INFORMATION FOR THE RESEARCH PROJECT

The effects of creatine on neural function

September 2010

You are being invited to take part in a 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 friends and relatives if you wish. 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.

What is the purpose of this study?

Creatine occurs naturally in the body and plays an important role in providing energy to the cells in our body. There is approximately 120g of creatine is present in the body. About half of this amount is 'made' by putting together smaller constituent molecules. The other half is in the food we eat and is therefore absorbed through the alimentary canal. Creatine can be taken as a food supplement and is commonly used by athletes to increase muscle bulk. More recently, creatine's role in neural function has become a topic of interest and some studies on mice indicate that creatine can play a neuroprotective role. The purpose of this study is to examine the role of creatine on neuralfunction. Previous work by the members of the investigative team from Royal Holloway has shown that the response of parts of the brain responsible for our vision is reduced by 20% after ingestion of creatine. In this previous work, the technique used to measure brain function was functional Magnetic Resonance Imaging (fMRI), which captures brain responses in an indirect way by assessing blood oxygenation changes, which occur when the brain is active. Other techniques can capture the electrical activity of the brain directly. One such technique is magnetoencephalography (MEG).

The purpose of the present study is to undertake further measurements of brain function using both fMRI and MEG. The results of the study will allow us to separate the effects of creatine on the activity in the brain and the blood oxygenation effects that have already been reported.

Why have I been chosen?

You have been invited to participate because you are a normally sighted individual, with no history of diabetes.

Who is organising the study?

Prof Antony Morland (University of York), in cooperation with Professor Andrew Smith (Royal Holloway University of London), has organized this study and will be very happy to answer any questions you may have concerning the procedures you will be asked to undertake. Prof Morland may be contacted at the address shown at the bottom of this sheet.

What will happen if I choose to take part and what will I have to do?

We will ask you to take part in a test of your vision whilst we are scanning your brain using (1) a Magnetic Resonance Imaging (MRI) system and (2) a magnetoencephalography (MEG) system. You will be required to look at a small cross on a screen and to keep looking at it for about 10 minutes at a time. While you look at the cross the screen will also show static or flickering patterns. It is important that you continue to look at the cross when these patterns appear. You will be shown the patterns and the cross before we start the test, so you will know what to look at.

On any one day, we will ask you to do this for 4 separate 10 minute runs in MEG, followed by 2 separate 10 minute runs in MRI. We will repeat these 6 tests on 2 further occasions, exactly one week and two weeks after your first scan date (at the same time of day). Participating in one session in no way obliges you to take part in the subsequent session. In the week between two subsequent scan days, we will ask you to ingest either creatine or a placebo. Neither the investigator nor you will know whether you have been given creatine or the placebo in week one/two. The chance of you receiving the creatine or placebo is 50:50 in week one/two. Creatine and the placebo will be taken orally (2 x 10g per day for 5 days, then 1 x5g per day for the remaining 2 days). We will administer the dose of the creatine and placebo. At the end of the study we will inform you whether or not you were treated with creatine/placebo in week one/two.

You are free to withdraw from the study at any time without giving a reason.

To scan your brain with an fMRI scanner we need you to lie on a bed that will slide into the scanner. We need you to lie very still and we will use some foam pads to help you keep your head still. You will be shown the scanner and will be able to practice lying down before we start any experiments. The scanner will make quite a lot of noise and you will be given ear-defenders to make it quieter for you. You will be given a button that allows you to alert us during the scanning, should you wish to. There is also two-way communication in the scanner, so you can talk to us and we can talk to you. If you do not like lying down in the scanner or find it unpleasant in any way, you can stop at any stage. After you have completed the scans when looking at the cross, there will be time for a break. After a break we will ask you to lie still for a further 15 minutes. This time you will not need to look at anything and can relax and even close your eyes. The whole session will last no more than an hour and a half.

The MEG scanner differs from the MRI scanner and the experience of being scanned is also different. The scanner is very much like a large helmet, similar to an old-fashioned hair dryer. The scanner is silent so you will not need ear defenders. You will need to be very still and we will use a dental impression onto which you will bite to help you stay in the correct position.

What are the potential risks of taking part?

Creatine monohydrate is a food supplement that may be bought in the supermarket. Creatine is not classed as a drug. There are no known adverse effects of creatine supplementation. A theoretical possibility of an adverse renal effect i.e. an adverse effect on kidney function, with long-term use has been suggested. However, no evidence of any such

adverse effect has been found in short- or long- (up to five years) term trials. This study will involve taking the recommended dose of creatine monohydrate for one week only.

The article by Wyss & Schulze is a scientific review of creatine research and pages 252–256 contain a detailed consideration of its safety. You can download a copy of this article at: https://www.ynic.york.ac.uk/~andre/P1119/CreatineResearch_Wyss2002.pdf

The basic conclusion of the review is that there are no known safety concerns for oral supplementation, the most common side effect is weight gain but this gain in weight is associated with creatine use for athletes who often take very high quantities of creatine before exercise. The weight gain is associated with creatine's ability to allow athletes to exercise for longer and thus build extra muscle. The effect of weight gain is unlikely to be seen in users who do not couple creatine ingestion with heavy exercise.

Other anecdotal reports of adverse effects such as muscle cramps, diarrhoea and so on have never been found in scientific studies and it is likely that these anecdotal reports are due to low quality creatine that has been corrupted with other substances and/or to dehydration in athletes who couple high doses with very heavy exercise. The creatine used in this study is 100% pure. The review also highlights the theoretical possibility that long-term use of creatine could possibly cause damage to kidney function. Whilst this theoretical possibility exists none of the scientific studies thus far conducted have revealed any evidence that creatine causes damage to the kidneys. The review concludes that further long-term studies (greater than 5 years) are needed but that *"...current evidence indicates that oral Cr[eatine] supplementation is safe...."*.

If you have any questions about creatine safety or any other issue we will be happy to explain. The placebo will be dextrose sugar, which has no known harmful effects on participants without diabetes. The MRI scanner is an instrument that is used in hospitals to take images of people's brains and it is not known to be harmful. MEG is harmless. The York Neuroimaging Centre takes pride and care in ensuring that no harm, or risk of harm, occurs to participants in research. In the event that something does go wrong and you are harmed during the research study and this is due to someone's negligence, then you may have grounds for a legal action for compensation against The University of York.' Regardless of this, if you have any cause to complain about any aspect of the way you have been approached or treated during the course of this study, then the complaints mechanisms of the University of York, the Department of Psychology, and the York Neuro-imaging Centre are available to you. Be certain that if you have any concern about the study it is perfectly normal and acceptable to seek reassurance from the investigators.

What are the potential benefits of taking part?

Please note that this study is for research purposes and will be of no direct benefit to you. You are under no obligation to participate in this study and if you choose to participate you are free to leave at any time. You will be paid a stipend of £50 for your participation on completion of the 3rd scan session (since scanning is foreseen to take 5 hours in total, this equates to £10 per hour).

Confidentiality – who will have access to the data?

Any information which you give us, and all of the measurements that we collect from you, will be confidential. No names will be used when the research is written up. We shall keep your data for 10 years and will then destroy it securely. We shall comply with the terms of the Data Protection Act 1988. We shall store the information and the measurements in anonymous computer files and in locked filing cabinets. We shall store names and addresses separately from other data. We shall use your data in this study and we may combine your data with data that we gather in future studies. Only three people in our research team will know the contact details of the participants. They are Professor Antony Morland, Dr Heidi Baseler, and Mr Andre Gouws. In addition, staff of the York Neuro-imaging Centre have privileged access to the computer systems and can link the names of participants with their data. Those people are under a professional obligation not to abuse this privilege. With the approval of the Research Governance Committee of the York Neuroimaging Centre, other researchers may be allowed access to the data which you will provide for use in research and teaching. Those researchers will be allowed access to your data in anonymous form only.

Will my G.P. be informed?

We will only contact your G.P in the event that we detect anything in your brain scans that require further investigation. In this unlikely circumstance we would contact your G.P. directly.

What will happen to the results of this study?

The purpose of the study is to learn more about the how the brain responds when creatine is ingested. The results of this study are intended to be prepared for publication in scientific journals and the results will also be disseminated to other scientists interested in brain function.

Thank you for considering taking part in this study. If you have any questions about the study that you wish to ask please do so.

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