Information Sheet for Head Injury Patients

Study title:
Major depression after traumatic brain injury: an investigation of D2/D3 receptors and dopamine transporter using PET.

Name of Principal Investigator: Prof David Sharp

You are invited to take part in a new research study. Before you decide, 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 a friend, relatives, and your general practitioner (GP) if you wish. Ask us if there is anything that is not clear or if you would like more information. Please take time to decide whether or not you wish to take part.

What is the purpose of the study?

Traumatic brain injury (TBI), damage to the brain caused by a head injury, is the most common cause of death and disability in young adults. It is commonly caused by road traffic accidents and assaults. Patients can experience problems with concentration, attention span, and memory, called cognitive impairment. Major depression is particularly common after traumatic brain injury (TBI), and may have a significant negative affect on quality of life. Across all types of TBI around a third of patients develop major depression, with a higher proportion of depression seen in those with more severe injuries. Depression can limits the recovery of patients, and is a significant cause of long-term morbidity.

It is likely that abnormalities of the brain chemical dopamine produced by TBI contributes to the development of depressive symptoms, although this has seldom been directly investigated. We will measure dopamine receptor levels in the living human brain with Positron Emission Tomography (PET) imaging, and MRI brain scans will help us interpret the data. PET scans work by using a radioligand which is a compound labelled with a radioactive tag. After injection into a person, radioligands specifically attach themselves to specific receptor proteins and give off a signal, which is detected by the PET camera. In addition, we will assess any associations between depression, dopamine abnormalities and certain genes linked to dopamine functioning and cognition after TBI.
The study may allow patients at risk of developing major depression to be identified early, which would allow targeted intensive treatment to improve clinical outcome. This could be widely used across the NHS to screen patients at risk of major depression following TBI.

**Why have I been invited?**

We are looking for people who have suffered a head injury and subsequently developed depression to take part in the study. We are also looking for people who have suffered head injury without depression to take part for comparison purposes. You have been invited because you have been identified as being potentially suitable for the study. Your doctor may have already discussed this with you, and may contact you by telephone to discuss your participation.

**Do I have to take part?**

No. You decide whether or not you want to take part. If you decide to take part, you will be asked to sign a consent form saying that you agree to participate. You can change your mind and stop taking part at any time. You don’t need to give a reason for changing your mind. If you don’t want to take part, this will not affect the standard of your medical care.

With your permission we will inform your General Practitioner of your participation in the study.

**Why may I not be eligible?**

It will not be possible to take part in this study if you are pregnant, breastfeeding or planning to fall pregnant during the study. If you have a cardiac pacemaker, heart valve or metal in your body that is not compatible with an MRI scanner or severe claustrophobia you cannot take part in the study either. There may be other reasons you cannot take part either due to medications that you are on or other medical conditions that may make it difficult to interpret the results. If you have been exposed to excess radiation in the last year e.g. multiple PET or CT scans then you may not be able to participate.

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

You will be asked to have a screening assessment that will help us decide if you can take part in the rest of the study. The assessment will involve a medical history and examination and psychiatric history involving a number of standardized questionnaires. We will ask you questions about your head injury, any current and past physical or mental health conditions, medicines that you take, history of radiation exposure and your use of any tobacco, alcohol and recreational drugs. It is important that we have a clear list of medications that you take and details of any pacemaker, heart valve or metal you may have in your body. If you have been asked to take part in this
research study from a TBI clinic, most of this will be performed as part of a routine clinical assessment and the information is reused.

We will take blood samples for laboratory tests to check your eligibility (total blood 10ml, about 2 teaspoons). Other routine blood tests will be performed including liver function, kidney function and blood count. We will also perform a routine urine drug screening test for recreational drugs, and a pregnancy test in female participants. If any of these tests show that you cannot be in the study, we will destroy all your samples. No information will be provided to you from the genetic testing.

If we decide you can take part and you still wish to do so, we will ask you to sign a consent form, and you will be asked to attend the imaging centres at Hammersmith Hospital for a further visit. MRI scans will be performed at the Clinical Imaging Facility and a PET-CT scan at Imanova Centre for Imaging Sciences, and tests of your memory and thinking, as well as a psychiatric assessment will be completed.

Here is a complete list of what will happen to you in the study. Each of the visits and procedures will be explained in more detail.

**Screening assessment (as described above)**
- Medical and psychiatric history and examination
- Routine blood tests

**Scanning visit (if you are eligible for the rest of the study after the screening assessment)**
- Blood test for genetic analysis, to look at genes and inflammatory markers important in cognition
- Urine test for recreational drug use
- Pregnancy test, if applicable
- Cognitive and psychiatric assessments
- MRI scans
- PET-CT scan

We will arrange the dates of each visit with you in advance. You can bring a family member or friend along to a visit if you want to.

Sometimes the order of procedures during a visit will vary. Also, sometimes it may not be possible to complete all of the procedures required in one visit, and so a further visit would need to be scheduled.

**Screening visit**

*Medical assessment including blood test*
This will take about 1 hour. It will involve a thorough medical and psychiatric history and examination including blood pressure, weight and height. We will
also take a blood sample (10ml, about 2 teaspoons) to test for routine medical conditions.

**Scanning visit**

**Blood and urine tests**
We will take a sample of blood (10ml, about 2 teaspoons) to look for certain genes (i.e. sequences of DNA) that are thought to affect cognition. We are investigating whether these genes influence recovery and the results will be completely confidential. We will take a urine sample to test for use of recreational drugs and pregnancy (in women).

**Cognitive and psychiatric assessments**
This will take between about 60-90 minutes. We will ask you to fill out some questionnaires relating to your quality of life, mood and sleep. We will ask you some questions about your mood, and you will do some cognitive tests, to see how your head injury has affected you. The tests involve remembering and recalling a series of pictures and words, as well as some timed tests of decision-making and reading.

**MRI scans at the Clinical Imaging Facility**
Magnetic Resonance Imaging (MRI) scanning uses a strong magnetic field to make pictures of the brain. Structural MRI scans show brain anatomy, including if there is any lasting damage from your head injury. The MRI scanner is a large circular magnet with a tunnel down the middle. During the scan you lie on your back inside the tunnel.

The whole MRI scanning procedure lasts about an hour and a half. You may be given one or more breaks from scanning, if required, to make it more comfortable.
During the functional MRI scans, you will do particular tasks. We will explain what tasks you will be doing during the scan and you can practise the task before the scan if necessary. You will make some simple decisions in the scanner to investigate brain function. You will see a small computer screen with instructions on it. You will have a keypad with buttons to press. During the scan, you will see words or pictures on the computer screen. You may be asked only to listen or look or you may be asked to make decisions about what you see or hear, and respond by pressing buttons on the keypad.

During the MRI scans you need to lie as still as possible. We will make sure you are comfortable before the scan starts. The scanner is noisy, so you will wear earplugs and protective headphones. You will be able to communicate with the scan operator through an intercom. You will have an alarm button to press if you are upset or worried during the scan. The scan can be stopped immediately if you are uncomfortable or you don’t like being in the scanner for any reason.

*PET-CT scan at Imanova Centre for Imaging Sciences*

A PET-CT (Positron Emission Tomography-Computed Tomography) scan is a type of brain scan which, when combined with an injection of a radioactive substance called a tracer, produces pictures of brain inflammation. The use of the tracer and the CT scan mean this scan involves a small dose of radiation. If you are a woman, you will have a urinary pregnancy test to confirm you are not pregnant before the scan.

You will have a cannula (a small plastic tube) inserted into a vein for injecting the tracer. This is a very simple procedure, like having a blood test.

The whole PET-CT scan takes about 1.5-2 hours. You will be helped into the PET-CT scanner. Near the start of the scan a doctor will inject a small amount of tracer. During the scan you need to keep your head as still as possible but you are able to move your legs and arms. You will be free to fall asleep if you
are able to. We will make sure you are comfortable before the scan starts. You will not feel anything whilst this is happening. You will be able to communicate with the scan operator through an intercom. You will have an alarm button to press if you are upset or worried during the scan. The scan can be stopped immediately if you are uncomfortable or you don’t like being in the scanner for any reason.

At the end of the scan, you will be helped out of the scanner and the cannula will be removed. You will be observed for a short period afterwards and given refreshments.

You will be given all the time you need before leaving. Simple checks of your heart rate and blood pressure will be assessed prior to discharge to make sure there are no problems before you leave. We will arrange for a taxi to take you home.

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

You will need to attend for the study visits as we have described. In case you have private insurance, you are advised to inform the insurer about your participation to the study

**What restrictions do I need to follow during the study?**

We ask that you do not drink alcohol for 12 hours before attending a study visit. Otherwise you can eat and drink as normal. You should take all your normal medications as usual before a study visit unless we instruct you otherwise.

**What if I am planning to become pregnant or breastfeeding?**

You cannot take part in the study if you are pregnant or breastfeeding. A urine pregnancy test will be performed on all women of child bearing potential prior to the PET-CT scan.

**Will I get paid to take part in this research?**

You will not be paid, but we will also reimburse travel expenses and refreshments for you and any one person who accompanies you. If you wish, you will be given a copy of some of your structural MRI brain images to keep.

If you are screened but found not to be eligible for the study we will pay your travel expenses.

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

You will not have any direct benefit from taking part in this study. The study may provide information useful to the understanding of depression and recovery after TBI.
What are the possible disadvantages and risks of taking part?

Radiation Risk

PET-CT scans involve exposing you to very small amounts of ionising radiation. To put this into context, we are all exposed to approximately 2.5 mSv (millisievert) of background radiation a year. A single PET-CT scan in this study will expose you to 2.2 mSv of radiation. Therefore if you have the PET scan in this study you will be exposed to an equivalent of the natural background radiation to which we are all exposed over one year.

Studies have shown that exposure to radiation (in excess of the natural background radiation) can increase your risk of developing a cancer in the future. We can estimate this risk based on the amount of radiation you receive. For example for each PET-CT scan you receive your estimated risk of developing a cancer is about 1 in 9000. This increased risk is very small compared to the average risk of a fatal malignancy for UK residents (about 1:4).

Other

Taking of blood samples from a vein or insertion of a cannula into a vein may cause minor discomfort and occasionally some bruising or irritation of the veins used for blood sampling. These effects normally clear up completely in a few days.

We operate the MRI scanner within the guidelines of the Medicines and Healthcare Products Regulatory Agency (MHRA) and there are not believed to be any risks. The scanner contains a large magnet, so metal or electronic objects must be kept out. We do not scan women who are pregnant.

What if new or unexpected information becomes available?

There is a small chance the tests we perform may show an unexpected abnormality. If this happens, we will discuss this with you. We will also inform your GP. If necessary, we will arrange for any further medical assessment, tests, and/or treatment that you may need on the National Health Service.

What happens when the study stops?

The specimens that you have given, and the data gathered about you will be looked after and stored at Imperial College London and Imanova, centre for imaging sciences. Data will be analysed by the research team within The Computational, Cognitive and Clinical Neuroimaging Laboratory (C3NL), at Imperial College London.
What if something goes wrong?

Imperial College London holds insurance policies which apply to this study. If you experience serious and enduring harm or injury as a result of taking part in this study, you may be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Prof David Sharp, contact details below). The normal National Health Service complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial AHSC Joint Research Compliance Office.

Will my participation in this study be kept confidential?

All information collected during this research will be kept strictly confidential. Brain images obtained during the study may be used for educational purposes, but only after all personal information has been removed so that you cannot be identified.

With your permission, we will tell your doctors and therapists the results of your scans and psychological tests, and write to your GP to tell him/her that you have taken part.

What will happen to the results of the research study?

The results of the research are likely to be published in peer-reviewed scientific journals and presented at research conferences. However you will not be identified in any report or publication because the data is made anonymous. We can provide you with a copy of any publications if you wish. We will offer a lay summary of the study results to you upon completion of the study as a courtesy and a thank you. You should be aware that the results of some of the tests done as a part of this research may not be available to you individually although we will make every effort to accommodate any of your requests for this information.

Who is funding and organising the research?

The study is being funded by the National Institute of Health Research. The study is sponsored by Imperial College London.

Who has reviewed this study?

The study has been peer-reviewed by expert colleagues working in this field and has been approved by an NHS Research Ethics Committee.
Short title: Major depression after traumatic brain injury: an investigation of D2/D3 receptors and dopamine transporter using PET.
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Thank you very much for taking time to read this information sheet.