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Centre Name: Centre for Psychedelic Research
Study Protocol number: 172258
REC Reference: 26/EM/0094
Short Study Title: FenDep

Study Title: PET imaging and serotonin release in depression and healthy controls

Study Summary

The document provides a summary of the FenDep study. If you wish to find out more information and participate, you will be required to read the full Participant Information Sheet.

What is the purpose of the study?

Depression is a debilitating condition and a leading cause of disability worldwide. Despite this, there has been very little progress on developing new treatments over the last 70 years, and approximately one-third of people with depression do not get better with antidepressants. Serotonin, a chemical messenger in the brain, is thought to play an important role in depression. Most antidepressants, including the first line treatment, selective serotonin reuptake inhibitors (SSRIs), are thought to increase serotonin levels. There is limited evidence, however, as to whether serotonin is depleted in the brains of people with depression. Moreover, at an individual level, it is very difficult to identify who will respond to SSRIs or other types of antidepressants. It is likely that there are several different causes of depression, of which altered serotonin is one. The purpose of this study is to understand how serotonin is altered in depression, whether this is in a particular subgroup, and if this can be used to predict response to SSRIs. To understand how other chemicals in the brain might

play a role, the study will also assess levels of dopamine and glutamate. Both individuals with and without depression will be required for the research.

To measure these different chemicals in the brain, the study team will use several different brain imaging techniques. Positron Emission Tomography (PET) scanning will be used to measure serotonin while Magnetic Resonance Imaging (MRI) will be used to measure glutamate, and indirectly, dopamine. Electroencephalograms, where electrodes on a special cap are placed on the head, will be used to look at brain activity. More details on the research methods can be found in the participant information sheet. The study will use questionnaires and tasks to collect psychological and behavioural information to determine how these relate to the brain imaging results.

While the methods used in this study will not be available in usual clinical practice, the hope is that the results will a contribute to a greater understanding of the underlying chemical alterations in depression, how to identify them, and eventually, how best to treat them.

To participate in this study, you will need to be:

- Older than 21
- Either have diagnosis of depression or enter the study as a healthy volunteer
- Have never taken an antidepressant
- Able to lie comfortably on your back for up to 2 hours

Please note, the study is looking for individuals with depression who are planning on starting an SSRI and willing to be followed up for 8 weeks. The study will also recruit individuals who do not suffer depression to compare results. However, those who do not suffer from depression, will not participate in the 8-week follow-up period.

You will not be able to take part if you:

- Been exposed to significant radiation within the last year
- Have contraindications to blood sampling and arterial cannulation
- Are pregnant or breastfeeding

Please note, that these criteria for participating are an overview and not the exhaustive list.

What does participation look like?

If you are interested in participating, then you will need to read the full participant information sheet. If you broadly meet the study criteria, you will be asked to attend a screening visit at the Imperial College Research Facility (ICRF). More information about the screening process can be found in the Participant Information Sheet. If are enrolled in the study, it will consist of attending two full days of scans and assessments at the ICRF. For volunteers with depression, there will be three remote follow-up calls to check in on how you are responding to the SSRI and complete further questionnaires.

Will I be reimbursed for my time?

Yes, we will reimburse all reasonable travel and food expenses. Participants will be offered £60 for completion of the screening visit, £250 for each full brain imaging day, and for volunteers with depression, £20 for each brief remote follow up call.

If you would like to find out further information about this study, please contact the study team at imperial.fendepMDD@nhs.net (individuals with depression) or imperial.fendepHC@nhs.net (healthy volunteers)

Thank you very much for your time!

APPENDIX 1: CONTRACEPTIVE GUIDANCE

Female participants of childbearing potential are eligible to participate if they agree to use methods of contraception consistently and correctly throughout the study.

Highly effective and acceptable contraceptive methods

Contraceptives allowed during the study include:

- Highly effective methods that have low user dependency:
- Implantable progestogen-only hormone contraception associated with inhibition of ovulation
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion
- Vasectomized partner (Vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the woman of childbearing potential),

and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used.

Highly effective methods that are user dependent:

- Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation
    - oral
    - intravaginal
    - transdermal
    - injectable

Sexual abstinence

- Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the subject.