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PARTICIPANT INFORMATION SHEET

Brain imaging of anaesthesia

We'd 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 the study?

General anaesthesia is often given to make sure patients are unaware, do not feel any pain and do not move during surgery. While anaesthetic drugs have been used safely for many years, the way in which they work is still not well understood. This means it is difficult for doctors to assess how deeply unconscious patients are during surgical procedures. Consequently, anaesthetists often give excess anaesthesia to ensure that the patients are unaware. Unfortunately, having too much anaesthesia can mean it takes some individuals longer to recover. We hope to understand better how these anaesthetic drugs affect the brain so that we can develop improved brain monitoring to help guide the amount of anaesthesia given to each patient.

Our previous research in healthy volunteers identified interesting changes in the brain's electrical activity during anaesthesia. We believe these electrical changes in the brain indicate the precise point when an individual loses awareness of the outside world under anaesthesia. We called this observation "**slow wave activity saturation**" and it can be measured by applying electrical sensors to the scalp - a technique called electroencephalography (or EEG). We believe that slow wave activity saturation (or SWAS) has great potential to improve brain monitoring during operations by allowing anaesthetists to give just the right amount of anaesthesia for each person.

We have recently developed a computer software program that will help guide the amount of anaesthesia given to each patient. It identifies when the SWAS level occurs by measuring the electrical activity of the brain. We have already tested this program retrospectively on hundreds of

EEG datasets acquired from patients having anaesthesia during surgery. In this study, we hope to improve how our computer program works in real-time and in the real-life operating room environment.

To do this, a consultant anaesthetist who both works in the Oxford University Hospitals and is part of our research team will use the program to deliver anaesthesia to patients and identify their SWAS level *before* they have their operation. We will then continue to improve the computer program after each patient until we can identify the SWAS level in less than 15 minutes (i.e. in approximately the same time it would take anaesthetists to put patients to sleep using current methods).

Why have I been invited?

You have been invited to take part in the study as you are due to have an operation, and your NHS surgeon and/or anaesthetist believe that you may be suitable for the study. We are seeking to recruit up to 30 male and female patients between the ages of 18 and 60 years, who are having surgery at the Oxford University Hospitals (OUH) NHS Foundation Trust. We would like to invite you to learn more about the study and to participate if you would like to.

You have been invited to take part in one of the two groups that are being recruited into the study. You would be recruited to the patient group that will help us optimise the SWAS model in an operating theatre. The other study group are healthy volunteers, who will have their brain scanned while they have anaesthesia delivered to SWAS. The information gathered from both groups will help us to optimise delivery of anaesthesia to SWAS and confirm that at SWAS an individual loses awareness of the outside world.

Do I have to take part?

No, it is up to you to decide. Please take as much time as you need to consider whether you would like to participate. If you decide not to, this will in no way affect your future clinical care. If you do agree to take part in the study, you are free to withdraw at any time without giving a reason. Withdrawing from the study will not affect your clinical care in any way.

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

If you are interested in participating after reading this information sheet, you can contact the research team on 01865 611 465 or by emailing anaesthesia.research@ndcn.ox.ac.uk to find out more about the study. Alternatively, if you express an interest in taking part to your clinical team, one of our research team will contact you to check to explain the study further. We can also see you at your pre-operative assessment appointment if this is easier.

You are under no pressure to decide quickly whether to participate. If you need more time, we just ask you to contact us when you have decided. If you decide to take part, we will ask you to provide written consent of your participation. This will take about 10 minutes, and can take place on the day of your operation or at your pre-operative assessment appointment.

Before your operation

You will attend the Oxford University Hospitals Trust as normal on the day of your operation, and you should follow the instructions given to you by your clinical care team.

When you arrive, as well as seeing the NHS anaesthetist, you will also meet with an anaesthetist who is part of the research team. They will again fully explain the study procedures to you.

Before your operation starts, you will be given anaesthesia while the researchers record and monitor the electric activity in your brain. The study anaesthetist will make adjustments to the amount of anaesthesia you receive based on your brain's electrical activity in order to identify your individual SWAS level. We will administer anaesthetic drugs that are commonly used for operations just at a slower rate so putting you to sleep may take slightly longer than usual. You will receive either an intravenous anaesthetic called propofol and/or an inhaled anaesthetic called sevoflurane to put you off to sleep. The anaesthetic you will receive will be assigned depending on the order of your enrolment into the study. Both of anaesthetic agents are equally effective. If you are one of the first 10-15 patients recruited into the study, you will receive sevoflurane anaesthesia throughout the study and your operation afterwards. If you are in the second 10-15 patients, you will receive propofol anaesthesia to put you off to sleep initially and then we will also give you sevoflurane to SWAS in order to prepare you for surgery.

As the anaesthetic dose is increased, you will become increasingly sedated and eventually lose consciousness altogether. Occasionally, the researcher will ask you to respond (for example by squeezing their hand) to indicate if you are still awake. When you are unconscious, your care will be transferred to the NHS anaesthetist assigned to your surgery. Your operation will then continue as normal. We will, however, continue to record your brain's activity during the operation, but this will not interfere with your clinical care.

Electroencephalography (EEG) recordings

In order to record the electrical activity of the brain, one of the research team will apply a snug fitting cap made of an elasticated cloth material on your head (see picture). This will be applied while you wait for your operation and will take 20-30 minutes. The EEG cap contains several metallic sensors and a water-based gel containing salts that conduct electricity is used to establish contact between the sensors and your scalp. In order to make a good connection, we will prepare the area of your scalp under each EEG sensor by cleaning it with alcohol and massaging it with an abrasive substance using a cotton swab, or by scratching the surface of the scalp lightly with a blunt wooden stick. The elastic cap will be removed once you are fully awake and responsive. As the gel is water-based it will wash out easily after your operation.

Questionnaires

While you wait, we will ask you to fill in some short questionnaires about how you feel about the operation, how good your sleep is usually, and some general questions about your personality. We are interested in how these factors can affect your brain's susceptibility to anaesthesia. This should only take about 15-20 minutes and can be filled out at the same time as we apply your EEG cap.

After the operation

When you awake from the operation, you will be asked to answer a brief questionnaire about any experiences you may have had when you were being put to sleep or during the surgery. It is very unlikely that you will remember anything during your surgery but, if you do, we may contact you again 3-4 weeks after your surgery. We would like to record your answers to these questions on both occasions if possible. We will also send you a feedback sheet a few weeks after the study is completed. Completion of this feedback sheet is entirely voluntary. Your answers would be used to help guide patient involvement in our studies in the future.

What should I consider?

Your participation may involve you being anaesthetised for longer than you would be as part of standard clinical care, particularly if you are one of the first participants in the study. We expect that on average it may increase your time in the anaesthetic room before surgery by 30 minutes, up to a maximum of 1 hour extra. If you are one of the later participants in the study, we hope that there will be no increase in time at all compared with the typical induction of anaesthesia.

As taking part in the study may extend the duration of your anaesthetic slightly, we will only recruit people with a very low risk of any adverse effects. The study research team will need access to your medical notes to make sure it is safe for you to participate. In the meantime, the following criteria in particular may **exclude** you from taking part in the study:

- Smoker (tobacco or electronic cigarettes)
- High alcohol intake (>14 units/week) or illicit drug use
- Pregnancy
- Obesity (e.g. body mass index >30 kg/m^2)
- Personal or family history of
    - allergies and/or adverse reactions to anaesthesia
    - blood clots or venous thrombo-embolic events (VTE) (e.g. deep vein thrombosis)
- Some neurological, psychiatric or psychological disorders (e.g. epilepsy, chronic pain, etc.)
- Some prescription medications (e.g. hormone replacement therapy)

What are the possible benefits of taking part?

There is no direct benefit to you from taking part in this study, apart from the knowledge that you are contributing to scientific research that we envisage will advance future medical care.

Are there any possible disadvantages or risks from taking part?

Anaesthesia

The increase in time that you will experience anaesthesia for will very slightly increase the very low risk of a developing a blood clot when being immobilised for a period of time during anaesthesia. However, you will only be recruited for this study if have a low-risk of developing a blood clot. In addition, we will use standard clinical measures such as compression stockings to further reduce the risk of this occurring.

Electroencephalography (EEG)

EEG is a procedure for measuring brain waves. It is harmless and painless and carries no significant risk to participants. EEG recording has been used safely for many years, and we are not aware of any cases of adverse events. EEG equipment we use comes from certified suppliers, who are obliged by law to adhere to published safety guidelines. If you feel any discomfort during the procedure, we ask you to please let the researcher know and they will stop the procedure without this having any negative consequences for you.

Questionnaires

The responses you give to the questionnaires will, like all the data gathered in the study, be kept entirely confidential.

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

Your GP will not be informed of your participation but you are free to discuss participation with them. In the very unlikely event of an incidental finding of an abnormality in your EEG recording that is deemed medically important to you, you will be contacted directly. Your GP may become involved later.

Will my taking part in the study be kept confidential?

Your participation in the study will be kept strictly confidential. The study will comply with the UK Data Protection Act, which requires data to be anonymised as soon as it is practical to do so. All data collected from you will be labelled with a code number rather than your name or initials. The keys linking these codes to personal details will be kept in lockable filing cabinets only accessible by the researchers involved in the study. The keys may also be stored in computer files either on the Wellcome Centre for Integrative Neuroimaging (WIN) central file server or will be encrypted appropriately on other University owned computers.

If you agree to be contacted for future studies, your personal data will also be stored in a separate password-protected database on an encrypted machine or on a protected server. Responsible members of the University of Oxford and the OUH NHS Foundation Trust may be given access to your personal data for monitoring and/or audit of the study to ensure that the research complies with applicable regulations.

Will I be reimbursed for taking part?

No. As this study should not involve any additional visits to the hospital, we do not expect there to be any additional costs for you. Should any visits in addition to normal care be required these will be reimbursed on production of receipts, or a provided mileage as appropriate.

What will happen to my data?

All personal and anonymised data collected about you will be handled and stored securely. This data is accessed locally via a password and firewall-protected server. All data will be backed up on storage tapes provided by the WIN Centre IT services. Audio recordings of your interviews will be encrypted and retained in voice format until the end of the study. After that point, anonymised transcripts of your interview will only be stored. Anonymised research data will be stored indefinitely to enable further analyses should new techniques arise in the future. The WIN Centre will also retain personal identifiable data for five years after the end of the study, after which it will be confidentially destroyed. If you have consented to future contact about other future projects then your personal contact details would be retained at the WIN and stored securely in a separate database.

With your consent, your fully anonymised data may be shared with other research institutions, including researchers outside of the European Union. In particular, this project is part of a European research collaboration called Luminous. Anonymous data from this study will be shared among partnered research groups in the consortium upon request. The consortium leaders, Starlab (Barcelona, Spain), will coordinate the data management, collection, storing and sharing of anonymous data between Luminous partners. Strict anonymization protocols are in place at every institution involved in the consortium.

After the publication of the study results by our research team, your anonymised data will be made publicly available to third parties to use as they need. This is part of a larger effort in science to open research findings to public scrutiny at all levels. All data shared in this fashion will be stored in a repository called the Open Access Infrastructure for Research in Europe (OpenAIRE), which has strict standards for ethical data sharing. It may also be stored in an equivalent University of Oxford open access database called the Oxford Research Archive - Data (ORA-Data, http://www.bodleian.ox.ac.uk/bdlss/digital- services/data-archiving). This repository will allow the data to be accessed by any user for a period of 20 years.

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

You may withdraw your consent to participate in the study at any time, for any reason and without affecting your legal rights. Withdrawal from the study will also not affect the care you receive from the NHS in relation to your surgery or any other clinical care you may be receiving. You have no obligation to give the reason for withdrawal. Any data collected up to the point of withdrawal will be retained and may be used unless you request otherwise. You are free to request that your data are destroyed at any time during or after the study.

What will happen to the results of this study?

We hope to publish the results of this study in scientific journals. We may also present the results at scientific seminars or conferences. Some of the research being undertaken will also contribute to the fulfilment of an educational requirement (e.g. a doctoral thesis). We may also publish results on our website. Finally, your anonymous data may form part of a future research grant application. It will not be possible to identify you in any report or publication. We may also use direct quotations from interviews with you but again these will be anonymised so that it will not be possible to identify you.

What if we find something unexpected?

It is important to note that we do not carry out EEG recordings 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 EEG recording 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. By agreeing to take part in the study, this means you are agreeing to be told about an unexpected finding in this way. You will 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.

Please note that an incidental finding may be detected either at the time the EEG recording is collected or may be identified some time later, potentially months or even years later. If you think you may have an undiagnosed medical condition affecting your brain then you should consult your GP. You should not take part in this study.

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 during the course of this study, you should contact Dr Katie Warnaby by telephone on 01865 611 465 or by emailing katie.warnaby@ndcn.ox.ac.uk. Alternatively, you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 572 224, or the head of CTRG, email 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 by telephone 01865 221 473 or email PALS@ouh.nhs.uk.

Who is organising and funding the study?

This research is organised by the University of Oxford and is funded by the European Union's Horizon 2020 research and innovation programme, as part of the LUMINOUS project.

Who has reviewed the study?

Research involving healthy subjects receiving anaesthesia 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 West Midlands - Coventry and Warwickshire Research Ethics Committee. Prior to this, the research was reviewed by the LUMINOUS Consortium's Ethical Advisory Board at the request of the European Union's Horizon 2020 research and innovation programme.

Participation in future research:

If you wish to be approached for potential future research, we will store your contact details securely beyond the duration of this study (see 'Will my taking part in the study be kept confidential?' above). Agreeing to be contacted does not oblige you to participate in future research.

Further information and contact details:

If you are interested in taking part after reading this information sheet, you should contact Dr Katie Warnaby and the research team, either by email on anaesthesia.research@ndcn.ox.ac.uk or by telephone on 01865 611 465.

Thank you for considering taking part.