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PARTICIPANT INFORMATION SHEET

Project Title: Neuronal mechanisms underlying the role of serotonin and its genetic polymorphism on compulsive behaviours

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish. Should you choose to participate you will be given a copy of this information sheet, as well as a signed consent form, to keep for your records.

Part 1 tells you the purpose of this study and what will happen to you if you take part.

Part 2 gives you more detailed information about the conduct of the study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1.

What is the purpose of this study?

The purpose of this study is to investigate how the temporal lowering of tryptophan activity affects learning and decision-making. Tryptophan is a naturally occurring amino acid found in protein rich foods such as meat and dairy products. This amino acid is a main building block of a brain chemical called serotonin. Temporarily lowering tryptophan levels is known to lead to a short-term reduction of serotonin in the brain and could affect people's learning capacity and decision-making. Serotonin is important in a number of psychiatric disorders, including depression, anxiety and OCD. By looking at how people learn and make decisions when serotonin is low we hope to better understand why different mental illnesses occur.

Who are we looking for to take part?

We are looking for healthy volunteers, aged between 18 and 45 years of age.

Do I have to take part?

It is up to you to decide whether or not to take part. If you decide to participate, one of the research team members will contact you to set up a time that is convenient for you. If you decide to take part *you are free to withdraw at any point and without giving a reason*.

Expenses and Payments

You will be given £50 for your time and we will also cover travel expenses incurred from taking part in this study. In addition, you will have the opportunity to win additional money (up to £10 per session) based on your performance on the cognitive tasks.

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

If you decide to take part in the study, we will ask you to come to the Wellcome Trust Clinical Research Facility (WTCRF) located at Addenbrooke's hospital in the morning on a particular day at your convenience. From the midnight prior to your chosen session you will be asked to fast and to drink only water.

After confirming your details and taking your consent, we will take a small blood sample (25 ml, approximately 2 tablespoons of blood). You will be given a special drink. This will either contain the balanced proportion of amino acids (natural substances) that you normally expect to eat in one day or a misbalanced proportion of amino acids – this is a tryptophan depletion drink– the idea of the study is that we don't know which you will have. You will then rest in a quiet area where you can read books or magazines, and watch television for three hours. We will offer you a snack during this period.

After the resting period, you will be given some questionnaires and computerized tests to complete. We will also take a small blood sample to assess the tryptophan levels in the blood. The computerized tests should take three and a half hours, after which you will be free to return home. You can expect to be at the research facility for no longer than eight hours.

What is the drug, device or procedure that is being used?

Tryptophan depletion is a dietary procedure that temporarily lowers serotonin levels in the brain. Tryptophan is a naturally occurring amino acid found in protein rich foods such as meat and dairy products. This amino acid is a main building block of a brain chemical called serotonin. Temporarily lowering tryptophan levels is known to lead to a short-term reduction of serotonin in the brain and could affect people's learning capacity and decision-making. In this procedure we will give you either a mixture of amino acids that you normally expect to eat in one day or a misbalanced proportion of amino acids – this is a tryptophan depletion drink. The amino acids administrated are part of a normal diet, although they are being given as a drink instead of food.
We will also ask you to complete some questionnaires to asses your mood and perform several computerized tests in which we will ask you to learn the association of symbols and win as many points as you can.

What are the side effects of any treatment received when taking part?

Some people find the taste of the drink unpleasant and you may experience mild nausea after drinking it but this diminishes within an hour. The overnight fast and blood tests may cause minor discomfort.

Are there some restrictions when taking part?

Tryptophan depletion has been used in multiple different studies and has never caused any major or lasting problems. If you feel unwell you should refrain from driving or operating machinery during 24 h after participation in the study.

What are the possible benefits of taking part?

There will be no direct benefit to you in participating but the information we get from this study will help improve the treatment of people with OCD and depression.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information on this is given in Part 2.

Part 2.

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

You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

What if there is a problem?

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 (contact: Yulia Worbe, yw327@cam.ac.uk, 01223 764425). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure (or Private Institution). Details can be obtained from the hospital.

NHS bodies are liable for clinical negligence and other negligent harm to individuals covered by their duty of care. NHS Institutions employing researchers are liable for negligent harm caused by the design of studies they initiate. For harm arising from the management of the research, the NHS indemnity scheme will apply. Insurance for negligent and non-negligent harm has been arranged by the University.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Cambridge University Hospitals NHS Foundation Trust and University of Cambridge but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Will my taking part in this study be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the department will have your name and address removed so that you cannot be recognized from it. All data is handled in compliance with relevant UK statutory and Data protection laws.

Any of the data collected during the computerized tasks may be inspected by the research team purely for the purpose of research and to analyze the results. From time to time they may also be inspected by people from the regulatory authorities to check that the study is being carried out correctly. Your name, however, will not be disclosed outside of the study and you will be assigned a code number so

that your data will be linked to this code rather than your actual name, to ensure confidentiality. The master list linking code names with subject names will be stored in paper form in a locked filing cabinet within the Department of Experimental Psychology. Only members of the study team and regulatory authorities (who monitor the quality of the research) will have access to this identifiable data.

Raw cognitive testing data will be extracted from the testing computers and stored in encrypted format in the Department of Experimental Psychology; this data will be anonymized via the use of code numbers for participants. Analysis will take place within the Department of Experimental Psychology by a named member of the study group.
The data will be reported in scientific journals, conference presentations, and internal research group reports. As per established guidelines, research data will be stored for 10 years after the end of the study, using subject codes to ensure anonymity.

Involvement of the General Practitioner/Family doctor (GP)

Before you participate in the study, we will send a letter to your GP notifying him/her of your potential participation. If your GP has the opinion that it is not safe for you to participate in the study, he/she will notify us before you begin the study.

What will happen to any samples I give?

We will collect two blood samples: one at the beginning of the day and one before the computerized tests. The primary reason for collecting blood samples is to confirm the levels of tryptophan in the bloodstream, because factors such as age, gender and food intake can affect the rate of absorption. This information will be stored in a database with your name removed. This data will not be reported by name in any report and will be entirely confidential. If you decide to withdraw from the study, your blood will be destroyed and any data gained from it will be removed from the study**.** All samples will be destroyed once the study is finished.

We will use one of the blood samples to extract DNA from your blood, to determine the variants of particular genes that are important for determining serotonin levels in your brain. If we have collected enough blood samples from a large number of people, we will be able to draw important conclusions on the role of particular genes in certain complex behaviours. For more information on genetic testing, see next question.

Will any genetic tests be done?

In addition to studying the main effects of lower tryptophan levels on cognitive performance, we will also be studying how genes influence individual differences in responding to this manipulation. We will analyse one of your blood samples for a gene that influences the serotonin system, called the serotonin transporter gene. Past research has indicated that this gene subtly influences the brain's processing of emotional material. For our study, we are interested in whether this gene influences the effects of serotonin-related drugs on learning and decision-making. Everyone has either a "long" or a "short" version of this gene. Both versions of the gene are normal and will not indicate anything about your health. No other genetic analysis will be performed and all analysis will be anonymous. This genetic analysis will only be carried out in conjunction with the main study and all samples will be destroyed once the study is finished.

What will happen to the results of the research study?

The results will be reported in scientific journals, conference presentations, and internal research group reports. As per established guidelines, research data will be stored for 10 years after the end of the study, using subject codes to ensure anonymity.

Who is organising and funding the research?

This study is being organized by the Department of Experimental Psychology at the University of Cambridge. This study is supported by funding from the MRC-Wellcome Trust Behavioural and Clinical Neuroscience Institute.

If you have any questions about the study (or if you wish to complain), please contact either of the following:

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24-hour contact number (in case of adverse event): 0033679854954