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PARTICIPANT INFORMATION SHEET
Losartan and emotional processing and memory
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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 discuss it with friends, relatives and your GP if you wish. 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?

Recent studies suggest that the blood pressure medication losartan might have the potential to improve psychological treatments, and we hope that the knowledge gained from this study will eventually contribute to the improvement of treatment for people who experience emotional problems such as anxiety disorders. We would like to test two groups of people: one who receives a single, low dose of losartan, and one who receives placebo (a substance not containing any medication). Your allocation to one of these groups will be randomised. In particular, we are interested in how this drug affects emotional processing in the brain.
To measure this, you will be working on a battery of computer tasks, responding to emotional and non-emotional stimuli. During some of these tasks, we will measure activation patterns in your brain using functional magnet resonance imaging (fMRI).

Why have I been invited?

We would like 40 healthy people aged 18-50 years to take part.

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

- are younger than 18 or older than 50 years.
- have a Body mass Index below 18 or over 30.
- have insufficient English skills.
- are smoking more than 5 cigarettes a day.
- are pregnant or breast-feeding.
- have been on certain medication that influences the central nervous system (e.g. antidepressants, sleeping medication) during the last 6 weeks.
- are currently taking blood pressure or other heart medication, especially a drug called aliskiren, or beta blockers.
- are currently diagnosed with intravascular fluid depletion or dehydration.
- have ever had a psychological disorder such as depression, bipolar disorder, eating disorder, anxiety 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, or other severe diseases such as kidney, liver, heart or respiratory problems, renal insufficiency, or systemic infection.
- Have any contraindication to MRI, such as some intra-uterine device (IUD) coils, some metal implants etc.
- participated in another study involving certain medication that influences the central nervous system (e.g. antidepressants, sleeping medication) during the last 6 weeks.

You will also not be able to take part in this research if you are left-handed.

Do I have to take part?
No. It is up to you to decide whether or not to take part. 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 ask you a few screening questions (for instance, regarding your general health and current medication) via email or phone to make sure it would be appropriate for you to take part in the study. Once we have established your general eligibility, we will invite you to the department for two visits:

1. Screening Visit (Department of Psychiatry/ Warneford Hospital)
Your first visit will be a screening session where we will make sure that it is safe for you to take part, and that you are suitable for this particular study. We will also give you the chance to ask any questions you might have.

This session will involve asking you to:
- sign a consent form
- give us some information about your medical history
- answer some detailed questions about your current and previous psychological well-being.
- complete a series of questionnaires asking about symptoms such as anxiety or low mood.

The screening visit will take about 30 minutes to 1 hour. Should a potential undiagnosed psychiatric or medical condition (such as high blood pressure) be identified during this visit, you will be encouraged to make contact with your GP.

Visit 1: Screening Visit (1/2 to 1 hour) *Department of Psychiatry/ Warneford Hospital* Giving informed consent Medical and psychiatric screening Questionnaires
Visit 2: Testing Visit (3 ½ to 4 hours) *Department of Psychiatry/ Warneford Hospital* Questionnaires Drug administration Losartan (50mg) vs placebo Experimental Testing Computer tasks and fMRI

2. Testing Visit (Department of Psychiatry/ Warneford Hospital)
We will ask you to have your last meal 2 hours before this visit. At the beginning of your visit, you will receive a capsule that will either be:
- a placebo capsule (not containing any medication; main ingredient: microcrystalline cellulose)
- a 50mg losartan capsule.

The treatment that you will be allocated to receive will be chosen at random, and neither you nor the researcher will be aware which treatment you have received. Losartan has been tested in similar studies before, and it has been shown that single-doses like the one you might be receiving are unlikely to cause any side effects. We will measure your blood pressure and heart rate before and after having taken the capsule.

One hour after having taken the capsule, we will ask you to take part in the fMRI scan. To undergo magnetic resonance scanning you would be asked to lie still on a table inside the MRI scanner. The scan will take about 45mins and we will ask you to respond via a button box to a Memory Task displayed on a screen that you can see whilst in the scanner. In this task, we will present images that you will be asked to categorise, using a left key for animals and a right key for landscapes. In a later test, we will find out how well you remember these images outside the scanner. While you are in the scanner, we may measure your breathing, heart rate, and the electrical characteristics of your skin. This will involve putting a band around your chest, and wearing a clip on one of your fingers. After the scan, we will ask you to complete some more tasks on a computer laptop. **It is essential that you can keep the appointment arranged for you as scanner time is highly sought after and cancellations must be made as soon as possible so that other researchers can use the time on the machine.** The total time of this visit is approximately 3 ½ to 4 hours.

What is losartan?
Losartan is a medication for high blood pressure which has had UK market authorisation for 20 years. Recent research suggests that this drug can also improve cognition and the effects of learning experiences. As a side effect, some participants experience symptoms such as drowsiness, muscle weakness, low blood sugar, headaches, hypotension or allergic reactions. However, if you are randomised to the losartan condition you will only be asked to take a very low, single dose. Recent studies have shown that taking such doses is very unlikely to cause side effects. Nevertheless, you will be closely monitored by a researcher during the testing session.

What is an MRI scan
MRI is safe and non-invasive and does not involve any ionising radiation (x-rays). The MRI scanner is a large tube which is open at both ends. You will enter the scanner headfirst and your legs will remain outside the tube. Participants will be introduced carefully to the scanner and allowed to leave at any stage. Whilst in the scanner participants have easy access to a call button should they wish to stop the scan or speak with the radiographer or operator.

Are there any possible disadvantages or risks from taking part?
Although we believe this is a very safe study, appropriate medical oversight will be in place. For the drug doses used here, no side effects have been reported in previous studies, and there is no evidence to suggest that MRI is harmful to unborn babies. Nevertheless, as a precaution, you will not be able to take part in this study if you are pregnant, planning to become pregnant, or breast-feeding. Pregnancy testing kits will be provided if you are unsure whether you might be pregnant.

MRI is safe and non-invasive and does not involve any ionising radiation (x-rays). However, because they use a large magnet to work, MRI scans are not suitable for everybody. Because of this, you will be asked pre-screening safety questions to help determine if you are able to take part. For example, if you suffer from claustrophobia, you are likely not to be comfortable in an MRI scanner. Normally, MRI scanning for research purposes would not be performed without further investigation if you have a heart pacemaker, mechanical heart valve, mechanical implant such as an aneurysm clip, hip replacement, or if you carry other pieces of metal that have accidentally entered your body. As some of the scans are noisy, we would give you earplugs to make this quieter for you. It is important that these are fitted correctly as they are designed to protect your ears. In preparation for your scan and for your comfort and safety we may ask you to change into pocketless and metal free "pyjama-style" top and trousers, which are available in a range of sizes. You may keep your underwear and socks on, but we would ask ladies to remove underwired bras. If you have a suitable sports type bra you may wear this instead. Please avoid any fabrics that contain metallic threads or have been silver impregnated (often marketed as anti-microbial/bacterial or anti-odour/stink). Metal jewellery, including body piercing, must also be removed. Eye shadow and mascara must also be avoided, since some types contain materials that can interact with the magnetic field. If you wish to wear eye makeup to your scan we can provide makeup removal wipes but you are advised to bring your own makeup to reapply. Lockers are provided to secure your personal belongings and clothing.

It is important to note that we do not carry out scans for diagnostic purposes, and therefore these scans are not a substitute for a doctor's appointment. Our scans are not routinely looked at by a doctor; rather our scans are intended for research purposes only. Occasionally a possible abnormality may be detected. In this case, we would have the scan checked by a doctor. If the doctor felt that the abnormality was medically important, you would be contacted directly and recommended to have a hospital (NHS) diagnostic scan arranged. You would not be informed unless the doctor considers the finding has clear implications for your current or future health. All information about you is kept strictly confidential.

What are the possible benefits of taking part?
There are no direct benefits to taking part in this research. However, we hope that the results of this study will inform the development of more effective treatments for anxiety disorders.

Will I be reimbursed to take part?
If you take part in this study, you will be paid £50 for participation upon completion of the study. For this, we will take your bank details at the end of your second visit and transfer your reimbursement into your account. If your screening visit indicates you are not eligible for the study, you will receive a pro-rata reimbursement.

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?
We believe that this is a safe study. The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. If you have a concern about any aspect of this project, please speak to the Principal Investigator, Dr. Andrea Reinecke, who will do their best to answer your query. The researcher should acknowledge your concern within 10 working days and give you an indication of how he/she intends to deal with it. If you remain unhappy or wish to make a formal complaint, please contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480, email ctrg@admin.ox.ac.uk, who will inform the chair of the Research Ethics Committee at the University of Oxford.

What will happen to my data?
We will be using information given by you in order to undertake this study. Research is a task that we perform in the public interest. The University of Oxford, as sponsor, is the data controller. This means that we, as University of Oxford researchers, are responsible for looking after your information and using it properly. We will use the minimum personally-identifiable information possible. We will destroy most identifiable information about you as soon as possible after the study has finished. However, we are required to keep consent forms, which contain your name, for 5 years after study completion. We will store these securely at the University of Oxford, separately from your anonymised research data

All electronic data will be anonymised and only contain a study ID, and this data will be stored on a password protected computer. 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 collection). Following appropriate reimbursement for your participation in the study, your bank details will be destroyed in our files (but may be kept by our department's finances department for up to 7 years). All other information that is collected about you during the course of the research will be kept strictly confidential. It 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 until the end of data collection, which will be stored in a locked filing cabinet). This information will be kept securely in paper or electronic form for at least 5 years following study completion.

Responsible members of the University of Oxford, host institution and regulatory authorities may be given access to data for monitoring and/or audit of the study to ensure we are complying with applicable regulations. Anonymised data collected during the course of the study may be used in future research.

Will my General Practitioner/family doctor (GP) be informed of my participation?
No, we will not inform your GP of your participation in this study.

What will happen to the 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. If you are interested in finding out about the results of this research, please let us know and we will make arrangements to inform you once the study is completed.

Who is organising and funding the research?
The University of Oxford is Sponsor of the research and it is being funded by an award from the MQ: Transforming Mental Health Charity, and the University of Oxford Medical Sciences Division.

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.

Participation in future research:
If you have indicated in the consent form that you would like to be contacted for further research studies, we will keep your contact details on file. However, this information will be kept separately from research data, on a password protected computer that can only be accessed by researchers involved in this study. Agreeing to be contacted does not oblige you to take part in future research.

Contact details
If you would like any further information on this study, or if you have any concerns, please contact Adele Holder or Theodora Thoroddsen. Email: adele.holder@psych.ox.ac.uk/ theodora.thoroddsen@kellogg.ox.ac.uk or telephone: 01865 618320.

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