Division of Cardiovascular Medicine,
Radcliffe Department of Medicine,
University of Oxford
<Professor Kyle Pattinson>
Tel: 01865 224644
email breatheoxford@fmrib.ox.ac.uk>

PARTICIPANT INFORMATION SHEET

Capturing **M**ulti**OR**gan **E**ffects of COVID-19

C-MORE Sub-study "COVID NEURO"

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 extra sub-study?

The purpose of this optional sub-study is to understand in much more detail the effects of COVID-19 on the brain. We are particularly interested in the way symptoms are perceived (e.g. breathlessness, fatigue, mood) and the way COVID-19 may potentially predispose some people to future brain conditions (e.g. stroke).

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.

In this sub-study we will collect additional brain scans using either our 7 tesla research scanner at the Wellcome Centre for Integrative Neuroimaging at the John Radcliffe Hospital in Oxford or the magnetoencephalographic (MEG) scanner at the Oxford Centre for Human Brain Activity (OHBA). Combining the knowledge we gain from these two scanners will help us understand the impact of COVID-19 on the brain in considerably more detail than is possible with more conventional brain scans. The decision as to which scanner is used will be based on the outcome of the magnet safety assessment, your own preference and the requirement to achieve a balance of participants across both scanning technologies. Please read this document fully even if a decision has been made at the time of reading.

Why have I been invited?

You have been asked to participate in this study because you have agreed to take part in the main C-MORE study, this additional sub-study is completely optional. Alternatively you may have not taken part in the original C-MORE study but have responded to an advertisement for research participants.

In this sub-study we would like to perform additional studies of the effects of COVID-19 on the brain) and compare this with people who have not had this infection.

We will study up to 100 people who have been infected with SARS-CoV-2, (the virus that causes COVID-19) and an equivalent number of people who have not been infected. We will use the control group as a benchmark to compare against the results of the other group.

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. 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?

You will be invited to attend one research visit. If you have had COVID-19 this would take place between 3 and 6 months after the infection. If you participated in the C-MORE study then the visit would take place soon before or after your visit for the main C-MORE study but on a different day.

The visit will all take place at the Wellcome Centre for Integrative Neuroimaging at the John Radcliffe Hospital or at the Oxford Centre for Human Brain Activity (OHBA). The visit will last approximately 2 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 additional eligibility assessment by telephone before you attend for this sub-study. This eligibility will mainly consist of additional MRI safety questions due to the considerations of the higher power 7T scanner used in this sub-study. . MEG does not pose health and safety issues, but you will be asked a number of screening questions in order to identify possible sources of artefacts (e.g., dental implants, pace-makers, etc.) that could compromise signal quality.

On your arrival

If you have not previously had COVID-19, on the day of the visit we will first check your temperature and 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 each visit?

Informed consent
MRI safety questions
Either Magnetic resonance imaging (MRI) scan (up to 1 hour)
Or MEG scan(up to 40 minutes)
Questionnaires (45 minutes)

The activities and assessments are described in detail below:

Informed Consent

We will 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 will be asked to sign a consent form.

If you would like to complete the questionnaires and cognitive tests before you attend for your study visit, then we will provide you with a link to a secure online platform which will enable you to complete the tests in your own time, on your own computer, tablet or smartphone. We would ask you to sign an electronic consent form pertaining to these tests.

MRI Safety questions, Medical history and physical examination

We will go through a Screening Form with you to make sure that it is safe for you to participate in the research. We will also 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 45 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.

Some of the computer tests may be performed on an internet site called "True Colours" This is a web platform that is hosted within the NHS, and your name, NHS number and contact information would be stored by the system that is hosted on NHS computer servers. It is already routinely used in both Oxford Health NHS Foundation Trust and

Oxford University Hospitals Trust as part of standard clinical care, and the data would only be accessible to those who are providing clinical care.

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.

MRI scan (up to 60 mins)

As part of this study you may have an MRI brain scan which will happen at the Wellcome Centre for Integrative Neuroimaging based at the John Radcliffe Hospital in Oxford.

You will be asked to lie still on your back while your brain is scanned. There will be breaks between the scans, with the shortest scans taking about 2 minutes and the longest scan 10 minutes. You will wear a respiration belt to measure your breathing rate and a finger clip to monitor your blood flow. These are standard instruments used to measure physiological parameters whilst in the scanner.

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 some MRI safety questions to help determine if you are able to take part. For example, if you suffer from claustrophobia, you could not be scanned.

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. While there is no evidence to suggest that MRI is harmful to unborn babies, as a precaution, the Department of Health advises against scanning pregnant women unless there is a clinical benefit. We do not test for pregnancy as routine so if you think you may be pregnant you should not take part in this study.

As some of the scans are noisy, we will give you earplugs, or headphones to make this quieter for you. It is important that these are fitted correctly as they are designed to protect your ears.

Some people scanned in MRI scanners, especially 7 Tesla scanners, may experience a mild dizzy sensation as they are moved into the scanner. This is normal and the sensation starts to go away as soon as you are in the scanner. You would be introduced carefully to the scanner and allowed to leave at any stage. Whilst in the scanner you will have easy access to a call button should you wish to stop the scan or speak with the radiographer or operator.

In preparation for your scan and for your comfort and safety we may ask you to change into pyjama style clothes or scrubs that we will provide. You may keep your underwear and socks on, but we would ask ladies to remove their bras. Metal jewellery, including body piercing, must also be removed and if you have any tattoos you will be asked

about them in the pre-screening MRI safety questions because some types contain materials that can interact with the magnetic field. Eye shadow and mascara must also be avoided, since some types contain materials that can interact with the magnetic field. We can provide you with make-up removal wipes or you can bring your own. Lockers are provided to secure your personal belongings and clothing.

MEG scan (up to 40 minutes)

As part of this study you may have an MEG brain scan which will happen at the Oxford Centre for Human Brain Activity (OHBA) based at the Warneford Hospital in Oxford.

MEG is a silent, safe and non-invasive and does not involve any ionising radiation (x-rays) or magnets field. There are no known risks associated with MEG.

You will be asked to sit in a chair while your brain is scanned using a helmet placed over your head. Before the MEG scan, the researcher will attach a few sensors to your wrists and face in order to record your heartbeat and your eye movements, and a respiration belt to measure your breathing rate. Some sensors are also attached your arms, to measure muscle activity. In addition, we will place 5 small coils on your forehead and above your ears to measure your head position during the scan.

To avoid disrupting the scan readings, you will be asked to remove metallic objects that you might be carrying or wearing, for example, jewellery, body piercings, removable dental braces and clothing with metal parts. If you wear glasses, you should inform the researcher in advance and they may be given special non-metallic glasses to wear. We may ask you to change into pyjama style clothes or scrubs that we will provide.

Once in the scanner, we will measure your brain activity while you are resting with your eyes open and closed. This is followed by simple tasks, including a task where you will passively listen to tones while watching a movie. Note that you can ask the researcher to stop the scan at any time.

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 would like to get pregnant, you would not be eligible for this study and should discuss this with the study doctor also.

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?

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 some MRI safety questions to help determine if you are able to take part.

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.

While there is no evidence to suggest that MRI is harmful to unborn babies, as a precaution, the Department of Health advises against scanning pregnant women unless there is a clinical benefit. We do not test for pregnancy as routine so if you think you may be pregnant you should not take part in this study.
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 hearing.

Some people scanned in MRI scanners, especially 7 Tesla scanners, may experience a mild dizzy sensation as they are moved into the scanner. This is normal and the sensation starts to go away as soon as you are in the scanner.

You would be introduced carefully to the scanner and allowed to leave at any stage. Whilst in the scanner you will have easy access to a call button should you wish to stop the scan or speak with the radiographer or operator.

In preparation for your scan and for your comfort and safety we may ask you to change into pocket less 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 non-wired 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.

If you are pregnant or breast-feeding, you should not take part.

Note that MEG silently and non-invasively records the magnetic fields that are naturally emitted from the working human brain. There are no known health and safety risks associated with MEG scanning.

Questionnaires: You might find the additional 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

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 on an incidental findings, such as high blood pressure, 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 paper 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 Division of Cardiovascular Medicine 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 the samples I give?

This sub-study will not collect additional blood samples.

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 is 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, 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.

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.

What will happen if I don't want to carry on with the study?

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 ask your doctors for a copy of any publication. Some of this research will contribute to the educational requirement of a doctoral thesis. None of the information published in the thesis, journal articles or scientific meetings can identify you. It is important to note that your personal information will not be disclosed. You would have no legal right to a share of any profits that may arise from the research.

What if we find something unexpected?

It is important to note that we do not carry out scans for diagnostic purposes, only for research. Our scans 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 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 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 Clinical Trials and Research Governance (CTRG) office on 01865 616480 ctrg@admin.ox.ac.uk.

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

We would normally like to hear the feedback of potential participants but the nature of this COVID 19 outbreak has meant that there has not been the opportunity or the time do this. So therefore, we would be very grateful to receive your thoughts and feedback about your experience in this study.

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/

www.nhs.uk/Conditions/Clinical-trials/Pages/Introduction.aspx

Who is organising and funding the sub-study?

This research is organised by the University of Oxford. If you wish to know more about any aspect of the main study, please contact Dr Betty Raman or the sub-study investigator Dr Kyle Pattinson. The sub-study research is funded by the Oxford University Covid-19 Research Fund

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 the North West - 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 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.

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.