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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 anaesthetists give just the right amount of anaesthesia for each patient.

This study builds on our earlier work that identified interesting changes in brain activity during general anaesthesia. We believe these changes in the electrical activity of the brain indicate when an individual loses awareness of the outside world. Our observation was that when the anaesthetic dose is increased, slow waves in the brain reach a maximum level, and then do not increase any further even though much more anaesthetic drug is given. These slow waves are low frequency oscillations (at around 1 Hz or 1 cycle per second) and are also an important feature of deep sleep. We have called this observation slow wave activity saturation (or SWAS) and it can be measured by applying electrical sensors- a technique called electroencephalography (or EEG for short).

This study firstly aims to confirm our original finding of SWAS and explore how different parts of the brain communicate at this level of anaesthesia. To do this, we will measure brain activity using

both electroencephalography (EEG) and magnetic resonance imaging (MRI) while individuals are given a commonly used anaesthetic medication called sevoflurane. Secondly, although it is clear that anaesthesia and sleep are very different states, there are some obvious similarities. We will also record the brain's response during sleep in the same people to explore whether there are any common brain mechanisms and whether sleep influences anaesthesia.

Why have I been invited?

Both patients and heathy volunteers will be recruited into the study. You have been invited to take part in the healthy volunteer arm of the study. We are seeking to recruit up to 30 right-handed, male and female healthy volunteers between the ages of 18 and 60 years. We would like to invite you to learn more about the study and to participate if you would like to.

The information gathered from both groups will help us to optimise delivery of anaesthesia to SWAS and confirm that SWAS indicates the precise point when an individual loses awareness of the outside world under anaesthesia. The patient group involving up to 30 participants will additionally help us optimise the SWAS model in an operating theatre.

Do I have to take part?

No, it is up to you to decide. We will describe the study in this information sheet, which is yours to keep. Please take as much time as you need to consider whether you would like to participate. If you are interested in taking part, you should contact the research team by email on anaesthesia.research@ndcn.ox.ac.uk or telephone on 01865 611 454. If you do agree to take part in the study, you are free to withdraw at any time without giving a reason.

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

If you express an interest in taking part, one of the research team will contact you by telephone to check whether you are suitable and to explain the study further. During this call, they will ask a number of general questions to make sure you can safely participate in the study. You will also be asked to complete a screening form to assess whether it is safe for you to have an MRI scan, and return this to us by post or email. You are under no pressure to decide whether to participate quickly. We just ask you to contact us when you have decided.

If you take part in the study, you will be asked to make three visits to the Wellcome Centre for Integrative Neuroimaging (WIN) at the FMRIB building, John Radcliffe Hospital in Oxford. We will arrange these visits at times to suit you as much as is possible.

- Visit 1 will be a screening visit and does not involve any brain imaging.
- Visit 2 will take place in the early evening. It will consist of several magnetic resonance imaging (MRI) scans that measure your brain activity without anaesthesia.
- Visit 3 will take place early the next morning. It will involve more MRI scans while you are given an inhaled anaesthetic called sevoflurane. During some of the MRI scans, we will ask you to respond to words and painful stimuli as the anaesthetic dose is increased. We will also use an EEG cap to record your brain's electrical activity in the MRI scanner.
- During the night between Visits 2 and 3, we will record the electrical activity of your brain while you sleep in the comfort of your own home.

Each study visit is explained in more detail below and outlined in the flow chart on the next page.

Visit 1 (Screening: 30-45 minutes)

We will arrange a convenient time for you to come to the WIN. You will be met by one of the study research team. They will go through this information sheet with you to make sure that you understand what is involved in the study. The researcher will ask you a series of questions about your health and lifestyle to make sure it is safe for you to participate. Please bring details of any kinds of surgeries or metallic implants that you have had in the past, and any prescription medication you are taking. Please also bring some identification and proof of address with you to ensure safe return of the sleep EEG kit. Please also bring your bank details if you would like to receive financial compensation for study participation directly into your bank account.

The researchers will also explain some of the procedures that will be carried out during Visits 2 and 3. In particular, the researcher will show or explain to you:

- how the inhaled anaesthetic will be delivered.
- how your heart rate, blood pressure and breathing will be monitored.
- how the pain and auditory stimulation will be delivered.
- how the EEG is measured during your sleep and in the scanner.
- how the MRI scans will be performed.

You are encouraged to ask questions throughout the visit if anything is unclear. If you are happy to take part, you will be asked to sign a consent form. It will be made clear that you are under no pressure to do so, and you can withdraw from the study at any time.

You will then see a medical doctor, who will give you a brief examination to check it is safe for you to receive sevoflurane anaesthesia. We may ask you to lie in the scanner briefly to check that the anaesthesia facemask fits you properly. If we have any other concerns about your suitability for scanning, we may also ask you to speak to one of the Centre's radiographers during this visit.

At the end of the visit if you are still happy (and eligible) to take part, we will schedule Visits 2 and 3. This may be done later by email or phone if you need more time to consider study participation.

Visit 2 (Baseline scan: 2 hours)

You will come to the WIN for Visit 2 in the early evening, usually around 6pm. We will describe what will happen during this visit and answer any questions you may have. Before scanning, you will complete an MRI Screening form to make sure that it is still safe for you to be scanned. You should let the researchers know if anything has changed in your circumstances since Visit 1.

Questionnaires

During Visit 2, we will ask you to complete a set of short questionnaires about your general levels of anxiety, sleep quality and some aspects of your personality. This will take approximately 15-20 minutes. The responses you give to these questions will be anonymised and kept confidential, like

all the other study data gathered from you. We will use these questionnaires to try to explain variability in the brain's response to anaesthesia between individuals.

Visit 1 (Medical Screening: 30-45 minutes)

- You will meet the researchers and go through the study in detail.
- You will be shown the facility and the equipment involved.
- You will sign a consent form if you are happy to participate.
- You will be screened by a medical doctor.

Visit 2 (Baseline Scans: 2 hours)

- You will come for an evening MRI scan lasting approximately 1 hour.
- You will complete questionnaires telling us about your sleep and aspects of your psychology.
- We will fit EEG electrodes to record your sleep that night. This will take about 30-45 minutes.
- There will be no anaesthesia given on this visit.

Going home after visit 2

- You will return home immediately.
- We will pay for and organise a taxi ride to your home.
- You will sleep in your own home

Visit 3 (Anaesthesia scans: 4-5 hours)

- You will arrive at approximately 8am, having fasted for at least 6 hours (i.e. no food or drink).
- You will have the sleep EEG electrodes removed.
- You will have the scanner EEG cap applied and a short EEG recording performed.
- You will fill in questionnaires about last night's sleep and your current anxiety levels.
- We perform several baseline EEG-MRI scans, including scans during painful stimulation.
- We will deliver sevoflurane anaesthesia to you while we play sounds until you lose responsiveness.
- We will repeat the EEG-MRI scans.
- We will increase the sevoflurane anaesthesia according to your EEG signals until you reach SWAS.
- We will repeat the EEG-MRI scans.
- We will turn off the anaesthetic
- You will wake up in the scanner room while having your EEG recorded.
- You will be asked questions about your experiences.

Going home after visit 3

- When you have fully recovered, we will give you lunch.
- We will pay and organise for a taxi ride to your home.
- You must have somebody with you overnight after the anaesthesia.

MRI scanning

You will then change into a pyjamas-looking top and trousers, which you will be provided with and are available in a range of sizes. You may keep your underwear and socks on, but we ask women 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).

You will be asked to remove any metal on you (such as hairpins). Metal jewellery, including body piercings, must also be removed. Eye shadow and mascara should 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. You will then be taken to the scanner room and be prepared for scanning. As some of the scans are noisy, we will 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.

We will then perform several non-invasive MRI scans to investigate your brain's anatomy, chemical composition and blood flow. There will be several breaks between the scans with the scanning session lasting approximately 1 hour. During MRI scanning, you would be asked to lie as still as possible on a table inside the scanner. We will make sure that you are comfortable by providing cushions around your head and give you a blanket to keep you warm if you need it. You will also be given a call button to hold throughout the scan. You can use this to get the attention of the researchers just outside the scanner room at any time. You can also speak to the researchers via a microphone when the scanner is not running. We may also monitor your heart rate, blood saturation levels and breathing rate during these scans to make sure that the changes in your brain scans are not artefacts produced by changes in your heart or breathing rates. More details about how this physiological monitoring will be carried out are included in the Visit 3 description.

Sleep EEG

We will measure your brain's electrical activity using EEG while you sleep at home that evening (i.e. the night between Visits 2 and 3). After the MRI scanning is completed, you will be able to get changed into your own clothes. You may choose to change into comfortable night clothing or pyjamas at this time. We will then fit you with a sleep EEG kit, which should take around 30-45 minutes. The researcher will attach a number of electrodes to your scalp and chest. The electrodes are connected by wires to a central unit that you will wear in a harness on your chest while you sleep. In addition, we will attach an oximeter to your finger to measure oxygen saturation in your blood, and place small cannulae (tubes) at your nostrils to analyse oxygen and carbon dioxide levels in air that you breathe out while you sleep.

To establish electrical contact between the scalp and the EEG sensors, a water-based gel containing salts that conduct electricity is placed under each metal contact. In order to achieve a good connection, we will prepare the area of the scalp under each EEG sensor by cleaning it with rubbing alcohol and massaging an abrasive substance using a cotton swab, or by scratching the surface of the scalp with a blunt wooden stick. We would ask you to let the researcher know if at

any time the procedure becomes uncomfortable. In the laboratory, there is a shower-head, shampoo and a hair dryer for removal of the gel after completion of the research.

After the sleep EEG kit has been applied, you will return home in a taxi and are asked to stay at home for the rest of the evening. You should go to bed at your normal bedtime or whenever you feel tired. In preparation for having anaesthesia the next day, you are asked to fast for six hours before the MRI scan. For most people, the best way to do this is to have a good meal in the evening and then refrain from eating or drinking on the morning of your visit. If you have any questions about the fasting rules, please ask your researcher during Visit 2. If you have taken any food or drink the next morning the experiment may have to be cancelled.

Visit 3 (Anaesthesia scan: 4-5 hours)

Having fasted overnight, you will return to the WIN the next morning for Visit 3. We will organise a taxi for you so that you arrive in time for your scan session. This will typically start at 8am. You may drink still water for up to 2 hours before receiving the anaesthesia.

EEG in the MRI scanner

When you arrive, we will describe what will happen during this visit and answer any questions you may have. Firstly, you will have the sleep EEG kit removed and a different EEG kit that is suitable for the scanner will be applied. The researcher will place a snug fitting cap on your head that is made of an elasticated cloth material and contains the EEG sensors. As with the sleep EEG kit, electrical contact will be made between the scalp and the EEG sensors using a conductive gel. When completed, a short EEG recording of resting brain activity will be performed outside of the scanner. This will take around 45 minutes to 1 hour in total.

Questionnaires

During set-up of the EEG, we will ask you to fill in more questionnaires about your current anxiety levels and how well you slept the previous night. You will also be asked to fill in another MRI screening form. This will take approximately 10 minutes in total.

MRI scanning during sevoflurane anaesthesia

You will be prepared for MRI scanning as in Visit 2. You will change into the pyjamas-looking top/trousers and you will be given earplugs as before. Additionally, we will supply you with some compression stockings to wear. You will have an intravenous cannula inserted into the back of your hand. This is purely for safety reasons and we do not expect to use this unless you have an unexpected (and rare) adverse reaction to the anaesthetic. You will then be positioned in the scanner and the facemask used to deliver the anaesthesia will be put in place. As in Visit 2, several different measures of your brain's activity, chemical composition and blood flow will be recorded. This time we will also record EEG and MRI data simultaneously both during baseline scans and while you are given sevoflurane anaesthesia. You will gradually become increasingly sedated and eventually lose consciousness.

We will repeat the same sequence of MRI scans three times: 1) before the anaesthesia starts, 2) when you have lost responsiveness to auditory stimuli, and 3) when you reach the SWAS endpoint as measured by the EEG. During one of the MRI scans, we will deliver brief painful stimuli to you and ask you to respond to the commands that will be played to you over headphones.

We expect it will take from 45 minutes up to 1 hour of scanning until you lose responsiveness under anaesthesia. Again, there will be several breaks between the MRI scans when you will be able to speak to the researchers until you lose responsiveness. You will also have the call button as in Visit 2 so you are able to get in touch with the researchers at any time.

Pain Stimulation

In order to assess your responsiveness to pain under anaesthesia, we will use either heat, mechanical and/or electrical stimulation. To produce heat pain, a thermal probe will be attached to your arm or leg that will heat up for typically three seconds in duration, causing a brief painful sensation. Your skin at the location of the thermal probe may become slightly red, but this will fade within a few hours. No lasting or permanent damage will be done to your skin.

We may also elicit mechanical pain by using sharp probes applied to your skin surface. The probe will not penetrate or damage your skin. For electrical pain, an electrode is applied to the surface of your skin prepared with a commonly used cream that enhances conductance. Current is only applied to this prepared surface area and will not pass internally into the body.

There are no known side effects from these procedures. All these methods to elicit pain are brief, safe and controlled, but adequately painful to produce a response in your brain.

Before the MRI scanning begins, there will be a brief thresholding procedure where pain stimuli of different intensities will be given to you. You will be asked to rate them on a scale of 0 to 10, where 0 is not painful and 10 is maximum pain. The purpose of this procedure is to determine the intensity that you rate as 8 out of 10. This is the intensity that will be used during the experiment.

Physiological monitoring

Your circulation and breathing will be monitored to ensure your safety during the anaesthesia. This physiological monitoring is similar to that used during operations is described below:

- We will use an electrocardiogram (ECG) to measure the electrical activity of the heart by placing electrodes on the skin at the front of the chest.
- We will measure the oxygen saturation levels using an oximeter placed on your finger or toe.
- We will measure your respiration using a stretchy band around your chest that moves as you breathe in and out.
- We will measure your blood pressure using an inflatable cuff that will be wrapped around your upper arm or wrist. This test may be slightly uncomfortable when the cuff is blown up.
- We will measure the concentration of sevoflurane, oxygen and carbon dioxide in the air you breathe out.

Recovering from the anaesthesia

Once the MRI scans are completed, you will wake up naturally from anaesthesia while the EEG recording continues. When you are awake, we will perform a short structured interview (10 minutes) to find out about your experiences during anaesthesia. We will perform an audio recording of this interview. When you feel able, you will be moved to an adjacent room where you will be taken care of until you recover fully. You will be given a sandwich lunch and we will arrange for a taxi to take you home. Due to differences in how susceptible people are to anaesthesia, the time to complete this session will vary from person to person. We expect the full session to last between 4-5 hours in total, of which about 2-2.5 hours will be spent in the scanner.

Please do not drive, use machinery, take alcohol or participate in any sports that evening as you may be quite tired. You must also have someone stay with you that night in case you feel unwell and need to contact us – this is highly unlikely but is an important precaution. One of the research team will also contact you later that evening to check that you are well.

What should I consider?

While both anaesthesia and MRI is normally safe for healthy individuals, some people should not undergo these procedures. We will perform a full medical screening in Visit 1 to make sure you are safe to participate. In the meantime, the following list could *exclude* you from participation:

- Smoking (tobacco or electronic cigarettes)
- High alcohol intake (>14 units/week) or illicit drug use
- Some types of facial hair and beards (that you are not willing to shave off for the study).
- Tattoos (depending on location)
- Pregnancy
- Obesity (e.g. body mass index >30 kg/m^2)
- Claustrophobia
- Certain metallic implants or metallic injury to eye
- Some prescription medications (e.g. hormone replacement therapy)
- Some neurological, psychiatric or psychological disorders (e.g. epilepsy, chronic pain, etc.)
- Personal or familial history of
    - allergies and/or adverse reactions to anaesthesia
    - blood clots or venous thrombo-embolic events (VTE) (e.g. deep vein thrombosis)

If none of the above apply and you decide to participate, please note surgeries of any kind you have had in the past, any metallic implants you have and any prescription medication that you are taking. This will be necessary for the medical screening.

Are there any possible disadvantages or risks from taking part?

MRI

The scanning is done using an MRI scanner, which is also routinely used in clinical practice to acquire images or various body parts. MRI is safe and non-invasive and does not involve any

ionizing radiation (x-rays). However, because it uses a large magnet to work, MRI scans are not suitable for everybody. Because of this, you will be asked pre-screening safety questions to help determine if you are able to take part.

Normally, MRI scanning for research purposes would not be performed 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.

EEG

EEG is a procedure for measuring brain waves. It is harmless and painless and carries no significant risk to participants, though some participants do report a brief itching sensation at the beginning of the recording. EEG recording has been used safely for many years and we are not aware of any cases of adverse events. EEG equipment comes from certified suppliers, who are obliged by law to adhere to published guidelines on electrical and mechanical safety (IEC-601). Our equipment is specifically designed for sleep or use in an MRI scanner. If you feel any discomfort, then please let the researcher know and they will stop the procedure.

Anaesthesia

Sevoflurane is a very safe medication that is commonly used to maintain sedation during surgery. However, it is possible that you can experience one of the side effects or rare reactions to sevoflurane anaesthesia (see table below). The WIN is appropriately equipped to deal with these reactions and the anaesthetists involved in the study are experienced in managing these situations. In the very unlikely event you experience a severe reaction you will be brought to the adjoining John Radcliffe Hospital for continuing care.

Common side effects (i.e. 1 in 10 cases)	***Uncommon (i.e. 1 in 1000 cases)***	***Rare or very rare side effects (i.e. less than 1 in 10,000 cases)***
Sore throat Headache Nausea/vomiting Dizziness, confusion and short-term memory loss	Low blood pressure or heart rate Reduced rate or depth of breathing	A serious allergic reaction to the anaesthetic (anaphylaxis) Heart attack or stroke Death (very rare - five deaths for every million anaesthetics in UK)

Painful stimulation

The mechanical, electrical or heat stimulation will elicit a brief painful or discomforting sensation, and can cause temporary redness of the skin. The researchers involved with this project have many years of experience using these methods for eliciting pain in a safe and controlled fashion.

Blood pressure

The method we use for measuring blood pressure is very safe, and is regularly used by doctors and nurses. You may feel uncomfortable when the cuff is inflated and there is a small chance of bruising to the upper arm. We have designed the research to make this less likely and we will stop the measurement if you find the measurement very uncomfortable, or your arm gets bruised. At the end of the measurements, we will let you know what your blood pressure was. If your blood pressure is high, this does not necessarily mean that you have high blood pressure. Blood pressure changes through the day and can be raised by things like stress and nervousness. However, if your blood pressure appears to be unusually high, we will advise you to discuss this with your GP, in case you need further tests or treatment.

If you are concerned about your blood pressure or any other aspect of your health, you should see your GP.

What are the possible benefits of taking part?

There is no direct benefit to you if you take part in this study. We hope that the information we get from this study may help us to better understand how anaesthetics work, as well as contribute to improve anaesthesia delivery in clinical practice in the future.

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 MRI that is deemed medically important to you, you will be contacted directly. Your GP may be 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 also 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 a name or initials. The keys linking codes to personal details will be kept in lockable filing cabinets only accessible by the researchers involved in the study. They may also be stored in computer files either on the WIN central file server or will be encrypted appropriately on other University owned computers.

Personal identifiable data (i.e. name and date of birth) will be held for at least five years after the end of the study to allow follow up in the rare event of a discovery of an incidental finding. The WIN will retain the Magnet Safety Screening form that is completed prior to each MRI scan, in-line with the local Oxford University Hospitals NHS Foundation Trust guidelines. If you agree to be contacted for future studies, your personal data will be stored in a separate password-protected database on an encrypted machine or on a protected server.

Responsible members of the University of Oxford 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?

We understand that taking part in the study will cause you inconvenience and take a significant amount of time. We will compensate you for the time and inconvenience of taking part in each of the experiment sessions. You will receive £10 for the screening visit (Visit 1), £25 for the first MRI session (Visit 2), £50 for the overnight EEG sleep recording, and £90 for the anaesthesia session (Visit 3). You will receive £175 in total if you complete all sessions. You will also receive a free sandwich lunch before returning home after Visit 3. Bank details will be collected to allow payment directly into your account. You will receive compensation for any reasonable travel expenses, including attending Visit 1 to learn about the study further and be screened for participation. Your taxi fares to attend Visits 2 and 3 will paid for, as will your return home after the anaesthesia on Visit 3.

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. Data acquired on laptop computers will also be copied to WIN servers. All data will be backed up on storage tapes provided by the WIN IT services. Audio recordings of your post-anaesthesia interview 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.

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 see fit. 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 (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. If you are a student of the University of Oxford, no academic penalty of any kind will incur for withdrawing from the study. 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. You will be reimbursed for the sessions attended up to the time of withdrawal (see 'Will I be reimbursed for taking part?' above).

What if we find something unexpected?

It is important to note that we do not carry out MRI scans or 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 scan checked by a clinical specialist. If the specialist felt that the abnormality was medically important, you would be contacted directly. They would discuss the implications with you and arrange for further investigations as necessary. For example, they may recommend that a hospital (NHS) diagnostic scan is arranged. Your GP may be informed at this time if you consent to this happening. Agreeing to take part in the study means that you agree to being 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 scan 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 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 PhD. 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 or images of your brain 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 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. 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 ctrg@admin.ox.ac.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 research and innovation programme Horizon 2020, 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?'). 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.