Serotonergic and Noradrenergic influences On Decision making in Anxiety (SODA)

We would like to invite you to participate in the SODA study, aimed at understanding how common drug treatments for anxiety affect psychological processes that are thought to play an important role in these conditions. Your participation could provide valuable insights into the immediate effects of antidepressants, which might would help us better understand how they work. Before you decide, it is important for you to understand why the research is being done and what participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part or not. Thank you for reading this information sheet.

What's involved?

What is the project's purpose?

This study will investigate the immediate effects of Citalopram, a selective serotonin reuptake inhibitor (SSRI) and Venlafaxine, a serotonin and noradrenaline reuptake inhibitor (SNRI) on learning and decision-making processes which may be affected in individuals with anxiety and depression. These drugs are commonly referred to as "antidepressants" but are frequently prescribed for treating both depression and anxiety. Currently, however, we know very little about how they work.

We want to know if administering these drugs will affect the way you learn and make decisions. In order to study their effects, we will be giving each participant one of the drugs or a placebo on three separate occasions. A placebo is like a pretend pill and is often called a "dummy treatment." It looks just like the real medicine but doesn't do anything because it has no medicine in it. We use it in studies to see if the real medicine works better than taking nothing at all. Please note that the placebo tablet you will be given contains lactose which is animal derived. In addition, each tablet (placebo or drug) will be encapsulated in a hard gelatine capsule, which is also animal derived.

Using electroencephalography (EEG), we will look at your performance and brain activity whilst you complete computerised tasks that will measure how you learn and make decisions. This research will help us to understand the immediate psychological effects of these drugs, which could provide important insights into how they treat anxiety and depression.

What are the drugs that are being tested?

SSRIs and SNRIs are used as first-line treatments for anxiety and depression. They are believed

to work by changing the levels of mood-enhancing chemicals in the brain called serotonin and noradrenaline, respectively. Both medications need time to work, and patients usually feel improvements after several weeks of treatment. The reasons for this delay in mood improvement are still unclear. So, despite their widespread use, the immediate effects of these medications on cognitive functions are not fully understood. You will contribute to a better understanding of these processes, which could lead to improved treatment strategies in the future.

Why have I been chosen?

You have been invited to participate in this study because you have satisfied the eligibility requirements via the information you provided in the online survey.

We are looking for people with high levels of general anxiety, but we do not require people to have received a formal diagnosis of an anxiety disorder. All participants must be between 18 and 55 years old. Participants with a past or current clinical diagnosis of a mood disorder (such as anxiety and depression) are welcome to participate in the study, provided they are not currently receiving medication therapy for their condition. We unfortunately cannot accept participants with psychiatric disorders other than the ones previously mentioned and participants who have taken any prescribed medication in the three (3) weeks prior to enrolment (with the exception of the contraceptive pill or hormone replacement therapy). The medication you will take as part of the study is contained in capsules that contain gelatine. People who do not eat meat products may not wish to participate because of this.

In addition, for your own safety you will not be eligible to participate in this study if you:
- are a heavy drinker (you consume more than 28 units of alcohol a week. You can estimate your alcohol consumption by reading the information on https://www.nhs.uk/live-well/alcohol-advice/calculating-alcohol-units/).
- drink more than 6 caffeinated drinks per day.
- are a heavy smoker (you smoke more than 5 cigarettes a day).
- have taken illicit drugs 7 days prior to admission to this study or intend to use illicit drugs during the study (including amphetamines, MDMA, cannabis or opioids).

What Would Taking Part Involve?

Your participation in the SODA study includes the following steps:

1. **Before Your Participation:**
    - ✓ **Receive Information:** You'll be provided with a detailed information leaflet about the study.
    - ✓ **Attend a Screening Visit:** You'll be invited to our Denmark Hill Campus in South London to attend a medical screening session lasting about **3-4 hours**, where we'll explain the study in detail and answer any questions you may have.
    - ✓ **Give Your Consent:** Before any study activities begin, we'll ask for your written consent.

- ✓ **Share Your Demographic Information:** You'll need to provide details about your sex, gender, age, and ethnicity.
- ✓ **Undergo a Medical Screening:** This includes a complete physical and neurological examination, as well as vital signs assessments and a 12-lead ECG. Additionally, you will need to provide a blood and urine sample which will be analysed for biomarkers relevant to your physical health, as well as for drugs of abuse and pregnancy. These samples are analysed only for the purpose of the medical screening and will not be used in the research in any way. The examination will be performed by a medically qualified professional.
- ✓ **Participate in a Mental Health Screening:** A trained psychiatrist will conduct an interview to confirm your eligibility and assess any psychiatric conditions that might prevent you from participating.

2. **During the Study:**
   - ✓ **Attend Three (3) Sessions:** If you successfully pass the medical screening, you will be invited to attend the three testing sessions. Each session involves taking a placebo, Citalopram (20mg), or Venlafaxine (150mg) capsules in a randomised order, followed by cognitive tasks and EEG recordings. Neither you nor the study team member will be told which drug you are being given. In our study randomisation means participants will receive the drugs and the placebo in different order. This helps ensure that the study results are due to the drugs themselves and not the order they were given. The exact sequence of drugs you will receive will be assigned to you by a computer system.

     While performing the tasks you will undergo an EEG, or electroencephalogram, which is a non-invasive procedure that records electrical activity in the brain. During this test, small sensors called electrodes are attached to your scalp to pick up the electrical signals produced by your brain cells when they communicate with each other. These signals are then recorded and analysed by a computer.
   - ✓ **Commit Your Time:** Each session lasts approximately **6 hours** (including preparation, drug administration and the testing itself), with at least an **8-day** gap between the sessions. Please note that the scheduling of the sessions will be made as flexible as possible to fit your personal schedule as long as the minimum gap of 8 days is maintained.

     In total, full participation in the study will involve a 3-4-hour screening session, plus 3 further study sessions lasting approximately 6 hours each.
3. **Throughout the Study:**
   - ✓ **Stay Informed:** We'll closely monitor your health and well-being, providing immediate support for any concerns.

Benefits and Disadvantages/Risks

What are the possible benefits of taking part?

While there are no direct benefits or guaranteed improvements in your condition, we hope you will find the study and tasks interesting. Additionally, your involvement will help advance research in anxiety treatment.

What are the possible disadvantages and risks of taking part?

Blood tests involve a small risk of bruising and may cause discomfort during the procedure.

There are no serious risks from performing the computerised tasks or from undergoing EEG.

The medications used are common treatments with known safety profiles. According to NHS information, the most common side effects that have been found during clinical treatment are:
- *Citalopram*: dry mouth, sweating a lot; being unable to sleep (insomnia); feeling sleepy, tired or weak; headaches; feeling sick (nausea).

- *Venlafaxine*: dry mouth; sweating and hot flushes; being unable to sleep (insomnia); feeling sleepy; feeling dizzy; headaches; feeling sick (nausea); constipation.

While it is unlikely significant side effects will occur from the single doses you will be given, we strongly recommend that you do not drive if you experience any drowsiness or dizziness, or any other side effects which might impair your ability to do so safely. A medically qualified team member will be available at all times during the study session for your safety and reassurance.

Both Citalopram and Venlafaxine are prescribed and can be used during pregnancy, as they are considered to pose low risk to pregnancy and babies' development. However, as a precaution participants who are pregnant or breastfeeding will not be eligible to participate in this study. For that reason, participants of childbearing potential will have to agree to use a medically accepted and highly effective method of contraception for the duration of the study. Additionally, urine pregnancy tests will be conducted at the screening session and before all subsequent testing sessions.

Will I be compensated for my time?

Yes, you will be compensated for the time spent on this study on a pro rata basis at the current London living wage (*£13.15/h*). If you take part in the screening session but are not eligible for the full study, you will still be compensated for the screening session (approximately £52.60 for 4 hours). The total amount you can earn by completing all parts of the study is £289.30, assuming a 4-hour screening session and three 6-hour study sessions). If you decide to withdraw from the study at any point, you will be compensated for any time spent up to your withdrawal (including the medical screening). The payments will be made via bank transfer.

Further Supporting Information:

- **Do I have to take part?**
  Participation is completely voluntary and deciding not taking part will not impact on any care you receive in the future.

  You may withdraw at any time without consequence. You are free to withdraw from the study, including during the interview, without having to give a reason. You will not be

disadvantaged in any way for withdrawing from the study and will be financially compensated for the time you have taken.

- **What will happen to my samples?**
  As part of the medical screening process, you will need to provide blood and urine samples.

  A blood sample will be taken by a phlebotomist – a healthcare provider with special training in drawing blood – by inserting a needle into your arm. This typically happens very quickly. You may feel the needle go into your skin. The sample needed will be no more than 2 teaspoons of blood. This sample will be used for a Complete Blood Count (CBC) test and a Comprehensive Metabolite Panel (CMP). These tests are part of standard healthcare assessment and are used to evaluate your overall health as well as to screen for diseases such as ones that affect your cardiovascular system, kidneys, liver etc. The tests will be conducted at the local laboratory, Synnovis KCH. After performing the tests, the results will be sent to the Clinical Lead or a medically trained delegate, who will be responsible for reviewing them. Samples will be taken at the King's College Hospital Clinical Research Facility and will be transferred to the laboratory within an insulated transport container. Your blood s

  The urine sample will be used for drug screening and pregnancy testing, which will be carried out at the Clinical Research Facility in King's Hospital by a medical professional. Once the results are obtained on each study day, the samples will be promptly disposed of. You will provide your sample in a small plastic container. You will be provided with the container and instructions on how to provide the sample during your visits.

  Both samples will be anonymised, and the IDs will only be able to be identified by the study team.

  Please note that if you participate in this study, your GP will be notified of your participation. You should also be aware that there is a possibility that your participation in the study and the screening tests may reveal an unexpected result that may have relevance for your physical or mental health. If this happens, we will discuss this with you and, if necessary, inform your GP who will arrange follow-up as required. If you do not wish for your GP to be informed of any significant findings or results, you should not take part in this study.

- **How will we use information about you?**
  We will need to use information from you for this research project.

  This will include your name, address, telephone number, email address and date of birth. People will use this information to do the research or to check your records to make sure that the research is being done properly.

  People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

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.
  - We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

- **Where can you find out more about how your information is used?**
  You can find out more about how we use your information:
  - at https://www.hra.nhs.uk/information-about-patients/
  - our leaflets available from https://slam.nhs.uk/personal-information-gdpr (SLaM) and https://www.kcl.ac.uk/research/support/rgei/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research (KCL)
  - by asking one of the research team
  - by sending an email to Claire Delaney-Pope, informationgovernance@slam.nhs.uk (SLaM) or Olenka Cogias, info-compliance@kcl.ac.uk (KCL)

- **What will happen to the results of this research project?**
  The data from this research project may be disseminated through standard scientific outlets, for example in peer-reviewed papers, conference presentations and posters, and website publications. This research project also forms the basis of a PhD studentship and a postgraduate student will be involved in the data collection procedures for this study. Additionally, the data will likely be included in a final submitted student report, or a PhD thesis. All study results will be anonymised and reported as aggregated data, ensuring that no individual participant can be identified. This means that your personal data will be combined with data from other participants, and any published findings will reflect the group as a whole rather than individual responses.

  In order to maximise the value of the data generated through this study to the wider research community, we will deposit anonymised research data in established data repositories so that other researchers can access and use the data for their own studies. This will exclude any data used for medical screening purposes.

  The data controller for this project will be King's College London (KCL). The University will process your personal data for the purpose of the research outlined above. The legal basis for processing your personal data for research purposes under GDPR is a 'task in the public interest'. You can provide your consent for the use of your personal data in this study by completing the consent form that will be provided to you. You have the right to access information held about you. Your right of access can be exercised in accordance with the General Data Protection Regulation. You also have other rights including rights of correction, erasure, objection, and data portability.

As co-Sponsor, King's College London has a responsibility to keep information collected about you safe and secure, and to ensure the integrity of research data. Specialist teams within King's College London continually assess and ensure that data is held in the most appropriate and secure way. This may include storage of anonymised or pseudonymised data with a contracted GDPR compliant third-party storage provider within the UK, where they are assessed as the best data storage option. In such cases the third-party storage provider will not have access to any data that could directly identify you.

The data collected in this study may be valuable for future academic research. To facilitate this, we may share your anonymized data with other researchers within the UK and the European Economic Area (EEA), ensuring that you cannot be personally identified. This data could contribute to a broader understanding of the field, although specifics of the future studies will be defined as they arise. If you have any questions or concerns about this, please feel free to discuss them with the study team.

- **Who is organising and funding this study?**
  This research is being organised by the Department of Neuroimaging at the institute of Psychiatry, Psychology & Neuroscience. This research is being funded by the Wellcome Trust and NIHR Maudsley BRC.

- **What if have further questions?**
  For more information, please contact:
  - Dr. Toby Wise at toby.wise@kcl.ac.uk
  - Marko Dimitrovski at marko.1.dimitrovski@kcl.ac.uk

- **What if there is a problem?**
  If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions [Dr Toby Wise, 020 3228 2121, toby.wise@kcl.ac.uk]. If you remain unhappy and wish to complain formally, you can do this through the SLaM Patient Advice and Liaison Service (PALS) on 0800 731 2864, pals@slam.nhs.uk. 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).

  You will also be provided with a 24-hour card with contact details for the study team to report any delayed effects.

Consent

Your participation is completely voluntary, and you will be asked to sign a consent form if you decide to participate, confirming that you have understood the information and agree to participate under these conditions. You will be given a copy of the information sheet and a signed consent form to keep.

Thank you for considering participating in the SODA study. Your contribution is invaluable to advancing our understanding of anxiety and depression treatment mechanisms.