RESEARCH PARTICIPANT CONSENT FORM

TITLE:	Decoding Emotional Dynamics Driving Mood Instability in Bipolar Disorder
PROTOCOL NO.:	2025-005 WCG IRB Protocol #20252305
SPONSOR:	Laureate Institute for Brain Research
INVESTIGATOR:	Masaya Misaki, Ph.D. 6655 South Yale Avenue Tulsa, Oklahoma 74136 United States
STUDY-RELATED PHONE NUMBER(S):	918-481-4100 (24 hours) Masaya Misaki, Ph.D. 918-502-5137 (office) Salvador Guinjoan, M.D., Ph.D. 918-502-5119 (office)

RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you have questions, concerns, or complaints, or think this research has hurt you, talk to the research team at the phone number(s) listed in this document.

How long will I be in this research?

We expect that your participation in this research will last approximately 2.5 hours on the first day and 4 hours on the second day. The second session will be scheduled to take place within 7 days after the first session. If needed, there is a 3-day window to reschedule the second session to allow for flexibility.

Why is this research being done?

The goal of this research is to learn more about how the brain causes mood swings in people with bipolar disorder (BD). People with BD often have unpredictable changes in their emotions, which can make daily life challenging and are sometimes difficult to treat. This study will use brain scans (MRI) and advanced methods to study complex patterns in brain activity. These methods help us track how brain activations change over time and understand how these changes may be different in people with BD compared to those without the condition. By learning more about these brain patterns, we hope to find better and more personalized ways to help people with BD in the future.

What happens to me if I agree to take part in this research?

If you decide to take part in this research study, your first visit will involve answering questions about your mood and emotional experiences. On a different day, you'll return for a brain scan (MRI). Before the scan, you will be asked questions about your current mood. During the scan, you'll do simple tasks like recalling emotional memories and trying to manage your feelings. After the scan, you'll answer more questions about how you're feeling.

Could being in this research hurt me?

Some of the questions asked on surveys or during interviews may make you feel sad, tired or uncomfortable.

During the MRI scan, you may feel discomfort from being confined in a small space, skin sensations or muscle twitching, dizziness from lying down, and discomfort from loud noises.

Emotional discomfort from recalling distressing personal memories during the tasks may temporarily worsen your mood.

Some participants may also feel fatigued or emotionally drained after the MRI session.

As with any research and even with strong data protections in place, there is a slight chance someone might obtain unauthorized access to your data through malicious acts.

Will being in this research benefit me?

It is not expected that you will personally benefit from this research. Your answers to the questions and/or results from MRI may help inform future research projects.

What other choices do I have besides taking part in this research?

The only alternative to participating is to not participate.

What else should I know about this research?

Other information that may be important for you to consider so you can decide whether to take part in this research is that:

- The study involves recalling and reflecting on personal emotional experiences, including negative memories, which some participants may find emotionally taxing.
- You will need to lie still in an MRI scanner for up to two hours.
- Participation requires attending two separate sessions.

- Alcohol and drug screening will be conducted before the MRI scan.
- A pregnancy test will be administered for female participants.
- There are no out-of-pocket expenses or medications required for this study.
- There is a possibility that your deidentified information may be used or distributed for future research studies without your additional informed consent.

DETAILED RESEARCH CONSENT

You are being invited to take part in a research study. A person who takes part in a research study is called a research participant.

Why is this research being done?

The goal of this research is to better understand how the brain causes mood swings in people with bipolar disorder (BD). People with BD often experience unpredictable changes in their emotions, which can make daily life difficult and are sometimes hard to treat. We want to learn more about how brain activity leads to these emotional ups and downs. To do this, we will use a brain scan called MRI, which lets us take detailed pictures of brain activity while you do simple tasks, like remembering emotional memories and trying to manage your feelings. We will also use advanced methods to study complex patterns in brain activity. These methods help us track how brain activity changes from moment to moment and how those changes relate to your emotional state. We will compare these brain patterns between people with BD and people without BD (healthy participants) to see how they differ. This could help us find out which parts of the brain are involved in mood changes and why these changes happen more often in some people. In the long run, we hope this research will lead to better and more personalized treatments for people living with BD.

About 64 participants (32 with bipolar disorder and 32 without any psychiatric condition) will take part in this research.

How long will I be in this research?

We expect that your participation in this research will last approximately 2.5 hours on the first day and 4 hours on the second day. The second session will be scheduled to take place within 7 days after the first session. If needed, there is a 3-day window to reschedule the second session to allow for flexibility.

What happens to me if I agree to take part in this research?

If you choose to take part in this study, you will be asked to come to the Laureate Institute for Brain Research (LIBR) in Tulsa, OK, for two separate visits.

You will be asked to participate in an MRI scanning session during which you will perform tasks while the MRI takes images of your brain working. For your safety, you will be given a brief pre-screening form to complete. The information on this form will tell us if you have any metal, or other items that affect safety in a magnetic field, inside your body. The pre-screening form may identify some unanticipated medical findings that prevent you from participating in the MRI scan. If so, these findings will remain as confidential as possible and will be discussed with you by a researcher involved in this study. Before the scan, you will also be asked to complete both a

breathalyzer and a urine drug screening test. Female participants will have an over-the-counter urine pregnancy test immediately before the scanning session. You will not be allowed to participate in the study if the pregnancy test reads positive.

The MRI scanner rapidly takes pictures of your brain without exposure to harmful radiation – there are no X-rays or anything like X-rays in an MRI scanner. The MRI scanner is based on a magnet with a metal cylinder with a strong magnetic field inside. During the MRI, you will lie on a table that can slide in and out of the magnet. You will be asked to lie still during scanning by remaining as relaxed as possible. While in the scanner you will hear loud knocking noises. You will be fitted with earplugs to muffle the sound. You will always be able to communicate with the MRI staff during your scan through an intercom and a squeeze bulb. You may ask to be moved out of the machine at any time. We may also monitor your heart rate and respiration using a device on your finger and a rubber belt that fits loosely around your chest.

The study will use two types of brain scans: anatomical MRI and functional MRI. An anatomical MRI takes detailed pictures of the structure of your brain. It helps us look at the shape and size of different brain areas. A functional MRI shows how your brain is working while you do simple mental tasks. It measures changes in blood oxygen levels in different parts of the brain. When a brain area is more active, it gets more oxygen-rich blood. This helps us see which parts of your brain are working harder during certain activities. These scans are painless, and do not use any harmful radiation or injections.

Below are the contents of the study sessions.

Visit 1: Preparation Session (about 2.5 hours)

- **Informed consent discussion and signing forms**
- **Clinical interviews and questionnaire**

  You will answer questions about your mood, emotions, daily functioning, and life experiences. These include:
  - Montgomery–Åsberg Depression Rating Scale (MADRS)
  - Young Mania Rating Scale (YMRS)
  - Ruminative Response Scale (RRS)
  - Brief State Rumination Inventory (BSRI)
  - Temporal Experience of Pleasure Scale (TEPS)
  - Emotion Regulation Questionnaire (ERQ)
  - Difficulties in Emotion Regulation Scale (DERS)
  - Positive and Negative Affect Schedule-X (PANAS-X)
  - PROMIS measures (e.g., Depression, Anxiety, Fatigue, Sleep, Cognitive Functioning)
  - Sheehan Disability Scale (SDS)
  - State-Trait Anxiety Inventory (STAI-T)
- **Recalling personal memories**

  You will think of 8 emotional memories, 4 positive and 4 negative, that you will use in the MRI tasks. You will write brief keywords to help you remember them.

Visit 2: MRI Scan Session (about 3.5 to 4 hours)

- **MRI safety screening**
  We will check to make sure it is safe for you to undergo MRI scanning.
- **Alcohol and drug screening**
  You will be asked to complete both a breathalyzer and a urine drug screening test.
- **Pregnancy test (if applicable)**
  Female participants will complete a urine pregnancy test.
- **Pre-scan questionnaires**
  These check your current mood and emotional state. They include:
  - Young Mania Rating Scale (YMRS)
  - Brief State Rumination Inventory (BSRI)
  - Positive and Negative Affect Schedule-X (PANAS-X)
  - Quick Inventory of Depressive Symptomatology – Self-Report (QIDS-SR)
  - State-Trait Anxiety Inventory (STAI-S)
- **Task explanation**
  We will explain what to expect during the scan and guide you through a brief demonstration of the computerized task performed in the scanner to ensure you are comfortable with it.
- **MRI scanning (up to 2 hours total)**
  MRI scanning procedures include:
  - Structural MRI
  - Resting-state fMRI
  - Functional scans during the Think and Regulate Affective states Task

  While in the task, you will:
  - Recall personal emotional memories guided by keywords shown on the screen
  - Rate how you feel using a slider tool
  - Try to boost positive feelings during certain blocks
  - Do a simple attention task to help reset your focus between emotional tasks
  - Rest quietly with your eyes open while looking at a crosshair on the screen

  We will also monitor your heart rate and breathing during the scan for safety and to help us better understand your brain activity.
- **Post-scan questionnaires**
  These check your current mood and emotional state. They include:
  - Positive and Negative Affect Schedule-X (PANAS-X)
  - State-Trait Anxiety Inventory (STAI-S)

  You will also be asked how you felt during the scan and whether you feel tired or emotionally drained.

  If you feel emotionally distressed, support will be available. A clinical staff can speak with you if needed.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

- Follow all instructions provided by the study team, including how to prepare for each session and how to complete the emotional memory and regulation tasks.
- Inform the study team of any changes to your health or medications between visits, especially if you start or stop any psychiatric or neurological treatments.
- Let the study team know if you experience emotional distress or unusual discomfort during or after any part of the study.
- Avoid recreational drug or alcohol use before the MRI scan, as these can affect brain activity.
- Follow all MRI safety procedures as explained by the staff.

Could being in this research hurt me?

We will do everything in our power to keep your private identifiable information private, however complete confidentiality cannot be guaranteed. As with any research and even with strong data protections in place, there is a slight chance someone might obtain unauthorized access to your data through malicious acts. We will protect against this by storing your personal identifiable information in password protected databases behind electronic firewalls. Paper records, if used for this study, will be stored in a locked file cabinet behind locked doors.

Some of the questions on the surveys may make you feel uncomfortable, sad, anxious, depressed, or tired. You may skip any questions you are not comfortable with answering. You may stop the survey at any time.

Emotional discomfort from recalling distressing personal memories during the tasks could temporarily worsen mood.

Some participants may also feel fatigued or emotionally drained after the MRI session.

People are at risk for injury from the MRI magnet if they have any of the following metal implants or fragments:

- pacemakers or other implanted electronic devices
- brain stimulators
- dental implants
- aneurysm clips (metal clips on the wall of a large artery)
- metallic prostheses (including metal pins and rods, heart valves, and cochlear implants)
- permanent eyeliner
- implanted delivery pump
- shrapnel fragments

You will be asked to complete an MRI screening form for the MRI scan. You will be screened for these implants or metal fragments before the study, and if you have any of them, you will not receive an MRI scan and cannot be in the study. Tell the study doctor if you are uncertain whether you have any metal objects in your body. In addition, all magnetic objects (for example, watches, coins, jewelry, and credit cards) must be removed before entering the MRI scanner room.

Welders and metal workers are also at risk for injury because they may be unaware of small metal fragments in the eye.

There are no known long-term risks or consequences of MRI scans. However, you may become uncomfortable because you will be lying in a small space. Some people are bothered by the loud thumping noises made by the scanner. You will wear earplugs to reduce the noise and increase your comfort during scanning. LIBR study staff will closely and continuously monitor you throughout the scanning procedure. You will be able to use an emergency call button at all times during the scan. You will be removed from the scanner immediately if you request to be removed.

If you are a female, it is best that you not be pregnant while participating in this study. A urine-based pregnancy test may be obtained prior to any MRI scanning.

If you are deemed to constitute a serious risk for suicide while on LIBR premises, LIBR policy requires that you be escorted to the onsite, 24-hour emergency facility at Laureate Psychiatric Clinic and Hospital (which is located approximately 100 yards down a sidewalk from the LIBR facility). If you refuse to be escorted to this facility and leave the LIBR premises, the study clinician will contact the Community Outreach Psychiatric Emergency Services (COPES – 918-744-4800), which is available 24 hours per day to send a mobile unit to your home.

If you identify suicidal ideation while not at a LIBR facility, you will be instructed to call 911 or to go to the nearest emergency room if you feel you are a threat to yourself or others. You will also be given the contact details of the Tulsa Community Outreach Psychiatric Emergency Services (COPES – 918-744-4800), if applicable.

Will it cost me money to take part in this research?

Neither you nor your health insurance will be charged for any of the study tests, procedures, or activities. If you need to be hospitalized, voluntarily or involuntarily, Laureate Institute for Brain Research does not intend to provide payment for this, and you or your insurance provider will be billed for these costs.

Will being in this research benefit me?

There are no benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research.

What other choices do I have besides taking part in this research?

This research is not designed to diagnose, treat or prevent any disease. Your alternative is to not take part in the research.

What happens to the information collected for this research?

Your private information and your medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsor
- People who work with the research sponsor

- Government agencies, such as the Food and Drug Administration
- WCG IRB, the Institutional Review Board (IRB) that reviewed this research
- Laureate Institute for Brain Research monitors and auditors
- ClinCard (for processing study compensation)

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

Data collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent. Any data or results obtained from these future research will not be shared with you because it is not possible to predict how they will be utilized by other Investigators.

Certificate of Confidentiality

We will do everything we can to keep others from learning about your participation in this study. To further help us protect your privacy, we have obtained a Certificate of Confidentiality from the United States Department of Health and Human Services (DHHS). With this Certificate, we cannot be forced (for example by court order or subpoena) to disclose information that may identify you in any federal, state, local, civil, criminal, legislative, administrative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except to prevent serious harm to you or others, and as explained below.

You should understand that a Certificate of Confidentiality does not prevent you, or a member of your family, from voluntarily releasing information about yourself, or your involvement in this study.

If an insurer or employer learns about your participation, and obtains your consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy. Disclosure will be necessary, however, upon request of DHHS for the purpose of audit or evaluation, and is limited only to DHHS employees involved in the review.

Who can answer my questions about this research?

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number(s) listed in this document.

This research is being overseen by WCG IRB. An IRB is a group of people who perform independent review of research studies. You may contact them at 855-818-2289 or clientcare@wcgclinical.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.

- You want to talk to someone else about the research.
- You have questions about your rights as a research participant.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What if I am injured because of taking part in this research?

If you are injured or become sick because of being in this research, call the study doctor immediately. In the event of an emergency, call 911. Be sure to tell the emergency staff and other healthcare providers of your participation in this study. If you are injured or become sick during your study participation, contact your healthcare provider or go to your local emergency room. You or your health insurance provider will be billed to cover the cost of the medical or emergency services provided. No funds have been set aside by study sponsor or Laureate Institute for Brain Research to compensate you if you are hurt or get sick because of or during study participation. However, you still have the right to bring a lawsuit if you think you were harmed and deserve compensation.

Can I be removed from this research without my approval?

The person in charge of this research can remove you from this research without your approval. Possible reasons for removal include:

- It is in your best interest to stop participating
- You are no longer able to safely undergo MRI scanning (e.g., due to new metal implants or health changes)
- You become pregnant
- You do not follow study instructions or miss scheduled appointments
- The research is changed or canceled by the sponsor, the Institutional Review Board (IRB), or a regulatory agency
- You begin taking a medication or receive a diagnosis that makes you ineligible for continued participation

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

What happens if I agree to be in this research, but I change my mind later?

Taking part in this study is voluntary. You may choose not to participate. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. If you agree to participant then later decide against it, you can withdraw for any reason and leave the study without penalty or loss of benefits entitled.

If you decide not to give permission to use your data, then you will not be able to be in this research study. You may withdraw or cancel your permission, but this permission will not stop automatically. You may withdraw or take away your permission to use and disclose your health information at any time. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be

gathered after that date. Information that has already been gathered may still be used and given to others. To withdraw or cancel permissions, *please contact Masaya Misaki in writing at the Laureate Institute for Brain Research, 6655 S. Yale Ave, Tulsa, OK 74136, or by email to mmisaki@laureateinstitute.org.*

Will I be paid for taking part in this research?

For taking part in this research, you may be paid up to a total of **$190**. Your compensation will be broken down as follows:

- **$50** for completing Visit 1 (Preparation Session, about 2.5 hours)
- **$140** for completing Visit 2 (MRI Scan Session, about 4 hours)

You will be paid through a ClinCard (similar to a debit card). Payments will be deposited within 24-48 hours of the visit.

The results from this study may lead to new commercial products or tests. If this happens you will not receive any additional compensation.

What If There Are New Findings?

We will provide you with any significant new findings developed during the research study that may affect your health, welfare, or willingness to continue your participation in this study. You may be asked to sign a new consent form if this occurs.

Statement of Consent:

By signing this consent document, you agree that you have read and understand the document and have had a chance to ask questions and you have received satisfactory answers to all of your questions. If you agree to be in this study, you will be given a signed and dated copy of this consent form. Your signature documents your consent to take part in this research.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

Your signature documents your consent to take part in this research.

Signature of participant	Date
Signature of person obtaining consent	Date