LETTER OF INFORMATION AND CONSENT FORM
Functional neuroimaging of intrinsic hemodynamic networks in bipolar disorder, unipolar depressive disorder, and healthy controls: Finding a biomarker for bipolarity.
Ethics #: 102586

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Co-Investigators: Peter Williamson, M.D., Jean Théberge, Ph.D., Kristen Ford, Ph.D., Richard Neufeld, Ph.D., Derek Mitchell, Ph.D., and Volker Hocke, M.D.
Sponsor: Pfizer Canada through the Pfizer Psychiatric Research Award.
Pfizer Canada is providing the funds for this study but has no investment in study results.

INVITATION TO PARTICIPATE IN RESEARCH

You are being invited to voluntarily participate in research looking at the way that the brain responds to certain events. The purpose of this letter is to give you the information you need to make an informed decision about whether or not you would like to participate. It is important that you know what the research involves. Please take the time to read this letter carefully and ask questions if you would like to understand some part of it better. You should feel free to ask the research staff any questions you may have about the study at any time. You will be given a copy of this Letter of Information and Consent Form once it has been signed.

PURPOSE OF THE STUDY

By comparing people with depression, bipolar disorder, and healthy controls we hope to learn more about these conditions and how to treat them more effectively. The purpose of this study is to look at how brain networks function in healthy people and people who have depression and bipolar disorder and to see if we can use these differences to distinguish between the two disorders.

EXPECTED DURATION OF STUDY AND NUMBER OF PARTICIPANTS

The study will include:

1) 40 participants who are depressed
2) 40 participants who have bipolar disorder
3) 40 healthy controls

This letter applies to you if you are in any of these three groups. This study will take approximately 6 hours and will be completed on two separate half days, although parts of the research may take less time. The MRI scan will take place at the Lawson Health Research Institute in the St. Joseph's Health Care Centre. The interview and questionnaire portions of the study will take place at FEMAP at 860 Richmond Street.

ELIGIBILITY

This study is an option for people 16 to 40 years old. You cannot participate if you have a major medical or a neurological disorder. Individuals in the depressed group will not be eligible if there is a family history of bipolar disorder. Healthy control participants will not be eligible if there is a family history of mood disorders. Some psychiatric conditions and some substance use patterns will exclude you from participation. This will be evaluated after you agree to participate in the study, if you decide to do so.

You will not be eligible to participate if you cannot have an MRI brain scan. If you have any history of head or eye injury involving metal fragments, if you have some type of implanted electrical device (such as a cardiac pacemaker), if you have severe heart disease (including susceptibility to heart rhythm abnormalities), you should not have an MRI scan unless supervised by a physician. Additionally you should not have a MRI scan if you have conductive implants or devices such as skin patches, body piercing that cannot be removed or tattoos containing metallic inks because there is a risk of heating or induction of electrical currents within the metal element causing burns to adjacent tissue.

PROCEDURES

If you take part in the study you will have the following evaluations. None of these procedures are experimental. That is, the procedures themselves are not under investigation. The only reason you would have them now, however, is as part of this study. They are not necessary for your medical or mental health care. For this study you will be asked to complete the following:

- Psychological interviews and questionnaires that ask about your socioeconomic status, personal and family history of psychiatric symptoms, current mood and psychiatric symptoms. This will take approximately 3 hours.
- In order to have a complete history of any mental illness in your family we will need to contact members of your family to confirm and possibly elaborate on the information you provide for us. On page six (6) you will find space to list the names and contact information of family members you consent to a member of the research team contacting.
- Functional magnetic resonance imaging (fMRI) brain scans will look at what is happening in your brain while you rest comfortably performing a simple visual task to identify faces, emotions and shapes you will see. You will need to set aside 2 hours for this scanning procedure. The MRI machine uses a strong magnet and radio waves to make images of the body's interior. You will be asked to lie on a long narrow couch for 45 minutes while the machine gathers data. During that time you will be exposed to magnetic fields and radio waves. You will not feel either. You will, however, hear repetitive tapping noises that arise from the magnets that surround you. You will be provided with earplugs or headphones that you will be required to wear to minimize the sound and protect your hearing. The space within the large magnet in which you lie is somewhat confined, although we have taken many steps to relieve the "claustrophobic" feeling.

There are no known significant risks with this procedure at this time because the radio waves and magnetic fields, at the strengths used, are thought to be without harm. The exception is if you have a cardiac pacemaker, or a metallic clip in your body (e.g., an aneurysm clip in your brain), have severe heart disease, body piercings, tattoos containing metallic ink or slow release pharmaceutical skin patches. There is a possibility that you will experience a localized twitching sensation due to the magnetic field changes during the scan. This is not unexpected and should not be painful. However, you can stop the exam at any time. The magnetism and radio waves do not cause harmful effects at the levels used in the MRI machine. However, because the MR scanner uses a very strong magnet that will attract metal, all metallic objects must be removed from your person before you approach the scanner. In addition, watches and credit cards should also be removed as these could be damaged. These items will be kept securely for you. This will take place at the Lawson Health Research Institute attached to the St. Joseph's Hospital.

RISKS AND DISCOMFORTS

Psychological Interviews and Questionnaires: You may experience some discomfort by being asked questions about your socioeconomic status, history of psychiatric symptoms, current symptoms, current mood state, and history of difficult childhood experiences. You are free to not answer any question(s) you like. A clinical research team member will be available to you at all times should you have questions or feel distressed by any of the procedures of this study.

Brain Scan Procedure: Part of your participation in this study will involve a research test with Magnetic Resonance Imaging (MRI) system, a common medical diagnostic tool that uses a strong magnetic field, a low frequency magnetic field, and a radio frequency field. No X-rays are used. As with any technology there is a risk of death or injury. For MRI, the risk of death is less than 1 in 10 million and the risk of injury is less than 1 in 100,000. These risks do not arise from the MRI process itself, but from a failure to disclose or detect MRI incompatible objects in or around the body of the participants or the scanner room. It is, therefore, very important that you answer all the questions honestly and fully on the MRI screening questionnaire.

Almost all the deaths and injuries related to MRI scans have occurred because the MRI operator did not know that surgically implanted metal hardware (such as a cardiac pacemaker) was present inside the participants during the MRI scan. Other remote risks involve temporary hearing loss from the loud noise inside the magnet. This will be avoided with ear headphone protection that also allows continuous communication between you and staff during the scan. For comparison, the risk of death in an MRI is similar to travelling 10 miles by car, while the risk of injury during an MRI is much less than the risks associated with normal daily activities for 1 hour.

You may not be allowed to continue in this research study if you are unable to have a MRI scan because, for example, you have some MRI incompatible metal in your body, you may

be pregnant or attempting to become pregnant, or you may have a drug patch on your skin that contains a metal foil.

International controlled studies of human brain development on relatively small sample sizes (546 participants) have shown no untoward effects of repeated MRIs between the ages of 0 and 18. Approximately 25 million clinical MRI procedures have also been performed on children, with no obvious effects. There is, however, a small chance that an as yet unknown problem or side effect may be discovered.

Arranging a time for the evaluations could take a few days. During that time we request that you not take over-the-counter medications that can affect the brain (some antihistamines, pain medication, sleep aids, etc.) but please continue with any usual medications that are prescribed by your physician(s), including your psychiatrist. Please answer fully all questions we ask about medications you are taking during the study.

Other mental tasks in this study involve the need to pay attention and answer a variety of questions with a researcher. These may cause you some mental fatigue and possibly mild frustration. No effects from these tasks are expected to be long lasting.

INCIDENTAL FINDINGS

The MRI experiments carried out for this study are performed solely for scientific purposes. The data which is collected is not optimized to make clinical diagnoses, and the research team involved in these experiments are not trained to make medical evaluations. By participating, you agree that the experimenters are not expected to arrive at a clinical interpretation of the data collected. Nevertheless, there is a small possibility that a potential abnormality might be observed – otherwise known as an incidental finding. If this occurs you will be notified of the issue by the principal investigator of the study who will assist you with your options for following up. Investigators are not responsible for the outcome of medical follow-up or for any incurred costs during medical follow-up. By participating, you agree to the possibility of being informed about a potential incidental finding, according to the above-described procedure. If you do not agree to the potential risk of an incidental finding you should not participate in this study.

RIGHT TO WITHDRAW FROM THE STUDY

Participation in this study is voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time with no effect on your current or future care. You do not waive any legal rights by signing the consent form.

If you are participating in another study please inform our research team to ensure that there is no problem with participating in both studies. Participation in this study will not affect your ability to participate in future research studies.

TREATMENT

If you are a participant in, or seeking treatment with any London Health Sciences Centre program you will remain in the process of obtaining care from a mental health care provider

regardless of whether or not you participate. This study does not interfere in your treatment and you should continue any medications that you have been prescribed. If you are not seeking and/or receiving treatment, your participation in this study is not affected.

ALTERNATIVES TO STUDY PARTICIPATION

If you decide not to participate or if you withdraw from the study before it is completed, you will proceed with your clinical care as before, if you are involved in obtaining or receiving clinical care. You will still be able to receive treatment through this clinic if you need it.

CONTACT PERSON FOR PARTICIPANTS

Please contact a research staff member at **(519) 646-6000 ext. 65196**:

- If you have any injury, bad effect, or any other unusual health experience during this study.
- To report concerns or seek help at any time, day or night: If a research staff member is not in the office, the voicemail outgoing message will give clear directions for what to do. To get immediate help, call the Hospital operator at **(519) 646-6000**, and ask them to reach Dr. Elizabeth Osuch. Dr. Osuch or her representative will return your call as soon as possible, and advise you of any necessary steps required to ensure your comfort and safety, including possible discontinuation of the study or referral for in-person evaluation at an emergency room.

FURTHER QUESTIONS

If you have any further questions about this study you may contact: Dr. Elizabeth Osuch or a research staff member at (519) 646-6000 ext. 65196. If you have any questions about the conduct of this study or your rights as a research participant you may contact Dr. David Hill, Scientific Director, Lawson Health Research Institute, telephone: (519) 667-6649.

REIMBURSEMENT FOR PARTICIPATION

You will be reimbursed $75 for the expense you accrue by your participation in this study. This is intended to include your travel costs, any child-care costs, parking, and all miscellaneous expenses you have from participation. Your reimbursement will not be more than $75 even if your expenses for participation are more than this. You will not be charged for any tests conducted for this study, including the MRI scan. In the event you are not able to complete the study your compensation will be pro-rated accordingly and will not be in excess of $20.

This letter of information is yours to keep.

CONSENT FOR FAMILY CONTACT
Using Hemodynamic brain networks to distinguish between unipolar depression and bipolar disorder in youth.

I consent to having a member of the research team contact the family members listed below ☐

I do not consent to having any family members contacted ☐

Family Member Name	Contact Information

_____
Name of Participant (please print)

_____ _____
Signature of Participant Date

_____
Name of person responsible for obtaining this consent (please print)

_____ _____
Signature of person responsible for obtaining this consent Date

CONSENT FORM

Using Hemodynamic brain networks to distinguish between unipolar depression and bipolar disorder in youth.

I have read the letter of information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

_____

Name of Participant (please print)

_____ _____

Signature of Participant Date

_____

Name of person responsible for obtaining this consent
(please print)

_____ _____

Signature of person responsible for obtaining this consent Date