during the research you may have grounds for legal action for compensation against King's College London and/or SLaM NHS Foundation Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate). King's College London has obtained insurance which provides no-fault compensation i.e. for non-negligent harm, you may be entitled to make a claim for this.

What if you no longer want to take part?

If you no longer want to take part that is fine, all you need to do is tell one of the research team. You are free to choose not to take part or withdraw from the study at any time without giving a reason: this will not affect treatment. You can also ask Dr Zahn to delete your data or part of your data at any time point before we anonymise your data and delete any identifying information. Data that have been anonymously included in published reports cannot be withdrawn once they are published.

What are the possible benefits of taking part?

There are no direct benefits to you. It is you who will benefit the progress of medical research. You will make an important contribution to a better understanding of depression by taking part in our research project. We will also give you a short report on the results of the diagnostic interviews that we have carried out which we will share with your GP. If you take part in the MRI session, a limited assessment of the MRI scans will be performed by a radiologist and identification of a major abnormality that requires action will be reported to the GP you specify on your MRI consent form. You will also receive an electronic copy of your MRI scan if you wish.

What will happen if relevant new information on a psychiatric or neurological disorder is detected that was not known before?

During our assessments, we may detect new relevant information which points to the presence of a mental health or neurological problem that you were not aware of before the study. In this case if the mental health or neurological problem is deemed relevant to your health and wellbeing we would inform your GP with your permission. If you have told us that you are feeling unwell first before seeing your GP/responsible clinician, we may get in touch with your GP/responsible clinician to make sure that you receive help, because unfortunately we are not able to provide treatment outside of the study. In this case, we may write a more detailed letter tailored to your individual circumstances which may include treatment suggestions if you would like us to do so. In a life-threatening situation such as when you report about acute suicidal thoughts that you cannot control, we have the duty of care to refer you for further help

and may have to give information on your health to other health professionals without your consent.

What can I do if I feel distressed after taking part in the study?
Some of the testing materials used require you to imagine how to feel about acting in certain ways or how to judge other people. This may evoke feelings such as guilt or anger. In case you feel distressed during or after taking part in the study, please tell the research team who will contact Dr Zahn or another psychiatrist/psychologist involved in the research project to arrange for further counselling.

What will happen to my samples?
Your saliva samples will be used to measure stress hormones, inflammation, and hormones linked to human bonding. They will be stored in anonymised form at the Maurice Wohl Clinical Neuroscience Institute at King's College London and we ask your permission to store it for future studies where we could look at other chemicals in your sample for research questions which would have to be approved by the ethics committee.

How will we use information about you?
We will need to use information from you for this research project. This information will include your name, date of birth and contact details. The research team will use this information to contact you and your GP. Your name, date of birth, or contact details will not appear on any records or samples containing your data collected during the study. A code number will be used to identify records stored separately in a password protected file which can only be accessed by our research team. The code file and signed consent forms will be kept for 5 years after publication of the research results by Dr Zahn and then destroyed. Confidentiality could only be broken in a life-threatening situation in which we would have the duty of care to refer you for further help. We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?
- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study which we will make available in anonymised form through our King's College data repository.

Where can you find out more about how your information is used?
You can find out more about how we use your information
- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by contacting King's College London's Data Protection Officer, Mr Albert Chan at info-compliance@kcl.ac.uk

Participation in Future Studies
We would also like to ask for your permission to contact you again in order to ask whether you would be interested in participating in a future study.

What will happen to the results of this study?
Anonymised results of this study will be presented at scientific conferences and published in international journals and as part of academic dissertations and you will receive a copy of the initial results via email within one year of completion of the study.

Who is funding this study?
This study is funded by the Medical Research Council and the NIHR Biomedical Research Centre at the South London and Maudsley NHS Trust.

Who has reviewed this study?
The research to be carried out has been approved by the London South East NHS Research Ethics Committee. This does not imply any endorsement.

Please contact us on the details below if you have any questions about the study. We very much appreciate you taking the time to read this and thank you for considering this request.

Contact for further information:
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