Department of Psychiatry
Addenbrooke's Hospital
Cambridge, CB2 0QQ

HEALTHY VOLUNTEER INFORMATION SHEET

Studying the psychological and interoceptive contributions to eating

You are being invited to participate in a research study. Before you decide if you would like to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if anything is unclear or if you would like more information.

Part 1 gives you information on the purpose of the study and what will happen to you if you take part.
Part 2 tells you more detailed information on the conduct of the study.

PART 1

What is the purpose of this study?

Our research looks at the important factors that contribute to appetite and eating patterns in healthy individuals and those for whom eating patterns may have become disrupted. Part of our intention is to understand overeating, which is a major cause of ill-health worldwide. We also want to understand eating behaviour and experiences of eating in people who may not struggle with controlling their consumption but who may have health problems that affect the normal communication between the gut and the brain. By putting these pieces together, we hope to improve our understanding of normal and disrupted eating patterns.

Over-consumption affects the population as a whole and is clearly driven by major changes in our environment and in the ways that these foods are marketed and made available. Yet not everyone is vulnerable to the so-called "obesogenic environment" and it is critical to understand why some people become obese while others, inhabiting the same environment, do not.

This study aims to explore how the body, the brain and the environment interact to cause over-consumption and obesity. To do this we will use a set of complementary measures including metabolic and hormonal markers in blood as well as psychological and behavioural tasks (including observations of eating patterns) and brain responses to food-related cues.

Lean and obese people as well as individuals from patient groups who have disturbances in body-brain signalling (either following surgery or because of genetic mutations) will be studied over the course of a two day visit (including an overnight stay) at the clinical research facility. We will be able to examine key differences in brain-body-environment interactions in lean and obese individuals and how different individual patterns of interactions relate to appetite and eating-related processes. In addition, studying how disturbances in brain-body communication in the affected patient groups affect these interactions, will help us better understand how this complex integrated system works.

Why have I been invited?

For this study, we are recruiting, as well as healthy volunteers of different weight status (lean and obese), two groups of people: those who are undergoing upper gastro-intestinal surgery (including gastrectomy) and people with an identified mutation in MC4R, LepR or SIM1 genes leading to trouble in reducing their food intake. You have been invited because you belong to one of these groups.

Do I have to take part?

No. It is up to you to decide whether or not to take part. Your decision will not affect your clinical care and treatment in any way. We will go over this information sheet with

you and answer any questions you have about the study. If you decide to participate, we will ask you to sign a consent form. You are free to withdraw from the study at any time without giving a reason.

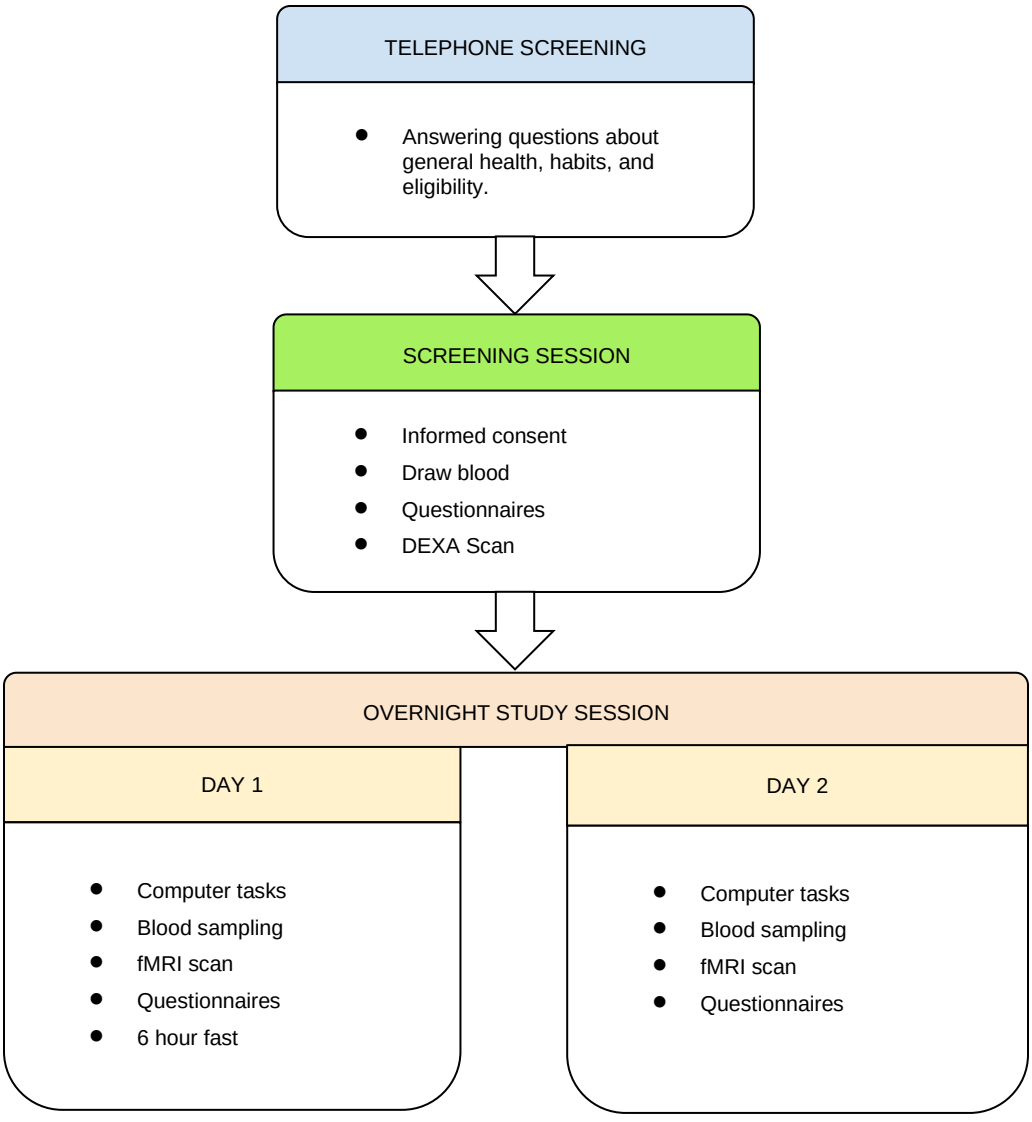
What does the study involve?

If you are interested in participating, a member of the research team will take you through a screening interview over the telephone to see if you meet the basic eligibility criteria. If you meet these criteria and would like to continue, we will arrange an outpatient screening session at Addenbrooke's hospital. In this session we will check if you have any health conditions that would prevent you from participating in the study session. If you do not, then you will be scheduled for a single, two-day study session at Addenbrooke's hospital, including an overnight stay.

To be eligible for participation in this study, you must be in good general health. You should be between 18 and 45 years old, right-handed, fluent in English language, have normal or corrected-to-normal vision, and have no history of neurological diseases, substance dependence or major psychiatric disorder. You should not have nicotine dependence. For reasons of MRI safety, you should not be pregnant, lactating or have any metallic implants in your body.

What will happen to me if I take part?

The general study timeline has been illustrated below.



Telephone screening: This will be arranged at your convenience and take about 20 minutes. You will be asked questions about your general health to see if you are eligible for the study. After the telephone screen, you will be sent a link to a set of online questionnaires. All information from the telephone screen and questionnaire will be kept

confidential. If you do not wish to proceed with the study after the phone screen, your responses will be destroyed.

Screening Session: If you are eligible, you will be invited to the Cambridge Translational Clinical Research Facility located at Addenbrooke's hospital. This is a clinical facility staffed by nurses and a dedicated study doctor. When you arrive, a member of the research team will meet with you to go through this sheet and answer any questions that you may have. You will then be asked to provide written, informed consent. A study nurse will then collect a blood sample. You will then complete some short questionnaires about your medical history, as well as a computer task and a DEXA scan. The DEXA scan usually takes about 10 to 20 minutes. You may be asked to put on a gown over your underclothes for the duration of the scan. You will be taken to the X-ray room and asked to lie down on a padded table. One of the ward team will operate the scanner and will be able to see, hear and speak to you during the procedure. The X-ray machine will slowly pass over your body and a detector will measure how much X-ray radiation passes through your body and will send this information to a computer. The computer will then calculate your body composition in terms of fat and muscle mass.

The screening visit will last about 1-2 hours in total. At this session, we will check for any medical conditions that would prevent you from taking part in the main study session. If it so happens that you are not eligible to continue with the study, we will reimburse you £30 for the time you spent at the screening. This will not impact any care or support you receive from NHS services.

If there are any abnormalities in your blood tests, we will send your result to your GP with your consent.

Overnight session: If you are eligible, you will complete a single, two-day overnight visit to the Cambridge Translational Clinical Research Facility at Addenbrooke's Hospital. We will ask you to refrain from consuming alcohol for 24 hours before your study session. For the overnight session you will stay in a private room. We suggest that

you bring an overnight bag with you. There will be periods of free time in between testing so you are welcome to bring your laptop, books, or anything else might make your stay more comfortable.

During the study session, you will complete a series of computer tasks as well as some questionnaires related to your body feelings, mood, habits, and decision-making. Furthermore, we will collect blood samples on both days of the session.

You will complete two brain scans – one on each day. All brain scans will be completed in the afternoon, and you will fast for about six (6) hours before one of the two scans. You will be provided meals throughout your stay in the Cambridge Translational Clinical Research Facility, however during the testing period (i.e. from morning to the end of the day's testing) you will not be able to have any caffeinated drinks. If you are receiving medical care at Addenbrooke's hospital at the time of the study, you will be able to return to your unit each day following the study procedures. The overnight session will last a maximum of 36 hours.

Please find below the detailed schedule of what will happen during the overnight visit:

	DAY ONE	
MORNING	**ARRIVAL TO THE UNIT**	On arrival, you will have the possibility to settle in your private room and get acquainted with the research staff.
	BREAKFAST	Shortly after your arrival, we will provide a standardised breakfast.
	MORNING TESTING	During the morning session we will ask you to complete a series of tasks on a computer. Some of these tasks will assess awareness of your own body, some will test how you discriminate different tastes (e.g., sweet vs bitter), and others will focus on cognition and reasoning. There will be several occasions to take breaks in-between tasks.
	LUNCH	You will then be asked to complete some more tasks on a computer. Again, there will be time for you to take breaks if you wish to do so.
AFTERNOON	**AFTERNOON TESTING**	You will be asked to complete some more tasks on a computer. Some tests will look at how your respond to stimuli in your environment, others will assess your impulsivity. Again, there will be time for you to take breaks if you wish to do so.
	blood sample	A nurse will place a cannula in your arm and draw 10ml of blood.
	BRAIN SCAN	You will then enter the MRI scan, where you will complete three tasks, one of which will explore your sensation of thirst before and after drinking water. You will remain in the MRI scan for about 90-120 minutes.
	blood sample	A nurse will draw 10ml of blood.
	AFTERNOON TESTING	You will be asked to complete a set of self-report questionnaires
	DINNER	You will be offered a buffet meal.
	FREE TIME	You will have free time to spend in your room, where you can read, watch TV, work, etc.

	DAY TWO	
MORNING	**Blood sample**	A nurse will draw 10ml of blood.
	BREAKFAST	Shortly after you wake up, we will provide a standardised breakfast.
	blood sample	A nurse will draw 10ml of blood.
	MORNING TESTING	The morning of the second day will be very similar to the first one. There will be several occasions to take breaks in-between tasks.
	LUNCH	On one of the days you will be given lunch, while on the other we will ask you to fast until dinner time.
AFTERNOON	**AFTERNOON TESTING**	You will be asked to complete some more tasks on a computer. Some tests will look at how your respond to stimuli in your environment, others will assess your impulsivity. Again, there will be time for you to take breaks if you wish to do so.
	blood sample	A nurse will draw 10ml of blood.
	BRAIN SCAN	You will then enter the MRI scan, where you will complete three tasks, one of which will explore your sensation of thirst before and after drinking water. You will remain in the MRI scan for about 90-120 minutes.
	blood sample	A nurse will draw 10ml of blood.
	AFTERNOON TESTING	You will be asked to complete a set of self-reported questionnaires
	DINNER	You will be offered a buffet meal.
	THE END	

What will I be asked to do?

As mentioned above, you should not consume alcohol 24 hours before the screening and study sessions. A urine test is mandatory for women to ensure that you are not pregnant. The urine sample will be tested by a research nurse and discarded. This will be completed prior to the MRI scans.

Will I be paid for my time?

You will be paid £250 for taking part in the study. We will also pay for reasonable travel expenses (bus or taxi fare).

Please note, this income may have implications for those claiming benefits. It is the responsibility of the individual to comply with the conditions of their benefits. People who receive anything that might be deemed to be earnings or income by Her Majesty's Custom and Revenue Service (HMRC) may put their benefit entitlement in jeopardy. Income can include any payments made, vouchers or financial gifts given.

Please make sure that you get proper advice from a benefits advisor or **Jobcentre Plus** at 0345 604719 before you make a claim for expenses or sessional payments. You may also seek advice from the **Cambridge Citizen's Advice Bureau (CAB)** at 0344 8487979. If you reside outside of the Cambridge area, you may use the national website (citizensadvice.org.uk) or hotline (0344 111444) to find your local CAB.

What is the brain scan like?

We use the brain scan to study the circuits in the brain that are involved in controlling appetite and feeding behaviours in response to certain states. We can learn a great deal about how the brain works by looking at blood flow in different parts of the brain. A brain scanning technique called Functional Magnetic Resonance Imaging (fMRI) enables us to do this. It uses harmless magnetic fields to generate a map of the levels of oxygen in the blood across the brain. The fMRI scanner is a large box with an open-ended tunnel through its middle. For the scan, you would lie on a comfortable, padded table that is moved into the opening of the scanner. Scanning would take around 90 minutes. For about 1 h of each session, you would perform some computer-based tests. These would be explained to you outside the scanner, and you would see the task on a computer monitor inside the scanner. You would make responses on a button box, which would rest on your chest. A study nurse would collect blood samples from you before and after the scan on each day. You would spend up to 120 minutes in the MRI suite.

The fMRI scan does not involve X-rays or radioactivity. There is no evidence of any risks to your health from fMRI. The scanner does use powerful magnetic fields, so all metallic items (coins, jewellery, keys, etc) must be left in lockers outside the scanning

area, and you must tell us if you have any metal in your body, such as surgical clips or heart valves, as these can be affected by the magnet. If you do have a heart valve or heart pacemaker, or other metal implants, and you go inside the scanner, it could be very serious (normal metal fillings in your teeth are not affected by the magnet though, so they are safe). Most people find the scan easy to tolerate, but some people can find it slightly confined and noisy. You will be provided with earplugs to cut down the noise, and you will be able to communicate with the researchers through a microphone at all times during scanning. You will also have an alarm that you can use in case you are finding it uncomfortable. You should tell us if you suffer significantly from claustrophobia.

Like faces, brains come in all shapes and sizes, so that there are many normal variations of what the scan shows. There is a chance of less than 1:100 that your brain MR scan may show a significant abnormality of which you are unaware. All brain scans carried out at the WBIC are reviewed by a neuroradiologist and if a significant abnormality is found, you be referred to the appropriate specialist department. This will be done in consultation with you and your GP and you will be appropriately counselled. Such early detection has the benefit of starting treatment early but, in a small number of cases, may have implications for future employment and insurance.

Blood sampling

During the overnight stay, we will draw your blood on 6 different occasions: before and after breakfast on Day 2, as well as before and after each of the two scans. At the time of the first blood sample a nurse will place an intravenous cannula in your arm and this will stay in place for the duration of your visit so that you will not need to have multiple pokes during the study session. We will assay the levels of gut-hormones and neuropeptides, such as acyl-ghrelin, GLP-1 and PYY_{3-36}, and metabolites, including triglycerides and glucose. On each occasion we will draw 10ml of blood (around 2 teaspoons).

Are there any drugs involved?

There are no drugs involved in this study.

What are the psychological tasks like?

These are approximately 10 tasks where you view a computer screen and respond by pressing a button or key on a keyboard. Some concern anticipation and responding to rewards, others concern awareness to body signals.

What are the possible risks of taking part?

The risks of the brain scanning are described in the brain scanning section above. You may get some slight bruising where the blood sample is taken from your arm but this will subside quickly. The DEXA scan does involve X-rays but only a very small amount, less than a tenth of what a normal chest X-ray will involve and equivalent to 8 hours of natural background radiation in the UK, and the risks are negligible.

If at any point in the study you feel uncomfortable and unable to continue, you can ask to stop the session. You will have the option of either withdrawing completely from the study at that point or only continuing with part of it. For example, if you feel claustrophobic in the scanner, you can press the alarm bell and we will stop the scan and get you out. You can still continue with other parts of the study even if you do not want to take part in the scanning session.

What are the possible benefits of taking part?

You will not benefit directly from taking part in the study, but any understanding that we can develop about the relationships between metabolism, brain function and behaviour can assist the understanding of eating behaviours and decision making.

What will happen at the end of the study?

At the end of the study session, you will be seen by one of the study team who will make sure you are okay and arrange the payment for your time.

After the study is completed and the data are analysed, we will publish the results of this research at scientific conferences and journals to share the results with other researchers. We will also post a summary of the results of the study on the Health Neuroscience's

website (https://www.health-neuroscience.org/). However, no-one will be able to identify you as one of the participants in the study.

Contact Details

If you have any questions about the study, please contact:

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Bernard Wolfe Professor of Health Neuroscience
Wellcome Investigator
Hon. Consultant Psychiatrist
Director of Studies for Preclinical Medicine, Clare College
Department of Psychiatry
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This completes Part 1 of the Study Information Sheet. If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

PART 2

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

You can withdraw from the study at any time without having to explain why. Any stored samples that can be identified as yours will be destroyed if you wish. If any samples have already been processed, we may not be able to destroy these data, but they will anonymised. Withdrawing from the study will not affect any medical care that you receive.

Are there compensation arrangements if something goes wrong?

In the unlikely event of anything untoward happening, insurance has been taken out to cover this study.

Will I be videotaped during this study?

You will be videotaped while in the MRI scanner to ensure that you remain awake throughout the scan sessions. The tapes will be destroyed after they have been reviewed by the research team.

You will also be videotaped when completing study procedures in the Eating Behaviour Unit at Addenbrooke's Hospital. These tapes will be stored on a secure server in the Department of Psychiatry. The videotapes will be analysed by the research team to account for differences in how different people experience the study tasks.

All audio and video recording data will be anonymised and stored on a secure, password protected server, or on an encrypted external hard drive in a securely locked cabinet in the Department of Psychiatry. Audio data will be stored for five years. Video recording data will be store for 15 years. Only members of the research team will have access to these data. We may show parts of the video recording data to closed scientific audience but the videos will be edited to conceal the participant's identity.

What will you do with the blood samples from the study?

We will collect two blood samples from you before and after the brain scans; each sample will be approximately 10 ml. We will also collect blood samples before and after breakfast on day 2. These samples will be used to test for levels of glucose, lipids and hormones like leptin and ghrelin that affect appetite. If you withdraw from the study, your samples will be destroyed and any data gained from them will be removed from the study. All samples will be stored at -80 °C in a dedicated freezer facility at the Dept. of Psychiatry at Addenbrooke's Hospital for use in future research. Members of the research team will have access to your samples. All samples will be stored with a unique ID and only the research team will be able to link this ID back to you, this is known as link anonymisation.

Will my taking part in this study be kept confidential?

All information collected about you during the study will be kept strictly confidential. The normal principles of confidentiality apply just as when you visit your doctor. There are rare occasions when doctors and researchers are obliged to break confidentiality, and this is when they are concerned for your safety or for the safety of others. In such situations, the doctors and researchers have a duty to inform the relevant authorities and take the necessary steps to ensure your and/or other people's safety.

What will happen to the data and results from the study?

All the data from the study will be stored for a minimum of 15 years. Brain imaging data will be stored at the Wolfson Brain Imaging Centre. The data will be kept secure, and your personally identifiable information will not be available to anyone outside the research team. Your data will be shared with other research teams with appropriate ethical approval but this will only be in non-identifiable form. More details are provided below.

The scanning data will be stored on a secure network and only members of the Wolfson Brain Imaging Centre (WBIC) and the research group will have access to the data. Data from the brain scan, psychological tests and questionnaires will be kept securely for a

minimum of 15 years in the WBIC data archive in accordance with good research practice. Imaging and personal data held at the WBIC will remain identifiable, i.e. your brain scan data will be stored under your name and unique WBIC ID number, but is kept securely on a password protected server with restricted access. The custodian for imaging data collected at the WBIC is the Assistant Director of Computing at the WBIC, University of Cambridge. Other researchers working at the WBIC on similar ethically approved research protocols may use the brain scan data. The same standards of confidentiality will apply. Data may also be disclosed to researchers working outside the EEC when that person is working in close collaboration with researchers at the WBIC. In that case, that person would have signed a Code of Conduct guaranteeing that the data will be kept confidential and secure.

Cambridge University Hospitals NHS Foundation Trust and University of Cambridge is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Cambridge University Hospitals NHS Foundation Trust and University of Cambridge will keep identifiable information about you for 15 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at https://www.cuh.nhs.uk/corporate-information/about-us/our-responsibilities/looking-after-your-information or email the Data Protection Officer at: gdpr.enquiries@addenbrookes.nhs.uk.

Cambridge University Hospitals Trust will use your name, and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from Cambridge University Hospitals NHS Foundation Trust and University of Cambridge and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Cambridge University Hospitals NHS Foundation Trust will pass these details to University of Cambridge along with the information collected from you. The only people in Cambridge University Hospitals NHS Foundation Trust and University of Cambridge who will have access to information that identifies you will be people who need to contact you to audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, or contact details.

Cambridge University Hospitals NHS Foundation Trust keep identifiable information about you from this study for 15 years after the study is completed.

Who is organising and funding the research?

This study is organised by the Department of Psychiatry at the University of Cambridge and funded by the Wellcome Trust and Bernard Wolfe Health Neuroscience Research Fund. This study is jointly sponsored by Cambridge University Hospitals Foundation Trust and the University of Cambridge. In the unlikely event of anything untoward happening, insurance has been taken out to cover this study. Cambridge University Hospitals NHS Foundation Trust, as a member of the NHS Clinical Negligence Scheme for Trusts, will accept full financial liability for harm caused to participants in the clinical trial caused through the negligence of its employees and honorary contract holders. There are no specific arrangements for compensation should a participant be harmed through participation in the trial, but no-one has acted negligently.

The University of Cambridge will arrange insurance for negligent harm caused as a result of protocol design and for non-negligent harm arising through participation in the clinical trial.

Who has reviewed the study?

This study has been reviewed by the Cambridge East Research Ethics committee.

What if I have any concerns or complaints about the study?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (details provided below). If you remain unhappy and wish to complain formally, you can do this by contacting the Patient Advice and Liaison Service at the Cambridge University Hospitals at 01223 216756 (during office hours), or at pals@addenbrookes.nhs.uk.

If you would like more information:

We encourage you to think about the points made on this information sheet. You can contact one of the research team members (see below) if you have further questions, and we would be very happy to discuss these with you.

If you have any questions about the study, please contact:

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