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**Participant Information Sheet**

Title of study

**Effect of intranasal insulin on memory, mood, and taste perception**

**Contact person**: Dr Maartje Spetter, email: [Bhamstudies@contacts.bham.ac.uk](mailto:Bhamstudies@contacts.bham.ac.uk) Tel: +44 (0) 121 414 3878

Other UoB investigators: Prof Suzanne Higgs and Dr Pia Rotshtein

Dear Madam,

*Please read this sheet carefully before deciding whether to take part in this study. Contact us if there is anything that is not clear, or if you would like more information.*

**What is the research about?**

Insulin is substance in your body that plays a key role in regulating your blood sugar levels, however there is evidence that insulin in your brain may also influence your memory and mood and taste perception. Our main aim is to investigate how the intake of one dose of insulin, administered via the nasal passages, influences your attention and memory for words and pictures, your mood ratings, and how you experience the taste of certain foods. Additionally we will look at the effect of insulin on your brain responses during certain tests by using a method called functional magnetic resonance imaging (fMRI).

This research will provide us information to get a better understanding about memory, mood and taste preferences in the brain, and could help us to improve the strategies for the development of treatments and drugs that affect certain psychological and metabolic diseases. We will not explain all of the goals of the study beforehand because doing so might influence how you behave while you are participating. However these goals do not affect the risks or any of the procedures explained below. When you have completed the study we will debrief you fully about the study goals.

**What is (intranasal) insulin?**

Insulin is a hormone that is produced in a body organ called the pancreas. When you eat a meal or snack, the release of this hormone promotes absorption of glucose (energy from your food) from the blood into your fat, liver and muscles. You can administer insulin directly into the blood; this is what individual’s with diabetes do before they eat because they do not produce insulin naturally. However, in this study we will administer insulin through the nose with the use of a nasal spray. The insulin will then act directly on your brain receptors, which is not harmful in any way. With this method, we can directly influence the level of insulin in the brain without affecting the levels in the blood. This method has been used in dozens of studies that have investigated the effect of insulin without any side effects. The dose we will use has been used in many previous studies.

**What is (functional) Magnetic Resonance Imaging?**

(functional) Magnetic resonance imaging ((f)MRI) uses strong magnetic fields to create detailed images of your brain and tells us about how the brain works. While you are performing a task, the MRI scanner takes pictures of your brain and we can calculate which brain areas are involved when doing the task. It is a safe non-invasive brain imaging technique, so no radiation or X-rays are used, and there are no side-effects or cumulative risks from having multiple scans. However, because of the strong magnet involved, any metal has to be removed before you go into the scanner. We will check with you during the whole scan to make sure you are okay.For a more detailed description of MRI you can read the standard MRI-information sheet provided by the Birmingham University Imaging Centre (BUIC) (see appendix).

**Who is eligible to take part?**

We are looking for 70 female participants aged 18-65 years to take part in this study. Half of them ((35 individuals) should have a a body mass index (BMI) between 18.5-25 and the other 35 participants a BMI between 30-40. You can calculate your BMI by dividing your weight (in kilograms) by your height (in metres) squared (see http://www.nhs.uk/Tools/Pages/Healthyweightcalculator.aspx).

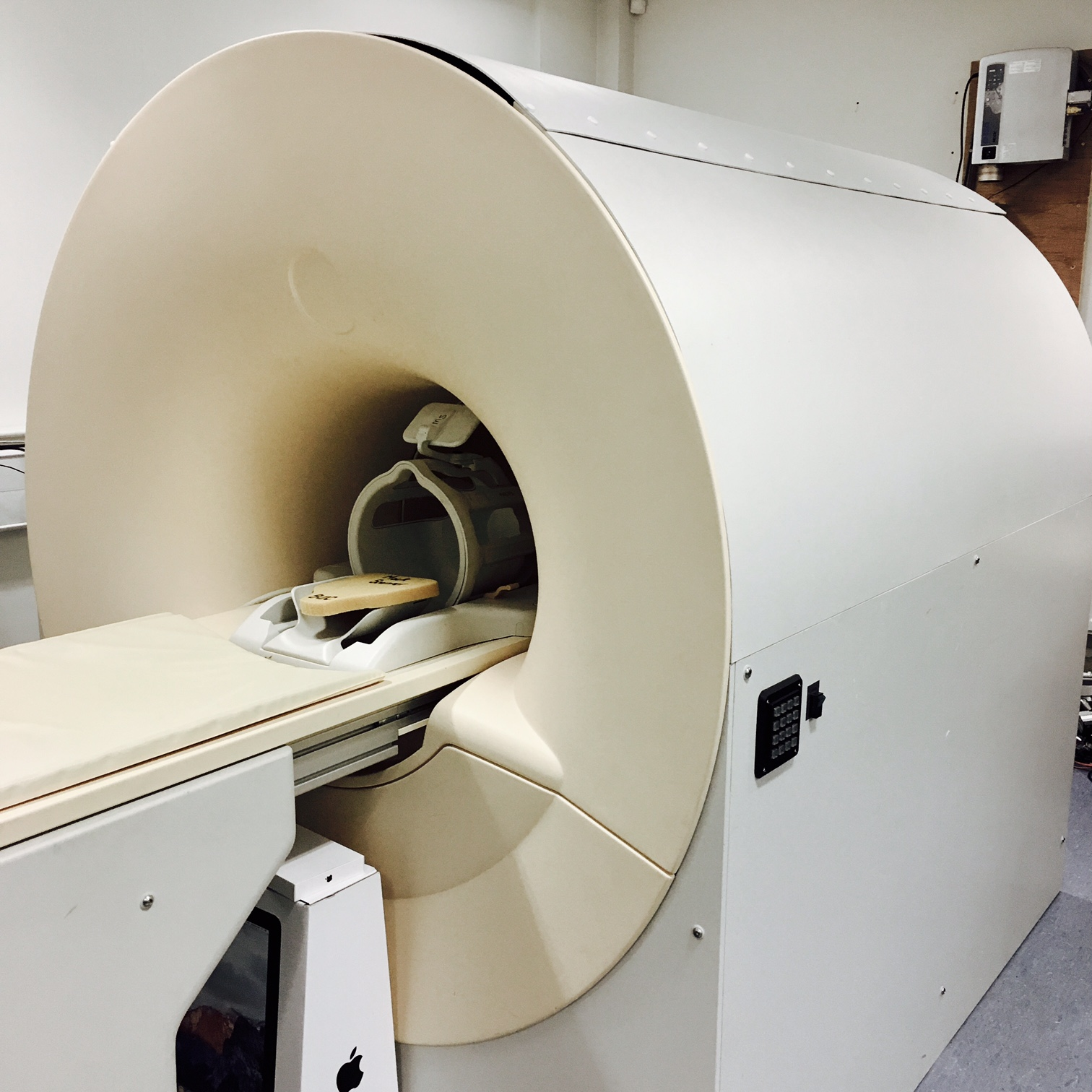
Other important criteria ALL of which you need to meet to participate are:

* Female
* Non-smokers
* Non-diabetic
* Fluent English speaking
* You cannot be pregnant or breast feeding
* No vegan, vegetarian, gluten-, lactose-free diet, or any food allergies
* No eating disorder or current weight loss of more than 5kg in last 3 months
* No metabolic (e.g. metabolic disorder, diabetes), physiological (e.g. depression) or neurological (e.g. epilepsy, headache disorder, multiple sclerosis, traumatic brain injuries) diseases or medication in relation these diseases
* Right handed (it is important for the brain scan that everyone is right-handed, because right- and left-handers show different patterns of brain activation that could make our findings unclear)
* No claustrophobia
* No metal in your body: e.g. pacemakers, mechanical heart valve, mechanical implant such as an aneurysm clip, hip replacement, or if you carry pieces of metal that have accidentally entered your body. This is to ensure that we do not take the risk of metal being in your body when you go into the scanner.
* Not sensitive to loud noises
* No surgical operations in the last 3 months
* No tattoos that are older than 15 years

**What would happen and what is expected of me if I take part?**

*Screening session (****1.5 hours****)*

* It is up to you to decide to join the study. If you decide to take part we will invite you to come to the **Clinical Research Facility at the Queen Elizabeth Hospital (CRF - next to the University of Birmingham** for a screening session. During this session we will explain what the study involves and find out whether you can take part. We will go through this information sheet with you and you can ask any question. After this, you will be asked to sign a consent form. When you have signed the consent form we will ask you to do the following things:
* Filling in an fMRI safety form to ensure eligibility
* Providing details of your medical history and additional a screening by a physician (The physical health check will consist of a measuring your blood pressure and recording your heart rhythm using electrocardiography (ECG). ECG records the electrical activity of your heart; this is a harmless and painless test, and will take about 5 minutes).

* Participate in a brief interview to determine your current and past experience of psychological symptoms and drug taking
* Complete some questionnaires
* Eat lunch (cheese sandwiches and crisps)
* Measurement of height, weight and calculate your BMI
* Go into the mock-scanner if you want to. This is a fake fMRI scanner (without the magnet), and gives you an idea of what it feels like to lie in an fMRI scanner (see figure 1).

This screening session will last approximately **1.5 hours**. After the screening session your GP will be informed of your wish to take part and he/she will notify us if they are aware of any medical reason as to why you cannot take part.

Figure Mock-scanner

If, following the screening, you are suitable, and willing to proceed with the study, you will be asked to attend two testing sessions in total at our Research facilities in the University of Birmingham. During both sessions you will be invited to come to the Clinical Research Facility at the Queen Elizabeth Hospital (CRF - next to the University of Birmingham) in the morning (around 11.30 am), and the session will be finished around 4.30-5pm. So each testing session will take about 5-5.5 hours.

***Test sessions (2x 5-5.5hours)***

On both testing days you will be asked to arrive at the CRF in the morning with prior instructions to consume your standard breakfast about 1 hr before coming to the CRF, and to avoid eating or drinking (except water) anything else in the meantime.

*Arriving at the Lab*

On both test days, you will first be screened by a nurse. He/she will perform a physical health check to confirm your health status, and additionally we test for pregnancy and recent alcohol consumption.

Once the nurse is okay with your participation we will continue with the testing session.

*The tasks you will perform during test sessions one and two:*

1. Questionnaires:

You will be asked to fill in several questionnaires during the whole day, asking you about your appetite and mood.

1. Administration of drug:

Either 1.6 ml/160IU of insulin (equals 8 puffs per nostril with a nasal spray) or placebo (a watery safe solution) will be administrated intranasally (through the nose, like a nasal spray), this will randomized between the two sessions and neither you nor the experimenter will know which one you get when (at the debriefing after you have completed both sessions we will tell you what you have received when).

1. fMRI scan:

During each test session you will undergo one scan session, lasting just under one hour. When in the scanner you will complete several tasks, while we measure your brain responses:

* A go/no-go task: here pictures will be presented for a very short period (a few seconds) on a computer screen. You will be instructed to press a key when items from one category appear, but to withhold responses when items from another category appear.
* Rating pictures task: several pictures will be presented on a computer screen; we will ask you to rate these pictures on pleasantness and appeal.
* In between the tasks mentioned above we will perform several technical scans, where you don’t have to do anything
* Between and during all scans we will be checking if everything is okay.

1. Blood drawn:

At 4 different time-points during the test day a nurse will take 12 ml of blood out of a small tube that is inserted into a vein (I.V. cannula). 12ml is about 3 tubes i.e. 3 to 4 teaspoons, so across all 4 time-points we will collect 48ml/12 tubes. The blood samples will be stored within the CRF, and then sent to a qualified laboratory to be analysed for glucose and insulin levels. We are interested in whether you insulin and glucose levels change due to the insulin administration.

1. Glucose Check

At 5 different time-points during each session a nurse will check your glucose levels with a blood glucose monitoring system. A nurse will use a special needle to prick into your finger; this will give a drop of blood that will be put on a testing strip. This strip is put into the monitoring system and this meter will read out your glucose levels automatically.

1. Lunch and Snack consumption

We will provide you a lunch (consisting of sandwiches, crisps, and water) and later on you will get a cookie snack. While eating we will ask you to rate the taste and how much you like the foods.

1. Money task:

In this task you will be asked to make preference judgments about hypothetical monetary and foodrewards.

1. Memory tests:

We will ask you to fill in questions about emotions and remember certain words and pictures, which we will test later.

Leaving the Unit

We strongly advise you not take part in any other drug studies within 3 months of taking part in this study. This is to exclude any possible interaction between the drugs.

Please note that:

* **You are free to withdraw from the study at any point up to the end of the final test day, and you do not have to give a reason (and your data will be removed at your request).**
* Your name will be removed from the information gathered in the study and it will not be possible to identify anyone from our reports on the study.
* Your medical notes and data collected during the study may be looked at by individuals on the study team, regulatory authorities, or members of the University of Birmingham where it is relevant to your taking part in the research.
* Your GP will be notified of your study participation and may need to disclose relevant medical information to the study research team.

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

*Insulin*

Whilst intranasal insulin is a safe drug and generally well tolerated, it has *possible* side effects, which include: transitory nasal irritation, rhinitis (inflammation of the inside of the nose which may be similar to that experienced during an allergic reaction to pollen), spontaneous nose bleeds and headache. However the likelihood of this occurring is very low. Additionally, there is a very small possibility a hypoglycaemia can occur. This means you have a very low glucose/sugar blood level after intranasal insulin administration, which you can also get after fasting or heavy exercise. Symptoms may include feeling shaky, sweaty, hunger, dizzy or tired. By drinking fruit juice or eating a sugar pill these symptoms should disappear. However, this side effect has never been reported after the use of intranasal insulin. In addition, during the whole study day we (researchers and nurses) will monitor you closely, check your glucose levels, make sure you are comfortable and watch you closely for any possible side effects.

As a precaution, you should not take part in this study if you are pregnant, suspect you might be pregnant, or if you are trying to become pregnant. As mentioned above, if you are a female of childbearing age, you must be using an effective means of contraception, and you will be asked to take a pregnancy test on the test day of the study.

*fMRI*

fMRI is a non-invasive procedure and does not involve any radiation (x-ray). However, the MRI scanner uses a strong magnetic field and therefore you will be asked to empty your pockets and remove any clothing containing metal such as belts. Any piercings must also be removed. The scanner can be very loud, so we will give you headphones and earplugs to block out the sounds. The scanner environment is quite small and confined, so people who are uncomfortable in small spaces may not be able to take part. However, if you feel uncomfortable, you may stop the scan. In the unlikely event that an unusual brain scan is identified, the following procedure will be followed: the scan will be reviewed by an independent radiologist, and if necessary the participant will be referred to their GP (with a covering letter indicating the radiologist’s concerns) in order to arrange clinical scans. Medical diagnostic follow-up will subsequently be arranged with an appropriate healthcare provider. Beyond these no other risks are anticipated.

*Blood*

The risk of drawing blood will be minimal; this may include minor pain, bruising and/or infection from the IV cannula. However it is one of the most common medical procedures.

*Benefits*

There are no direct benefits to taking part in the study. However, you will be making a contribution to our scientific understanding of the brain mechanisms underlying attention and taste preferences.

**Expenses and payments**

If you take part in this study, you will be given £100 (or the option of 10 course credits, for Psychology students via the Research Participation Scheme (RPS), which allows psychology students to participate in studies in exchange for course credit), upon completion of the study. Those who complete only the first screening day will be compensated with £10 for their time.

**Would my taking part in this study be kept confidential?**

All information which is collected about you during the course of the research will be kept strictly confidential and will be accessible only to the research team, the research governance and regulatory authorities. Any information (except the consent form and medical check form) about you will be assigned a number, and will not have your name on it so that it is kept confidential. Your data may be looked at by responsible researchers from the University of Birmingham. The fully anonymised data (which will contain no information that would identify individuals) will be submitted to an online archive in line with the requirements of our funding body. This means your anonymised data can be accessed by researchers beyond the immediate research team. All information will be stored in accordance with the Data Protection Act; this means all data will be stored at the School of Psychology in a locked cupboard. Consent forms and medical checks will be stored in a separate locked archive cupboard, and only the CI can access this. We are obliged to keep all anonymised data for a period of 10 years. After this time, it will be destroyed.

**What will happen to the results of the research?**

The results may be published in a scientific journal. Any research publication would not identify you individually. If you wish to obtain a copy of the published results, please inform the researcher by ticking the appropriate box on the consent form, and we will be delighted to send you a summary of the results.

**Insurance**

The University has in force a Public Liability Policy which provides cover for claims for "negligent harm" and the activities here are included within that coverage.

**Who has reviewed the study?**

The study was reviewed, and given a favourable opinion, by the Sheffield Research Ethics Committee.

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

The study is being sponsored by the University of Birmingham (RG 17-102). Funding will be provided by the University of Birmingham and the Biotechnology and Biological Sciences Research Council (BBSRC), a government funded research council.

**Do I have to take part?**

It is up to you to decide whether or not to take part. If you are interested to hear more about this study or ask for further information in confidence, with no obligation to participate you can contact the researcher Dr. Maartje Spetter (m.s.spetter@bham.ac.uk). This will give you the opportunity to discuss any questions that you may have about the study. If you decide to take part you will be given this information sheet to keep and given at least week to consider whether or not to participate. If you decide to take part you are still free to withdraw from the study at any time and without giving any reason up until the end of the final test day. Choosing to withdraw will not affect any current or future treatment within the NHS. Your GP will also be informed of your participation and will notify us if they are aware of any medical reason as to why you cannot take part. This may involve the GP disclosing relevant medical information about you to the research team. For students, if you decide not to take part, this will not affect any aspect of your university education.

**What do I have to do if I want to take part?**

If you are interested to take part in the study, please let us know and we will make an appointment for a screening session. If following the screening you are suitable, we will make two appointments for the test sessions. If you have any questions do to hesitate to contact us.

**The research team**

During this study a whole team of people with different expertise is involved to make it as comfortable and enjoyable for you as possible. This team includes the chief investigator Dr Maartje Spetter, a PhD-student Elizabeth Schneider, our physician Dr Elizabeth Sapey, nurses from the CRF, the hospital pharmacy, and BUIC personal. If you have any questions or concerns during the study please do not hesitate to talk to one of us.

**What if there is a problem?**

If you have any concern or complaint regarding any aspect of this study, you can contact:

*University of Birmingham:*

Prof Suzanne Higgs (s.higgs.1@bham.ac.uk)

Principal Investigator, School of Psychology

*or*

Dr Sean Jennings

University of Birmingham’s Research Governance and Ethics Manager

Phone - 0121 415 8011

Email researchgovernance@contacts.bham.ac.uk

*CRF –QEH:*

Dr Elizabeth Sapey (e.sapey@bham.ac.uk)

Physician

*or*

Patient Advice and Liaison Service (PALS) complaints department

Phone - 0121 371 3280 email: [complaints@uhb.nhs.uk](mailto:complaints@uhb.nhs.uk).

**Contact for further information**

If you have any further questions about this research, please contact Dr. Maartje Spetter; Bhamstudies@contacts.bham.ac.uk

**Thank you for taking the time to read this information sheet and considering whether to take part in this research.**

**You will be given a copy of this information sheet and a signed consent form to keep if you do take part.**