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PARTICIPANT INFORMATION SHEET (age 16 and 17)
Biomarkers and emotional processing
CUREC Ref: R65602/RE007
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You are being 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 a moment to read the following information carefully, and please show it to your parents and discuss your potential participation with them. Take time to decide whether or not you wish to take part.

PART 1: ABOUT THIS STUDY AND PARTICIPATION

What is the purpose of this study?

This study investigates how growth factors, substances naturally produced in the body, are related to anxiety, mood and the processing of emotional information. The growth factors we are interested in are proteins usually involved in cell growth and healing, but recent research suggests that people with lower levels of these proteins might also be more likely to feel anxious or sad at some point in their lives. In this study, we will ask 120 young people to give a small blood sample so that we can measure their individual levels of these growth factors. We will then assess to what degree these levels correspond to the processing of emotional information presented on computer screens (e.g. faces with varying emotional expressions), anxiety levels and mood. The findings might help develop a simple blood test indicating the risk of developing anxiety or depression in the future.

Why have I been invited?

We would like 120 people aged 16-35 years to take part.

Exclusion Criteria

You will not be able to participate in this study if you:

- are younger than 16 (or older than 35) years
- have insufficient English skills.
- are smoking more than 5 cigarettes a day.
- have been on certain medication that influences the central nervous system (e.g. antidepressants, sleeping medication) during the last 6 weeks.
- participated in another study involving certain medication that influences the central nervous system (e.g. antidepressants, sleeping medication) during the last 6 weeks.
- Have been on steroid medication in the last 6 weeks, such as beconase, cortisone or prednisone
- have ever had a severe psychiatric illness such as bipolar disorder, psychotic disorder, alcohol or substance abuse.
- have a close family member with a history of a severe psychiatric disease
- have a history of epilepsy or another neurological disorder
- are female and have no regular cycle (menstrual cycles of less than 21 or more than 32 days), are pregnant or are on hormonal contraception
- have a hair length smaller than 3cm

In case have consumed alcohol, caffeine, or nicotine within 12 hours of the testing visit, or have engaged in vigorous physical activity within 24 hours of the testing, you are not able to participate and we will have to reschedule the session.

Do I have to take part?
No. It is up to you to decide whether or not to take part. Your parent or guardian must also give their consent. If you decide to take part you will be given (or can print) this information sheet to keep. You will still be free to withdraw at any time and without giving a reason. The national advisory group INVOLVE (http://www.invo.org.uk) is an independent contact point where potential participants can seek general advice about taking part in research.

What will happen to me if I take part?
If you decide to volunteer, we will initially send you an email with a link to our brief online *screening* to make sure you are eligible to take part in the research. Alternatively, we can set up a phone screening call, if you prefer this over the online screening. Once we have established your general eligibility, we will invite you to the department for the *Testing Visit* and contact you again 6 months later via email to send you a link to the brief online *Follow-up Assessment*.
We will ask you to give us verbal or online consent for the screening and confirm that your parents/guardian are aware that you are taking part in the screening. At the testing visit your parent/guardian has to accompany you, so that we can obtain written consent from them that they are happy for you to take part in this research and obtain written assent from you that you are happy to take part in this research as well. Your parent/guardian does not need to stay with you during the whole testing visit.

<u>Screening (online or phone, 5min)</u>
First, we will ask you a few screening questions (for instance, your age, current medication, history of severe psychiatric illness, oral health and duration of menstrual cycle). After this, you will fill in a brief questionnaire consisting of yes/no questions, which measures thoughts, feelings, and behaviours, which might be relevant for anxiety and depression. We are looking for a wide range of people with different scores on this questionnaire to ensure that we get a balanced sample of participants. This means, that you might be excluded based on your scores on this questionnaire, once our capacity to include people with this score is reached. If you are ineligible and excluded from the study, all screening data will be destroyed.

<u>Testing Visit (Department of Psychiatry, 4 hours)</u>
This session will ideally take place between 12pm and 6pm. Please note that a few days before your appointment, we will send you a reminder to **please refrain from vigorous physical activity within 24 hours, from alcohol, caffeine, or nicotine within 12 hours, of this visit.** We will have to reschedule your appointment if you are not able to comply with these instructions.

The Testing Visit will involve:
- Chance to discuss this information sheet and any further questions
- signing consent and assent forms
- asking you for some sociodemographic information (e.g. gender, years of education, or the day of your menstrual cycle)
- answer some detailed questions about your current and previous psychological well-being in an interview and a battery of questionnaires
- give us saliva samples using a collection tube.
- Give us a small blood sample
- Give us a small hair sample

We will collect 2 Saliva samples using a special collection tube called Salivette (Sarstedt). In this tube you will find a cotton swab to place in your mouth for about 60 sec, so that it can absorb the saliva. After that, you will place the cotton swab back into the collection tube. This method is pain-free and involves no risk.

We will collect a blood sample (9ml in total), which will be taken by a trained and experienced researcher, similar to when your blood is taken during a GP visit. However, as with all blood tests, this can lead to slight discomfort or bruising where the needle goes in and there is a slight risk of fainting. To ensure your safety in case you feel faint, blood samples will be taken in a chair with support or lying down.

Furthermore, we would like to take a small strand of hair (~3 mm diameter) from the lower back of your head. This sample will be taken from different locations so that you will not notice any change in appearance

During this visit, you will also be working on different computer tasks for about 3 hours. These will, for instance, include two *Gambling Tasks* where you will repeatedly be presented with two abstract stimuli on the screen, each of which will be associated with a hidden probability of winning or losing points, and you will try and figure out these hidden patterns and make use of them to earn as many points as possible. In another task, a *Visual Search Task*, you will be asked to find and select a face with an emotional expression different from all the others shown on the screen as quickly as possible, using a computer mouse. In the *Foraging Task*, you are a little fish who needs to gather food while not being caught by predators. In the Challenge Task, we will ask you to solve simple mathematical, verbal, and attention challenges. During this task, we will measure your heart rate via a sports watch and chest strap, which is commonly used by athletes, and you will complete brief questionnaires about how you are feeling. The total time of this visit is approximately 4 hours. You will be able to stop the research at any point.

It is essential that you can keep the appointment arranged for you as testing time is highly sought after and cancellations must be made as soon as possible so that other researchers can use the time in the laboratories.

Follow-up Assessment 6 months later (via Email, 10min)
Six months after your testing visit, we will contact you again via email and send you a link to complete two online questionnaires assessing your current levels of anxiety and depression.

Risks and Benefits
There are no direct benefits to participants. We also do not expect any disadvantages or risks. You will be asked to provide a small blood sample during this study. Blood will be taken by a trained and experienced researcher. As with all blood tests, this can lead to slight discomfort or bruising where the needle goes in and there is a slight risk of fainting. Should you become distressed, please tell the researcher and the tests will be stopped immediately.

Expenses and payments
If you take part in this study, you will receive £40 upon completion of the testing visit (with the option to win up to an additional £5 in one of the experimental tasks), and another £10 for filling in the two online follow-up questionnaires 6 months after your visit.

PART 2: DATA PROTECTION AND INDEMNITY

What will happen if I do not want to carry on with the study?
Even after you have signed the consent form, you are absolutely free to withdraw from the study at any point without giving any reason and without medical care/legal rights being affected. Any identifiable data will then be destroyed.

What would happen if there is a problem?
If you have a concern about any aspect of this study, please contact Anoushka Sharma (Anoushka.sharma@psych.ox.ac.uk) or Dr Andrea Reinecke (andrea.reinecke@psych.ox.ac.uk), and we will do our best to answer your query. We will acknowledge your concern within 10 working days and give you an indication of how it will be dealt with. If you remain unhappy or wish to make a formal complaint, please contact the Chair of the Research Ethics Committee at the University of Oxford who will seek to resolve the matter as soon as possible:
Chair, Medical Sciences Inter-Divisional Research Ethics Committee; Email: ethics@medsci.ox.ac.uk; Address: Research Services, University of Oxford, Wellington Square, Oxford OX1 2JD

What will happen to my data?
All paperwork containing personal information, such as the consent forms, will be kept in a locked filing cabinet. Personal information such as names, email addresses, and phone numbers will be destroyed at the end of the study (which equals the end of data analysis). Only the consent forms will be kept for 5 years after the end of the study and then destroyed by shredding. All other information that is collected about you during the course of the research, including the data from the screening and your health information, as well as the

heart rate recordings will be kept strictly confidential. All data will have your name replaced by a code so that you could not be recognised from it (unless by the involved researchers who will hold a key linking this code to your name (stored in a locked filing cabinet) until the end of data analysis collection, when this link will be destroyed. The data will be kept securely in paper or electronic form for at least 5 years following study completion. All electronic data will be stored on a password protected computer. Paper records and paper questionnaires will be stored in a locked filing cabinet and then securely shredded.

Your saliva samples will be pseudonymised, cells will be removed & discarded, and the liquid part stored in the Department of Psychiatry until the measurement of the biological markers.
A part of your blood sample will be sent to the Haematology Department of the John Radcliffe Hospital on the day of collection using the hospital blood transport system. There, it will be analysed within 48 hours. Only c-reactive protein levels will be assessed – no other tests will be performed. Once your sample has been analysed, it will immediately be disposed of by the laboratory. The other part of your blood sample will be pseudonymised, cells will be removed and discarded, and the liquid part stored in the Department of Psychiatry until the measurement of the growth factors (fibroblast growth factor-2 and Brain-derived-neurotrophic factor) in the Department of Psychiatry in Oxford. No other analyses will be carried out, and we will dispose of your samples within six months of the end of the study.

At the end of the study, anonymised hair sample and saliva samples of all our participants will be sent to our collaborator at the Department of Biological Psychology at Dresden University of Technology in Germany (Prof. Clemens Kirschbaum) for analysis. Our collaborators will not receive any personal information associated with the samples (e.g., your name), and samples will only be identifiable by the study team at the Department of Psychiatry/Oxford, based on a unique identifier code attached to the samples. Our collaborators will measure the concentration of steroid hormones in each sample, but no genetic analyses will be carried out. After analysis, samples will be destroyed.
Responsible members of the University of Oxford may be given access to data for monitoring and/or audit of the study to ensure we are complying with regulations. With your permission, anonymised data collected during the course of the study may be used in future research.

What will happen to the other results of the study?
Anonymised results may be published at conferences and in scientific journals. However, no information which could be used to identify any individual participant will be published. Prior to study participation, we will ask for your consent to use your anonymised data in future studies if new research questions emerge. However, you can opt out of agreeing to this, and this will not affect your study participation. If you indicate at the end of your participation that you are interested in finding out about the results of this research, we will make arrangements to inform you once the study is completed.

Who is funding the research?
The research is being funded by an award from the Oxford University Medical Sciences Division Clarendon Fund.

Who has reviewed the study?
All research studies are checked by an Ethics Committee to ensure the research is conducted safely and to the highest standards. This research has been reviewed by and received ethics clearance through the University of Oxford Central University Research Ethics Committee.

Contact details
If you would like any further information on this study, or if you have any concerns, please contact Anoushka Sharma email: anoushka.sharma@psych.ox.ac.uk.

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