SUBJECT INFORMATION AND CONSENT FORM

Sponsor / Study Title:	**Bausch Health / Evaluating Motivation and Reward Mechanisms and Brain Substrates in Adults with Obesity: Further evidence that Obesity affects physical and mental health**
Investigator (Study Doctor):	**Roger McIntyre, MD, FRCPC**
Telephone:	**(416) 669-5279 (24 Hours)**
Address:	**Brain and Cognition Discovery Foundation** **750 Dundas Street West, Suite 2-221** **Toronto, ON M6J 3S3**

If you are transferred to an answering machine, please leave a message and the study team will call you back. If you do not receive a call back within 10 minutes, please call again.

Introduction

You are being asked to take part in a research study. Please read this explanation about the study and its risks and benefits before you decide if you would like to take part. You should take as much time as you need to make your decision. You should ask the study doctor or study staff to explain anything that you do not understand and make sure that all of your questions have been answered before signing this consent form. Before you make your decision, feel free to talk about this study with anyone you wish. Participation in this study is voluntary.

Background

You are being asked to take part in a study because you have been diagnosed by a health care professional with a mood disorder, either major depressive disorder (MDD) or bipolar disorder (BD), and obesity; and are between the ages of 18 and 65. A diagnosis of MDD or BD means that you have had episodes of depressed mood and/or of abnormally elevated mood. This study will be completed at the Brain and Cognition Discovery Foundation.

Medical research has shown that for many people with mood disorders, mood symptoms and changes in emotional processing, as well as difficulties with energy and

motivation, interfere with their quality of their life and their ability to function normally at work and with their families. It is believed that in part the difficulties that you're having with your mood and thinking processes are a consequence of obesity.

Scientific evidence now indicates that obesity is associated with changes in the structure of the human brain and its function. The human brain is comprised of circuits connecting brain regions very similar to a motherboard on a computer. Along with changing the structure, obesity appears to change the function of these circuits. It has been often observed in obesity that people with excess weight have significant impairment in their level of motivation, as well as the pleasure they experience in day to day activities. It is believed that the effects of obesity on the body are directly reducing levels of motivation and pleasure. Scientists now have a way that they can test your level of motivation and desire for rewards, to get a better sense of how obesity is affecting your brain.

Purpose

The purpose of this study is to determine to what extent obesity is associated with changes in brain circuits in people who have a mood disorder. This study is primarily interested in looking at select brain circuits known as the cognitive circuit, the affect circuit, the reward circuit, the motor circuit, and the default mode network. These circuits are thought to play a critical role in underlying reward and motivation in adults with obesity. We are primarily interested in three overlapping, yet distinct aspects of anhedonia (inability to feel pleasure). These areas include motivation, reward valuation, and reward learning tools.

Study Design

A total of 20 participants with Major Depressive Disorder (MDD) or Bipolar Disorder (BD), who are also classified as obese, will take part in the study. All participants will be recruited by the Brain and Cognition Discovery Foundation (BCDF). The BCDF is a non-profit organization dedicated to identifying the causes and cures of mental illness.

<u>Study Visits and Procedures</u>

The study procedure will be a single visit where you will meet with a research coordinator and they will gather information related to the age of onset, number of episodes, severity, comorbidity and number of medications and treatments you've taken for your mood disorder. The research team will also be completing a set of measures to assess your mood symptoms, cognitive function, level of motivation and pleasure, as well as quality of life and function. Sociodemographic information will also be collected at this time. Along with mental health measures, the research team will check your weight and height, as well as waist circumference, and will take a blood sample in order to determine your blood-glucose levels, as well as your cholesterol and its

subcomponents (e.g. HDL). The research team will also take blood to evaluate your inflammatory markers, oxidative stress markers, and level of insulin (about 25-30mL). The reason they will be checking this is because it is now known that many of these measures are abnormal in obesity.

After the research team gathers information about your illness history, you will be asked to participate in two tasks. The first task is called the Probabilistic Reward Task (PRT) and measures your learning associated with reward. The second task is called the Monetary Incentive Delay (MID) task and assesses your anticipation of rewards. Both tasks take approximately 20 minutes each to complete.

You will then be asked to have an MRI scan completed on the same day. The MRI scan will take place at the University of Toronto. The research team will coordinate this and make sure you are chaperoned through the entire process. During the MRI you will be asked to participate in a measure of motivation and reward. The measurement tool is called the Effort Expenditure for Rewards Task (EEfRT). The test will be very simple and takes approximately 20 minutes to complete. You will be asked to push a button on a button box. The pushing of the button will either be simple, using pushing of the index finger, or complex pushing where you will be using your fifth finger to push the button 10-30 times. You will be rewarded with money proportionate to how many times you push the button. For the simple task, you will receive $1 for every time you push and for the complex task, you will be variably rewarded between $3-$5. The research team will make it very easy for you to understand when you do it. Upon completion of the MRI scan, your involvement in the study will be completed. It is estimated that the total duration of the assessment with the research team will be 1-2 hours and the MRI scan takes approximately 1 hour.

Risks Related to Being in the Study

This study has risks. Some of these risks we know about. There is also a possibility of risks that we do not know about that have not been seen in study participants to date. Some can be managed. Please call the study doctor if you have any side effects even if you do not think they have anything to do with this study. The risks we know of are:

a) MRI risks: There are few potential risks of having an MRI scan, as it is a non-invasive procedure and does not involve any radiation. The main potential risk comes from loose metal objects, which, if taken near the scanner, could be dangerous. The combination of the noise of the scanner and confined space can also be stressful for people who feel uncomfortable in closed spaces.
b) Blood draw risks: Drawing blood may cause very mild pain, bruising, redness, and rarely infection at the needle stick.

c) Other risks: In addition to medical risks, being in this study may make you feel uncomfortable. You will be asked personal questions about your psychiatric and medical history. You may refuse to answer questions or stop the interview at any time if there is any discomfort. Administering the cognitive testing may sometimes be frustrating particularly if you are not performing as well as you think you should, and may also lead to mild mental and physical fatigue.

Benefits to Being in the Study

You may or may not receive any direct benefit from being in this study. Information learned from this study may help other people with mood disorders in the future.

Voluntary Participation

Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now and then change your mind later. You may leave the study at any time without affecting your care. You may refuse to answer any question you do not want to answer, or not answer an interview question by saying “pass”.

We will give you new information that is learned during the study that might affect your decision to stay in the study.

Alternatives to Participation

This research study is for research purposes only. The only alternative is to not participate in this study.

Confidentiality

Personal Health Information

If you agree to join this study, the study doctor and his/her study team will look at your personal health information and collect only the information they need for the study. Personal health information is any information that could be used to identify you and includes your:

- telephone number
- email address
- month and year of birth
- new or existing medical records, that includes types, dates and results of medical tests or procedures.

The information that is collected for the study will be kept in a locked and secure area by the study doctor for 25 years. A list linking your study number with your name will be kept by the study team, in a secure place, separate from your study file. Only the study team or the people or groups listed below will be allowed to look at your records. Your

participation in this study will also be recorded in your medical record at this site. This is for clinical safety purposes.

Representatives of the research ethics review board - Advarra IRB (an independent ethics committee that reviewed the ethical aspects of this study to help protect the rights and welfare of study participants), may have access to the information collected for this study, at the study site.

The blood samples will only be used for current study purposes. The samples will be labelled with your study ID and no personal identifiable information will be recorded on the samples.

Study Information that Does Not Identify You

Some study information will be sent outside of the site. Any information about you that is sent out of the site will have a code and will not show your name or address, or any information that directly identifies you.

All information collected during this study, including your personal health information, will be kept confidential and will not be shared with anyone outside the study unless required by law.

You will not be named in any reports, publications, or presentations that may come from this study.

By signing this information and consent form, you consent to the collection, access, use and disclosure of your information as described above.

Rights as a Research Participant

If you are harmed as a direct result of taking part in this study, all necessary medical treatment will be made available to you at no cost.

By signing this form, you do not give up any of your legal rights against the investigators, or involved institutions for compensation, nor does this form relieve the investigators, or involved institutions of their legal and professional responsibilities.

Withdrawal from Study

You may withdraw early from this study for reasons such as:

1. Voluntary discontinuation by you without prejudice to further treatment
2. Worsening of symptoms and/or emergence of suicide thinking

If you decide to leave the study, you have the right to request withdrawal of information collected about you, your blood and your MRI scan, as well as of any information obtained from these samples. Let your study doctor know.

If you do not request withdrawal of data collected on you, the information collected before you left the study will still be used in order to help answer the research question. No new information will be collected without your permission.

The study doctor may also withdraw you from the study if your condition worsens, if you do not follow the doctor's instructions, if the study doctor feels it is in your best interests to be withdrawn, if the study sponsor discontinues the study, or for administrative reasons. You can be withdrawn without your consent, but the study doctor will tell you why.

Costs and Reimbursement

You will be provided the amount of money earned during the EEfRT task. Also, you will be provided with $400 for volunteering your time. You will be paid following each completed visit.

There is no cost to you, your private medical insurance (if any), or the public health insurance plan, for study procedures.

Incidental Findings

Incidental findings are previously undiagnosed medical or psychiatric conditions that can be, potentially, discovered in the study assessments, for example, a MRI scan. Results will be discussed with you, individually, in a separate visit. If necessary, additional tests and assessment will also be arranged by the study doctor.

Conflict of Interest

Researchers have an interest in completing this study. Their interests should not influence your decision to participate in this study. You should not feel pressured to join this study.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call toll free: 877-992-4724
- or by email: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00032575.

Consent

The study doctor has my permission to tell my regular doctor about my being in this study: ❒ YES ❒ NO

This study has been explained to me and any questions I had have been answered. I agree to the use of my information as described in this form. I know that I may leave the study at any time. I agree to take part in this study.

Print Study Participant's Name	Signature	Date

(You will be given a signed copy of this consent form)

My signature means that I have explained the study to the participant named above. I have answered all questions.

Print Name of Person Obtaining Consent	Signature	Date

Signature of Investigator

Print Name of Principal Investigator	Signature	Date