**Participant Information Sheet**

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**Study title:** Evaluation of a NAsal Spray in AnxioLytic treatment (E-NASAL) trial

**Project Lead:** Dr Nathan Huneke

**Supervisors**: Prof Matthew Garner, Prof David Baldwin, Prof Nic van der Wee

**Other researchers:** Dr Robert Gordon, Dr Naomi Phillips, Dr Hannah Rowlatt, Dr Harry Fagan, Dr Laura Molteni

**ERGO number**: 52726

You are being invited to take part in the above research study. To help you decide whether you would like to take part or not, it is important that you understand why the research is being done and what it will involve. Please read the information below carefully and ask questions if anything is not clear or you would like more information before you decide to take part in this research. You may like to discuss it with others but it is up to you to decide whether or not to take part. If you are happy to participate you will be asked to sign a consent form.

**What is the research about?**

This study has been funded by the Medical Research Council. Dr Nathan Huneke is working towards a PhD in Clinical Neurosciences.

Anxiety disorders are the most common psychiatric disorder and because they typically result in impairment of daily life, are among the most burdensome of medical conditions. Generalised Anxiety Disorder (GAD) is a common anxiety disorder, yet it is often not diagnosed or treated properly. Patients who suffer from GAD experience excessive anxiety and worry, and a range of symptoms including muscular tension, restlessness, dizziness, difficulty in concentrating, and a feeling of being ‘on edge’, often with increases in heart rate, blood pressure and sweating.

If there was a human model of GAD, (that is, a way of temporarily producing some of the symptoms of GAD, but in a healthy person) it could be used to discover new and potentially more effective treatments and help us to understand what is happening in the body. We have been working on the development of a human model of GAD, using the inhalation of air enriched with 7.5% carbon dioxide (CO2) for 20 minutes. In healthy volunteers, this temporarily makes some people feel anxious and tense and reduces feelings of being relaxed and happy. It also temporarily increases blood pressure and heart rate as well as alters attention and emotion processing, which is commonly reported in anxious patients. The effects of CO2 are different from the inhalation of normal room air and we believe that this model could be used to explore how and whether treatments work in GAD.

In this study, we will examine the extent to which a widely used anti-anxiety drug, lorazepam, alters how healthy volunteers respond to inhalation of air enriched with 7.5% CO2 compared with a placebo. In particular, we will be testing a new way of delivering these anti-anxiety effects: a nasal spray. In a pilot study, this nasal spray was found to be safe and appeared to lower blood pressure and anxiety during inhalation of air enriched with 7.5% CO2.

We are recruiting healthy male and female volunteers, aged between 18 and 55 years, to be administered lorazepam nasal spray or placebo prior to inhaling 7.5% CO2.

**Why have I been asked to participate?**

You have been invited to participate since you have enquired about our advertised studies. We plan to recruit 60 participants for this study.

**What will happen to me if I take part?**

There are two parts to this study:

1. **10 minute telephone screening**

Before entering the research study, the researchers will contact you and ask specific questions about your physical and mental health, to check that you are fit to take part in the study. This will take about 10 minutes, will be arranged at your convenience and can be completed over the phone. All information will remain confidential.

You should be generally healthy, have no history of or current asthma, migraine, seizures, renal, cardiac or hepatic impairment or glaucoma, and have no present or past anxiety disorder or other mental health complaint. You should not take part if a close member of your family suffers from regular panic attacks or has been diagnosed with panic disorder.

Your alcohol intake should not be more than 21 units per week. Note that one unit of alcohol equals one 25ml single measure of whisky (ABV 40%), or a third of a pint of beer (ABV 5-6%) or half a standard (175ml) glass of red wine (ABV 12%). You should not be a regular smoker (more than 6/day). You should not have used medication in the preceding 8 weeks, apart from occasional paracetamol, or local treatments. Females should be using adequate methods of contraception and should not be pregnant or breast feeding, or be considering becoming pregnant. If you meet our list of entry criteria, then you will be invited to the testing session.

1. **Testing Session (9.30-11.30: 2 hours)**

Prior to the testing session you should refrain from alcohol for 36 hours. You also should not drink any caffeinated drinks after midnight prior to the test day. This is because alcohol and caffeine have effects on blood pressure and heart rate measurements; and alcohol may enhance the effects of the gas. However, the exception from this is if you regularly ingest caffeine in the morning, in which case you should have your usual caffeinated drink to avoid withdrawal effects during the study. You should not be a regular (i.e., daily) smoker and should not have smoked within 12 hours of the study session.

At the beginning of the session, you will complete some questionnaires that ask about your physical and mental health. Throughout the session we will take several measures of your current mood (short questionnaires), blood pressure and heart rate (arm cuff).

You will complete three 20-minute inhalations of air enriched with 7.5% CO2. The 7.5% CO2 gas is a mixture of carbon dioxide and air, with the air containing the usual amount of oxygen. The gas will be administered through a mask that covers your mouth and nose. This will be fitted prior to the inhalation of the gas to enable you to become accustomed to wearing it. You will wear the mask and remain seated in a comfortable position throughout the inhalation.

During each inhalation you will complete a short (8 minute) computerised task that measures your attention. During this task you will be presented with a set of widely used experimental pictures of emotional faces. Before you agree to participate you will have the opportunity to view examples of these faces. Please remember that you are free to withdraw at any time. During the task we will measure your heart rate, skin conductance and eye movements through 6 electrodes placed on the surface of your skin (i.e. non-invasively).

You will be given a nasal spray, either lorazepam or placebo, prior to the second and third inhalations.

**Are there any benefits in my taking part?**

The study will last approximately 2 hours and you will be reimbursed £15 for your time when you complete the testing session. If you prefer, then you can ask to receive 24 course credits instead of the £15. You will also receive £15 towards travel costs to the test session site at College Keep. Beyond this you should not expect to directly benefit from taking part in this research study. However, the information we obtain from this study might help us to understand and treat patients with anxiety disorders in the future.

**Are there any risks involved?**

Participants who meet any of the exclusion criteria should not take part in the study. This includes pregnant women or women who are breastfeeding, and women who plan to become pregnant. All women will therefore be asked to answer some short questions about their use of contraception to exclude the possibility of pregnancy. The screening procedure will ask participants some questions about their physical and mental health. Information about local support services will be available to any participant that is concerned about their physical and mental wellbeing.

Since the testing session requires you to attend the department in person, there is a small risk of contracting covid-19. We have put in place a number of measures to minimise this risk. You will be given a fluid-repellant facemask to wear throughout the session. The experimenters will wear full personal protective equipment, and only one experimenter will be allowed in the room with you at any time. There is enough space to maintain 2 metres physical distancing. Finally, the department and all study equipment is thoroughly cleaned between testing sessions. You will be contacted the day after the study day to check your wellbeing and we will advise you about the actions you will need to take should you develop symptoms of covid-19.

During the testing session, you will receive either a lorazepam nasal spray or placebo nasal spray. You will also complete three 20-minute inhalations of air enriched with 7.5% CO2.

1. **Lorazepam**

Lorazepam is a well-tolerated drug that is commonly used throughout the world, usually in multiple repeated doses rather than the two doses we will be using in this study. Lorazepam is usually available in tablet form, or as an injection. Administering lorazepam as a nasal spray is new. Despite this, we would expect possible side effects to be similar to those that occur with tablets. Commonly reported side effects include: drowsiness, dizziness, blurred vision, and nausea. The purpose of the medical screening at the start of the study is to make sure that it is safe for you to take the drug. It is unlikely that you will experience any side effects from two doses of lorazepam.

Participants can discuss any concerns or side effects with the study medical team led by Professor David Baldwin (Consultant Psychiatrist). Contacted at [dsb1@soton.ac.uk](mailto:dsb1@soton.ac.uk) and 02382310764.

1. **Inhalation of air enriched with 7.5% CO2**

Our research group has carried out in excess of 300 CO2 inhalation tests. Any effects of the gas inhalation are temporary and typically resolve within a minute after inhalation. Carbon dioxide inhalation may cause feelings of anxiety or unpleasantness. Other physiological effects that may occur include racing of heart, dizziness, pins and needles, and breathlessness. Some people also experience a mild headache afterwards.

People experience and describe the effects of inhaling 7.5% CO2 gas in different ways, and there is no way of knowing in advance how you will respond. Some people do not notice it at all, and some experience more marked anxiety. Most people will notice some effects, and if you do not like the effects, you can ask to stop. These feelings should be short-lived (typically resolving within a couple of minutes) and should not cause any lasting harm. The researchers will remain near you at all times and will offer reassurance if necessary. If you feel uncomfortable breathing the gas at any time during the procedure you may indicate that you wish the procedure to stop.

At the end of the study session you will remain in the testing room until you feel that any effects of the gas have worn off. We will contact you the day after the study day to check that you are healthy and well.

**What data will be collected?**

As part of the screening process, we will collect personally identifiable information including date of birth, ethnicity, gender identity, telephone number, address and medical history. We collect this information to ensure that the study groups are reasonably balanced in terms of demographics and to ensure that you are eligible to participate in the study. This information will be stored in an electronic database and on paper. We also collect your contact details so that we can maintain contact with you during the study, and to make any necessary follow up contacts. We will not retain your contact details for future studies.

During the testing session we will collect data on current mood (from questionnaires), blood pressure and heart rate, other psychophysiology measures including skin conductance, and measures of attention from the computerised task. These data will be stored in an electronic database and on paper.

All electronic databases containing personally identifiable information will be encrypted and password-protected. Where data has been collected using paper documents (e.g. questionnaires), all documents will be number-coded and stored in a locked filing cabinet. Personal data and consent forms will be stored separately from non-identifiable data.

**Will my participation be confidential?**

Your participation and the information we collect about you during the course of the research will be kept strictly confidential. However, if you were to provide the study team with any information that gives us concern about your safety or wellbeing, then we will have a duty to disclose this information. If we were to disclose this information, then we will discuss this with you at the time.

Only members of the research team (including supervisors) and responsible members of the University of Southampton may be given access to data about you for monitoring purposes and/or to carry out an audit of the study to ensure that the research is complying with applicable regulations. Individuals from regulatory authorities (people who check that we are carrying out the study correctly) may require access to your data. All these people have a duty to keep your information, as a research participant, strictly confidential.

**Do I have to take part?**

No, it is entirely up to you to decide whether or not to take part. If you decide you want to take part, you will need to sign a consent form to show you have agreed to take part.

**What happens if I change my mind?**

You have the right to change your mind and withdraw at any time without giving a reason and without your participant rights being affected.

If you withdraw from the study, you can request that we destroy the data we have gathered about you up until we have entered it into our secure database (approximately May 2021).

**What will happen to the results of the research?**

When the study has been completed, we shall analyse the data and report the findings. This will be reported in an appropriate scientific journal or presented at a scientific meeting. Your personal details will remain strictly confidential. Research findings made available in any reports or publications will not include information that can directly identify you without your specific consent. If you would like a copy of the final paper, you may request this.

Once the project is complete, all data will be transferred and stored in the University Research Repository. This will be held in an anonymised form and unlinked to any personal identifiable information. This allows other researchers to use the data for future research without being able to identify you. Data will be stored here for a minimum of 15 years.

**Where can I get more information?**

For further queries, please contact Dr Nathan Huneke ([n.huneke@soton.ac.uk](mailto:n.huneke@soton.ac.uk), tel: 02382 310 775).

**What happens if there is a problem?**

If you have a concern about any aspect of this study, you should speak to the researchers who will do their best to answer your questions.

If you remain unhappy or have a complaint about any aspect of this study, please contact the University of Southampton Research Integrity and Governance Manager (023 8059 5058, [rgoinfo@soton.ac.uk](mailto:rgoinfo@soton.ac.uk)).

**Data Protection Privacy Notice**

The University of Southampton conducts research to the highest standards of research integrity. As a publicly-funded organisation, the University has to ensure that it is in the public interest when we use personally-identifiable information about people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use information about you in the ways needed, and for the purposes specified, to conduct and complete the research project. Under data protection law, ‘Personal data’ means any information that relates to and is capable of identifying a living individual. The University’s data protection policy governing the use of personal data by the University can be found on its website (<https://www.southampton.ac.uk/legalservices/what-we-do/data-protection-and-foi.page>).

This Participant Information Sheet tells you what data will be collected for this project and whether this includes any personal data. Please ask the research team if you have any questions or are unclear what data is being collected about you.

Our privacy notice for research participants provides more information on how the University of Southampton collects and uses your personal data when you take part in one of our research projects and can be found at <http://www.southampton.ac.uk/assets/sharepoint/intranet/ls/Public/Research%20and%20Integrity%20Privacy%20Notice/Privacy%20Notice%20for%20Research%20Participants.pdf>

Any personal data we collect in this study will be used only for the purposes of carrying out our research and will be handled according to the University’s policies in line with data protection law. If any personal data is used from which you can be identified directly, it will not be disclosed to anyone else without your consent unless the University of Southampton is required by law to disclose it.

Data protection law requires us to have a valid legal reason (‘lawful basis’) to process and use your Personal data. The lawful basis for processing personal information in this research study is for the performance of a task carried out in the public interest. Personal data collected for research will not be used for any other purpose.

For the purposes of data protection law, the University of Southampton is the ‘Data Controller’ for this study, which means that we are responsible for looking after your information and using it properly. The University of Southampton will keep identifiable information about you for 15 years after the study has finished after which time any link between you and your information will be removed.

To safeguard your rights, we will use the minimum personal data necessary to achieve our research study objectives. Your data protection rights – such as to access, change, or transfer such information - may be limited, however, in order for the research output to be reliable and accurate. The University will not do anything with your personal data that you would not reasonably expect.

If you have any questions about how your personal data is used, or wish to exercise any of your rights, please consult the University’s data protection webpage (https://www.southampton.ac.uk/legalservices/what-we-do/data-protection-and-foi.page) where you can make a request using our online form. If you need further assistance, please contact the University’s Data Protection Officer ([data.protection@soton.ac.uk](mailto:data.protection@soton.ac.uk)).

**Thank you.**