

Nuffield Department of Clinical Neurosciences

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**PARTICIPANT INFORMATION SHEET (OXFORD)**

**Brain and Brainstem Basis of COVID-19**

**Virtual Reality Substudy**

**(BBB-COVID-VR)**

We would like to invite you to take part in our research study. Before you decide, it is important that you understand why the research is being done and what it would involve for you. Please take time to read this information and discuss it with others if you wish. If there is anything that is not clear, or if you would like more information, please ask us.

# What is the purpose of this study?

The purpose of this study is to understand the effects of COVID-19 on the brain. We are particularly interested in the way symptoms are perceived (e.g. breathlessness, fatigue, mood).

In some people, the symptoms of COVID-19 can continue for many months after the infection, which may adversely affect their quality of live. For example many people complain of persistent breathlessness and fatigue. The virus may affect the function of the brain in ways that are not yet fully understood.

The persistent breathlessness in long COVID-19 is often very difficult to treat, particularly when for some people their feelings of breathlessness do not match the physical status of their lungs. Because we know that breathlessness is not just about the lungs but also about the brain, it may be that for some people, over time the senses become mismatched leading to unexplained breathlessness.

In this study we want to investigate the brains role in creating this mismatch by using virtual reality to change the way your brain generates sensations of breathlessness. We are asking people with LONG COVID-19 and healthy volunteers to visit us in our laboratory for one 3-hour session which will include cycling on an exercise bike whilst wearing a virtual reality headset that takes you on a bike ride in the countryside.

# Why have I been invited?

You have been asked to participate in this study because you either have had COVID-19, have LONG COVID-19 or shown an interest in participating in the study as a healthy volunteer.

We will study up to 60 people who have LONG COVID-19 and 60 healthy volunteers who do not have symptoms of LONG COVID-19 or might have had COVID-19 in the past but do not have ongoing symptoms of LONG COVID-19. We will use the healthy volunteers control group as a benchmark to compare against the results of the patient participants group. In order to make this comparison, we require healthy volunteers to be of the similar age, sex, ethnicity and medical history as patient participants.

# Do I have to take part?

It is up to you to decide whether or not you would like to take part. If you decide to take part, you are free to withdraw consent at any time without giving a reason. This would not affect the standard of care you receive or may receive in the future. If you participate and then decide that you no longer wish to continue with the study, we would still retain any data already obtained from you unless you request otherwise.

# What will happen to me if I decide to take part?

***Informed Consent***

Firstly, we will explain the study to you and answer any questions you might have. We will then check if you are eligible for the study, if you are satisfied with the information you have been given about the study and would like to participate. If you agree to take part you we will ask you to sign an electronic consent form to allow us to check your medical records for additional MRI safety screening and complete the questionnaires and cognitive tests before you attend for your study visit on site. Alternatively this can be done on paper.

We will provide you with a link to a secure online platform which will enable you to complete the questionnaires and tests in your own time, on your own computer, tablet or smartphone. If you however prefer you can complete these questionnaires on paper when you come for the study visit.

You will then undergo an eligibility assessment and be invited to attend one research visit. If you are participating in the study as a healthy volunteer it will be at a time that suits you.

The visit will take place at our laboratory in Oxford University or Oxford University Hospitals NHS Trust. The visit will last approximately 3 hours.

You should avoid smoking for 24 hours before your visit, and avoid drinking alcohol or drinks containing caffeine (e.g. tea, coffee or coke), strenuous exercise or eating large meals for a few hours beforehand.

***Eligibility assessment***

An eligibility assessment will be conducted by telephone before you attend for the study.

***On your arrival***

On the day of the visit may check your temperature and if you have not previously had COVID-19, ask you if you have developed any COVID-19 related symptoms. You will be admitted to the building only if you have a normal temperature and report no symptoms.

***What will happen during the study?***

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| Informed electronic consent to allow for medical records checks |
| Questionnaires and cognitive tests (60 minutes) (these may be done at home or on site when you attend for the study) |
| COVID-19 symptoms checks before the visit |
| Medical history (allergy, medications) and physical examination (weight, height) during the visit (10 minutes) |
| Written consent during the visit |
| Cycling tests on a static exercise bicycle (two tests, each approximately 10 minutes, with a good rest between them). |

The activities and assessments are described in detail below:

***Medical history and physical examination***

We will check that you can enter the study safely by reviewing any illnesses you may have or have had, any medicines you may have taken or are currently taking and look at your height, weight, blood pressure and heart rate.

***Questionnaires, cognitive and olfaction tests (up to 60 mins)***

You will be asked to perform additional computer-based or paper and pencil tests in a separate room before or after the scan. If you wish you can complete these tests online before you attend for your visit. You will also be asked to complete questionnaires asking in more detail about symptoms you may be experiencing.

You may be asked to take part in an olfaction test to measure your sense of smell. This will involve being presented with, and asked to identify, several different types of smells.

***Exercise test*** *(two tests that last about 10 minutes each, with a good break between them)*

Firstly, you will be able to familiarise yourself with a static exercise bike and do a brief warm up (about 5 minutes of gentle cycling).  You will then be asked to cycle on the static bicycle for two short tests (about 10 minutes each) with a break between them. During both tests you will breathe through a mouthpiece or soft face mask which allows us to measure your breathing. You will wear a virtual reality headset (see photograph and video link below) and during the exercise we will change the virtual terrain to measure how hard it is to cycle in these different settings while hearing your own breathing sounds. We will ask you how hard you are finding it to cycle and how breathless you feel. The exercise effort will be set as a percentage of your own capacity and so should not be unpleasant. During the task we will record your heart rate using a finger monitor and breathing rate using an elastic belt across the chest.

The results of this study will help us find out whether people with breathlessness due to LONG COVID-19 experience breathlessness in the virtual world differently to those people who do not live with breathlessness, and this will help us design new ways to diagnose and treat long COVID-19.

A video demonstrating the virtual reality cycling experience can be found here:



<https://medicalxr.molbiol.ox.ac.uk/breathlessvr.html>



Figure: Cycling on the exercise bike with a view of the 'virtual world'

# What should I consider?

If you have any pre-existing medical problem for which you are seeing a doctor, you may not be eligible and should discuss this with the study doctor. If you are pregnant or are trying to get pregnant, you would not be eligible for this study and should discuss this with the study doctor as well.

You can continue to take your regular medications or other prescribed or over-the-counter medicines.

# Are there any possible disadvantages or risks from taking part?

***Virtual reality*** has been shown to make some people dizzy in some situations. This rapidly resolves once the headset is removed. If at any point in the study you become dizzy then we will help you remove the headset and you may stop the session should you wish to.

***Exercise tests*:** The cycling tests proposed in the study are routine widely-used tests and very safe. They may make you breathless, cause your heart to race or may make you feel light-headed, dizzy or nauseous. The tests will be tailored to your individual fitness level, and you can stop at any point you wish. You will be monitored throughout and medical personnel will be available.

***Questionnaires***: You might find the questionnaires are long or upsetting, or tiring. You might not like some of the questions or feel uncomfortable answering them. You do not have to answer any questions that make you feel uncomfortable

***Time:*** This study will take about 2.5-3 hours of your time (including time for the questionnaires and cognitive tests if you have not done them earlier at home). You will be required to travel to either the hospital or University site at Oxford.

***COVID-19 safety***: The study will be carried out taking appropriate COVID-19 precautions during the study visit to mitigate risks to you and to researchers. We will follow appropriate guidance on infection control and personal protective equipment as advised by the hospital. If you have symptoms of COVID-19 then you should not attend for the research.

**What are the possible benefits of taking part?**

You should not expect any direct benefits from taking part. Your help and the information we obtain from this study may improve our understanding of the effects of COVID-19 on the general health and well-being of people months beyond the acute period. If successful, this study could guide doctors to find better treatments.

# Will my General Practitioner/family doctor (GP) be informed of my participation?

We would not routinely inform your GP of your participation. There may be instances where GPs may be informed of your participation and be asked to follow up if we detect an abnormal result during the study tests that may be of clinical significance. We will ask for your consent to do this.

# Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The only identifiable information we hold about you will be your name on the consent form and an electronic list linking your name and contact details to the study code number you have been allocated. This information will be held on a high security server on the University network specially designed by Medical Sciences IT to hold personal information securely and in accordance with legal requirements. The paper consent forms will be locked securely within the Nuffield Department of Clinical Neurosciences offices. All data collected in the study will be de-identified and labelled with a participant study code number.

Responsible members of the University of Oxford and Oxford University Hospitals NHS Foundation Trust may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

With your consent the study researchers would like to access your medical records and information held by NHS Digital. NHS Digital (https://digital.nhs.uk/) is the national information and technology partner for the health and care system. This will enable them to collect all the relevant health information about you that relates to the aims of this research study.

# Will I be reimbursed for taking part?

You will be reimbursed reasonable expenses. On the day of your visit please make sure to keep your receipts for travel expenses, parking and meals so that you can be reimbursed these costs. We will also pay you £20 as a thank you for taking part in the study.

# What will happen to my data?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is ‘a task in the public interest.’ The University of Oxford the data controller and is responsible for looking after your information and using it properly.

We will be using information from you and your medical records (if you are a patient), NHS Digital, and other central NHS registries in order to undertake this study and will use the minimum personally-identifiable information possible. We will keep identifiable information about you for 1 year after the study has finished. This excludes any research documents with personal information, such as consent forms, which will be held securely at the University of Oxford for 10 years after the end of the study.

If you agree to your details being held to be contacted regarding future research, we will retain a copy of your consent form until such time as your details are removed from our database but will keep the consent form and your details separate.

If you are a patient, the Oxford University Hospitals NHS Trust will use your name, NHS number and contact details to contact you about the study, and to oversee the quality of the study. They will keep identifiable information about you from this study in accordance with their local policy for medical notes retention.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at

<https://compliance.web.ox.ac.uk/individual-rights>

You can find out more about how we use your information by contacting study investigators*breatheOxford@fmrib.ox.ac.uk*

# [What will happen if I don't want to carry on with the study?](http://hra-decisiontools.org.uk/consent/content-sheet-support.html#two)

If you decide to withdraw from the study, unless you state otherwise, any brain scans or other measurements which have been collected whilst you have been in the study will be used for research as detailed in this participant information sheet.

# What will happen to the results of this study?

The results of this study may be published in a professional journal, or presented at scientific meetings so that other doctors can see them. You can contact the study investigators for a copy of any publication. None of the information published in journal articles or scientific meetings can identify you. It is important to note that your personal information will not be disclosed.

#  What if we find something unexpected?

It is important to note that we do not carry out these tests for diagnostic purposes, only for research. The results are not routinely looked at by a doctor and are therefore not a substitute for a doctor’s appointment. Occasionally, however, a possible abnormality may be detected. In this case, we would have the test results checked by a doctor. If the doctor felt that the abnormality was medically important, you would be contacted directly, we will ask for your consent to inform your GP. 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 if there is a problem?

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.

NHS indemnity operates in respect of the clinical treatment which is provided.

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact Professor Kyle Pattinson on 01865 231 509 or kyle.pattinson@nda.ox.ac.uk. You may contact the University of Oxford Research Governance, Ethics & Assurance (RGEA) office on 01865 616480 or ctrg@admin.ox.ac.uk.

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study. If you wish to contact the PALS team please contact **01865 221473** or PALS@ouh.nhs.uk.

**How have patients and the public been involved in this study?**

We have discussed the study with people who have had COVID-19 and they have helped design the study to make it less tiring. For example we have followed up on the suggestion to allow questionnaire and cognitive test completion at home when possible.

If you are interested in taking part in other studies there is more information available here:

[www.crn.nihr.ac.uk/can-help/patients-carers-public/how-to-take-part-in-a-study/](http://www.crn.nihr.ac.uk/can-help/patients-carers-public/how-to-take-part-in-a-study/)

[www.nhs.uk/Conditions/Clinical-trials/Pages/Introduction.aspx](http://www.nhs.uk/Conditions/Clinical-trials/Pages/Introduction.aspx)

**Who is organising and funding the study?**

This research is sponsored by the University of Oxford and organised by the Nuffield Department of Clinical Neurosciences at the University of Oxford. If you wish to know more about any aspect of the study, please contact Dr Kyle Pattinson. The study is funded by NIHR Oxford Biomedical Research Centre

# Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants’ interests. This study has been reviewed and given favourable opinion by Preston Research Ethics Committee.

# Participation in future research

We will ask if we can contact you about future studies. This is optional, you can take part in this study but decline to be contacted again. If you consent, we will keep your contact details separately from research data you have provided and it will be under the custodianship of the PI for about 10 years. You can withdraw your consent for future contact at any time.

**What will happen to my data?**

If you agree to your details being held to be contacted regarding future research, we will keep your contact details separately from this study on a password protected computer in the Nuffield Department of Clinical Neurosciences. All contact about future research studies will come from our research team in the first instance. Agreeing to be contacted about future studies does not oblige you to take part in future research, and you can request that your details are removed from this register at any time you wish.

# Further information and contact details

Please contact Kyle Pattinson on phone 01865 224644 or email breatheoxford@fmrib.ox.ac.uk.

*Thank you for considering taking part.*