University of Pittsburgh

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: Anhedonia, Development, and Emotions: Phenotyping and Therapeutics (ADEPT) Study

Phase 1: Anhedonia Phenotyping

Version for Adults

PRINCIPAL INVESTIGATOR:
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If you have any questions about your rights as a research subject or wish to talk to someone other the research team, please call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668. You may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during your participation. You may request a copy of this consent form.

SOURCE OF SUPPORT: Wellcome Leap MC Psych

Summary of Key Points

- The goal of the ADEPT Study is to understand anhedonia in young people and how it changes based on treatments targeting the brain circuit underlying it. Anhedonia is a challenging mental health symptom that involves difficulty with motivation to experience pleasant events. This study could help develop treatments for people whose depression does not improve with traditional treatments.

- The ADEPT Study includes two phases. This consent form specifically details the information relevant to Phase 1 of the study. In Phase 1, participants are asked to go through a series of activities to measure anhedonia, including MRI scans, blood draws, behavioral tasks, clinical interviews, questionnaires, and app-based assessment of experiences and behaviors.

- Phase 2 of the ADEPT Study, not outlined in this consent, involves therapeutic activities, such as transcranial magnetic stimulation (TMS) and positive affect training. If you qualify and are interested, you may choose to do Phase 2 activities in addition to Phase 1. This would involve a separate Informed Consent Form.

Introduction

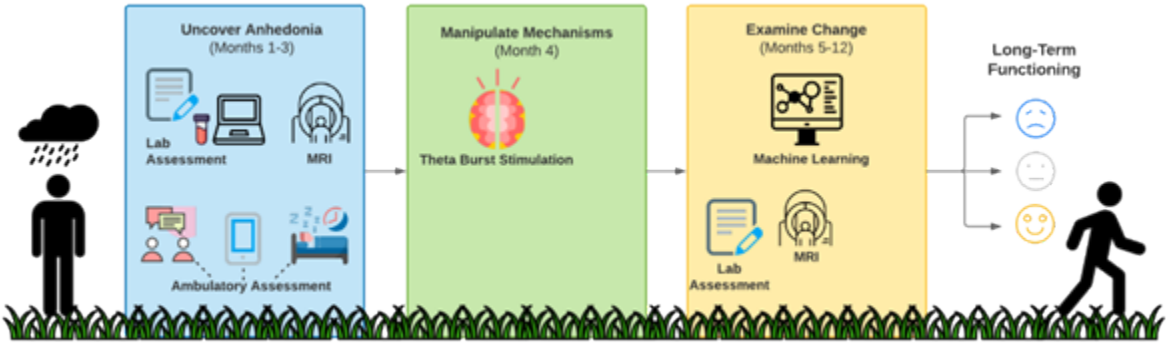
Before agreeing to take part in this research study, it is important that you read and understand the following information. This consent document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternatives that are available to you and your right to withdraw from the study at any time. No guarantees or promises can be made as to the results of the study.

If you are not completely truthful with the study team and investigators regarding your health history, you may be harmed by taking part in this study. You must think about the information in this consent document for yourselves. You must then decide if you want to take part in the study.

<u>Why is this research being done?</u>

In this research study, we are trying to understand and change anhedonia in young people with depression. Anhedonia is experienced by many people who have depression, and it involves difficulty with motivation, energy, and anticipation of pleasant events. People who experience anhedonia often have more severe depression, experience depression for longer periods of time, and don't easily get better with traditional treatments. We want to understand anhedonia early in life so that we can find ways to help young people develop along healthy pathways and avoid chronic illness. Anhedonia is related to function in the brain's reward circuit, inflammation in the body, and people's experiences and behaviors, and will measure all of these. We also want to see whether we can understand anhedonia by using treatments that could improve it. To do that, we are using neuroscience to guide us, providing activities that have been used to treat depression and target the brain's reward circuit, which is believed to be the

source of anhedonia. Finally, we will measure anhedonia over approximately 1 year to see how it changes with time, development, or treatment-based experiences. Eventually, the findings of this study might be useful for treating depression and improving people's quality of life.



What will happen in this study?
We are asking 300 young people (aged 15-25) who are currently experiencing depression to participate in our research study. In Phase 1 of our study, we will conduct a series of activities to understand that characteristics of anhedonia, including MRI scans, blood draws, behavioral tasks, clinical interviews, questionnaires, and measurement of real-life experiences and behavior using a phone app. We call this "phenotyping" because these characteristics are also called phenotypes.

Consent and Eligibility

The eligibility process for Phase 1 will include:

- An interview with questions about your mood, experiences, behaviors. This interview will take approximately 2-3 hours. With your permission, interviews will be video recorded to facilitate training and supervision of study staff.
- Questions checking for certain types of metal in your body because you cannot participate in the MRI scan if those metals cannot be removed.
- Questions about your health, including your treatment history.
- A 5–10-minute conversational task to compare vocal data

Study Procedures

The study will include 4 visits over approximately 1 year. These may be broken into two sessions per visit for scheduling reasons. In addition, the study will include ongoing smartphone app-based assessment of mood, experiences, and behavior.

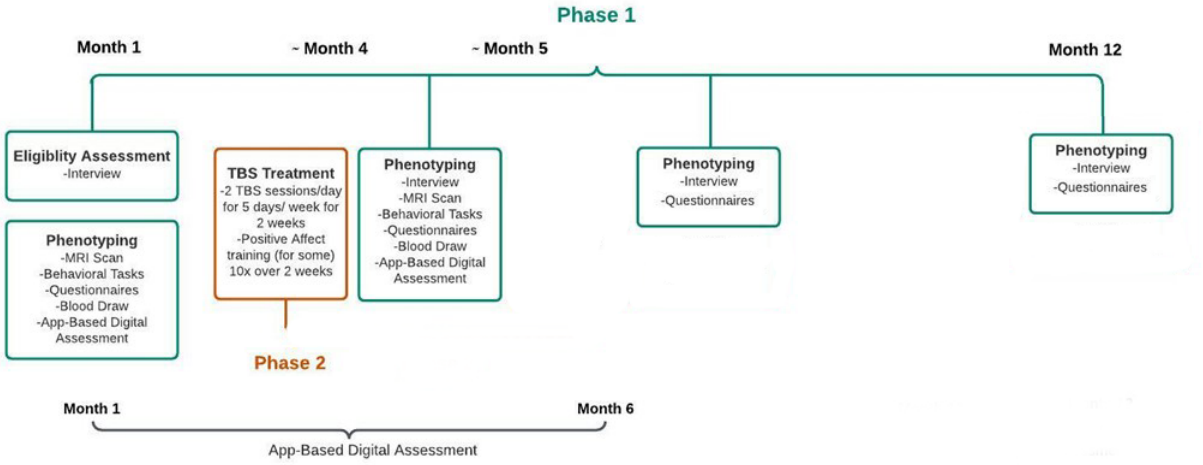
Visit 1
Participants will complete

- an MRI scan and an optional hand grip task where we test your grip strength
- questionnaires about thoughts, emotions, and experiences

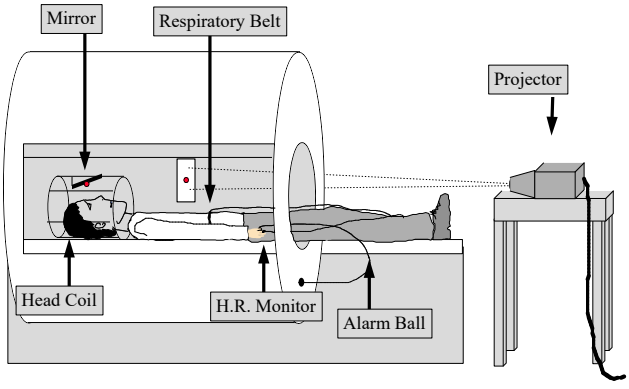
- tasks on a computer
- a cognitive task
- a blood draw by a trained phlebotomist
- instructions on starting the app-based study procedures

Visits 2-4
At approximately 4, 5, and 12 months after starting the study, participants will complete

- an MRI scan and an optional hand grip task (visit 2)
- questionnaires about thoughts, emotions, and experiences (visit 2-4)
- tasks on a computer (visit 2)
- a cognitive task (visit 2)
- a blood draw by a trained phlebotomist (visit 2)



<u>What is MRI?</u>



MRI is a type of imaging technique that uses a magnetic field to create detailed images of the brain. The MRI machine is a large, tube-shaped magnet that measures signals that reveal the brain's structure (its appearance) and function (its activity).

fMRI, or functional MRI, is a type of MRI that gets 3-dimensional pictures of the brain while people are experiencing and doing different things. The pictures that the scan creates show the parts of the brain that are active and how they coordinate their activity. fMRI is a painless procedure that does not use radiation, but uses radio waves, a large magnet, and a computer to create images.

The MRI scan sessions will take place at the BRIDGE Center, which is jointly operated by the University of Pittsburgh and Carnegie Mellon University, or at the Magnetic Resonance Research Center (MRRC) at UPMC Presbyterian Hospital. At the scan sessions, a team member will help you fill out an MRI Safety Screening Form to make sure that there are no known risks (for example, metal fragments in your body) to your participation. Before beginning the real brain scans, you will be given a chance to practice a game you will be playing in the scanner and be able to lie in a realistic MRI scanner simulator to become comfortable in the scanning environment. While the scanner is recording, you will complete tasks during some parts of the scan and will lie awake quietly during other parts . The team member or technologist will talk to them while you are in the scanner through a microphone; you should tell the technologist if anything is uncomfortable. You can also choose to stop scanning at any time.

It is important in these studies that you remain still while in the scanner because movement in the head, arms and legs can make the brain pictures blurry. You should experience no physical discomfort, except that associated with remaining still for the actual scanning period. You will not be informed of the results of the brain imaging scans because these MRI recordings are for research purposes, and this type of scan can't be used to get clinically meaningful information such as neurological health. However, if there is something unusual on the scans that requires further clinical evaluation (as determined by a radiologist) we will tell you this information and offer information about clinical care.

What are the computer tasks?

The computer tasks are about rewards. The tasks you will complete in the scanner involve (1) guessing numbers for a chance to win money and (2) making decisions and using a hand grip to get rewards. The tasks you will complete outside of the scanner also involve effort and decisions to win rewards.

What is the cognitive task?

The cognitive task will take approximately 1 hours and will be completed remotely. You will receive a link by email and can complete the task whenever it is convenient for you. This task will look at effort, reward, and decision making.

What do the questionnaires ask?

We will be asking questions about your emotions, experiences, and behaviors. These will cover things related to your mental health, as well as your life events, activities, and your age, gender, race/ethnicity, health, and household income.

What is app-based assessment?

The app-based assessment uses an app installed on your phone to collect two kinds of data: ecological momentary assessment (EMA) data and passive sensor data. EMA

data will be collected daily, one week per month, for the first 6 months and last 3 months of the study. On other days of those months, you will answer one very short survey (1-2 questions). Passive sensor data will be collected for the entire year each person is in the study.

EMA is a way to measure people's experiences and behaviors in real life as they are happening. In some ways, it can tell us more accurate information than questionnaires that ask about past experiences. In this study, EMA includes surveys several times per day in which you provide information about your mood and experiences. Passive sensor data refers to data that are collected automatically through sensors that are included in every smartphone. These sensors measure things like movement, rotation, and location. We use passive sensor data to measure patterns of physical activity (i.e., walking, exercise, sedentary activity, driving), location (e.g., going to different places), and sleep (bedtime and wake time). We will also measure social activity through collecting data on screen-time/social media app usage (minutes) and phone/messaging activity. The app will also collect text entered into the phone's keyboard to measure emotional states through language features and facial expressions. All information is encrypted two separate times: (1) as it is being uploaded to the cloud managed by the company that developed the app, (2) once the data is stored.

Some days' EMA surveys will include a question about your thoughts about dying or hurting themself. If you indicate a high intensity of these thoughts, the EMA system will (1) provide you with a list of crisis resources; and (2) alert an on-call study team member, who will contact you shortly (within approximately 24 hours) to assess your safety and help you develop a plan for remaining safe. Because Phase 1 of the ADEPT Study is not a treatment study and does not have clinicians available 24/7, study team members are not able to respond immediately to the responses you may provide during EMA. If you appear to be in a clinical emergency based on discussion with a team member, the team member may contact local crisis resources or recommend that you do so.

The app will continuously collect data as long as it is installed on the phone and activated. All the mobile sensing data streams are collected while the app is running in the background. The app will get data collected through the app and store them in a HIPAA-secure cloud server. They will then provide our research team with coded, de-identified data. Data is coded with the ID number that our study assigns for you and the device ID (a code the identifies the specific device that the app is running on). Neither ID contains or is linkable to personally identifiable information. Data sent to the research team will not include photos, text contents or text recipient/senders. You can stop the app from collecting data any time simply by deactivating it (e.g., swiping it out of memory) or uninstalling it. We automatically deactivate data collection remotely at the end of each participant's data collection period.

<u>What are the risks in this study?</u>

For MRI, there are no known dangers of exposure to the magnetic fields used and the

scan involves few physical risks. But you should be aware of the following:

- The magnet used in the MRI machine is very powerful and may attract and may move metal objects. If you have certain types of metal in your body, you cannot participate in the MRI part of this study. We will ask you questions before the MRI scan to make sure you are safe.
- Since the machine is loud, you will be given and must wear earplugs.
- Some people become uncomfortable while in the machine. You will have a chance to get comfortable before scanning starts.
- Sometimes people feel concerned about how well they do on tasks or become tired.
- There are no known risks to a fetus.

After a blood draw, you may get a bruise (a black and blue mark) or experience discomfort from the blood draw location. There is also a small risk of infection, lightheadedness, and/or fainting.

Some of the questions about your mood and experiences during interviews, questionnaires, or EMA may cause you to feel upset or distressed for a short period of time. The interview or questionnaire activity may be stopped at any time if you feel undue psychological or physical discomfort. It is also important that you express any concerns and/or ask any questions throughout the whole study. You may also experience distress or discomfort from unpleasant sounds in the cognitive task.

During EMA, there is a chance that someone around you will see your responses. You will be required to use a password for your phone to restrict access to the app. You can choose a convenient and private time/place to complete the survey if you receive a prompt at an inconvenient time or location. If your phone is stolen or lost, we will remotely erase the data on the app.

Although every reasonable effort has been taken, confidentiality during Internet communication activities cannot be guaranteed and it is possible that additional information beyond that collected for research purposes may be captured and used by others not associated with this study. Through the collection of identifying and sensitive information, a breach of confidentiality is possible, although this is an infrequent risk.

Additionally, we will offer you the option of communicating with us over text-message during your time in this study. Although we will do everything within our power to protect your information, text messages are not encrypted or secure during their transmission and it is possible they could be intercepted and used by others not associated with this study.

<u>What are the benefits of this study?</u>

You will not receive direct benefit from Phase 1 of this study. You may feel reassured or relieved from describing your experiences or symptoms, however, and you may feel satisfied about contributing to science. While Phase 2 includes treatment activities that

could improve depression or anhedonia, Phase 1 is more about understanding anhedonia and how it changes over time. Information from Phase 1 can be used to investigate whether the therapeutic activities in Phase 2 work, how they work, and in which people they work. Thus, knowledge from Phase 1 can contribute to future treatment studies that may to reduce suffering and improve health.

What is the compensation?

You will be compensated for your time and for transportation (parking or bus fare). For your first visit to the lab, you will receive $75 for the interview to assess eligibility. Based on the study activities, you could receive

- up to $175 for Interviews and Questionnaires ($25/visit x 4 visits for questionnaires; $75/visit x 1 visit for interview)
- $30 for the affect induction task during the interview
- up to $300 for MRI and Tasks Earnings ($150/visit x 2 visits + task winnings)
- up to $48 for the hand grip task (up to $24/completion x 2 timepoints)
- up to $40 for Blood Draws ($20/visit x 2 visits)
- up to $300 for EMA during Months 1-6 (Completion of at least 80% of EMA surveys per month: $50/month)
- up to $50 for the computer task ($25 for completing the task each time)

Payment to participants is considered taxable income regardless of the amount. If a participant receives $600 or more in a calendar year from one organization, that organization is required by law to file a “Form 1099 – Miscellaneous” with the IRS and provide a copy to the taxpayer. We are required to give your name and social security number to the Accounting Office. Participants who do not provide a social security number may still participate in the research, but the IRS requires that 24% of the payment be sent by the institution to the IRS for ‘backup withholding;’ thus you would only receive 76% of the expected payment.

You will have access to the University of Pittsburgh paid transportation services such as private car service or ride-share app (e.g. Uber) within a 50-mile radius if needed for any study procedures or appointments. Additionally, beverages and snacks may be offered to you.

Will I learn about new information that researchers learn?
We will tell you about any new information that we learn that may cause you to change your mind about staying in the study. We will also share some of our findings on depression and anhedonia in young people.

Will this be confidential?

To protect your privacy and maintain the confidentiality of information we obtain, we will keep all information we obtain in a secure location and use a number rather than your name as identification. All paper records that could identify you will be kept in a locked filing cabinet, and all electronic records will be stored in password-protected files. Although we will do everything in our power to protect your privacy and the

confidentiality of research records, we cannot guarantee the confidentiality of research records. However, no third party, including relatives, personal physicians, employers, insurance companies or other researchers will be provided with names or other identifying information.

There are 4 exceptions to your confidentiality in this study where individuals may have access to research records, which may include medical records. First, staff at the medical facilities where the study procedures will take place (BRIDGE Center, MRRC, WPH Phlebotomy Lab) will have access to your identifiable information related to the eligibility screening for participants and for handling internal hospital operations. Second, authorized representatives of the University of Pittsburgh Office of Research Protections may review your identifiable research information for the purpose of ensuring the appropriate conduct of this research study. Third, if the study staff learn that you or someone with whom you are involved is in serious danger of harm, they may need to inform, as required by Pennsylvania law, the appropriate agencies. The authorized representatives of UPMC or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders made by the investigators for hospital and health care services (e.g., laboratory tests) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance). In rare cases, identifiable records may be released in response to an order by a court of law.

What else is important to know?

Information from this study may be shared with other researchers here and at other research institutions, but those researchers will never be provided with any personal identifiers that would allow them to learn who you are. We will be sharing data with Wellcome Leap MC Psych, which is the sponsor of our study and 11 other studies, all focusing on anhedonia and depression, that are part of the MC Psych program. We are collecting some of the same information as other MC Psych studies, even though some of the procedures in our study at Pitt are unique. Confidentiality/security of data we share will be maintained by Vanderbilt University, where data integration will take place. Any data we share will be identified by a study-assigned number, and we will not share identifying details such as your name.
Some of your behavioral task data and questionnaire/interview data will be shared with our collaborators at Princeton University. The shared data will be deidentified, so it will not include your name or any other confidential data about you. The data can only be accessed by our collaborators and authorized members of their team. When we share this data, you will not be asked for additional informed consent.We may send blood and related samples to Mt Sinai School of Medicine, where Dr. Scott Russo's lab can perform assays. Additionally, we may send related samples to Dr. Walt's lab with the Massachusetts General Hospital at Harvard University. The samples will only be labeled with IDs, site if appropriate (University of Pittsburgh), and the date of sample, not with identifying information.

Your data and specimens used in this research study may contribute to a new discovery or treatment. There are no current plans for whole genome sequencing, but it is possible for future use of blood samples. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights, nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may realize. No individual results will be disclosed, but the research team will communicate study findings to participants as they emerge.

Per University of Pittsburgh policy, all research records must be maintained for at least 7 years following the final reporting or publication of a project. However, these records may be kept indefinitely by the research team.

A description of Phase 2 of this study, involving therapeutic activities aimed at reducing anhedonia and depression, will be available on http://www.clinicaltrials.gov, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Your participation in this study is completely voluntary, at all times.

What if I want to withdraw from the study?

Your decision to participate, or later withdraw, from this study will not affect your current or future relationship with the University of Pittsburgh, current or future medical care at a UPMC Health System hospital or affiliated health care provider, and current or future relationship with a health care insurance provider. If you decide no longer to participate after you have signed the consent form, you should contact Dr. Forbes or her research staff with the information on the front of this form. You may withdraw from the study at any time. If you choose to withdraw, we will typically continue to use information already collected. However, if you prefer that we no longer use any information from your participation, you should provide a written and dated notice to Dr. Erika Forbes.

It is possible that you may be removed from the research study by the researchers for failing to follow study procedures. You may also be removed from the study by the study staff if you no longer meet the eligibility criteria (for example, if you are not safe to undergo an MRI scan or is found ineligible during the interview) or if you are unwilling or unable to follow study procedures.

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this

follow-up care. At this time, there is no plan for any additional financial compensation. You do not waive any rights by signing this form.

Compensation in Case of Injury—BRIDGE Center
There is no compensation available if you are injured. You do not waive any rights by signing this form.

Neither you, nor your insurance provider will be charged for the costs performed only for the purposes of this research study. You will be charged in the usual manner for any procedures performed as part of your standard medical care (care you would receive even if you were not participating in this research study).

VOLUNTARY CONSENT
By signing below, I agree to have my interview audio- or videotaped. Recordings are for training, supervision, and quality purposes.

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions and voice concerns about any aspect of this research during this study, and any future questions I ask will be answered by the researchers listed on the first page of this form at the telephone number(s) given. By signing this form, I agree to participate in this research study.

By signing this form, I agree to participate in this research study.

_____
Participant's Printed Name

_____ _____
Participant's Signature Date

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____	_____
Printed Name of Person Obtaining Consent	Role in Research Study
_____	_____
Signature of Person Obtaining Consent	Date

University of Pittsburgh

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: Anhedonia, Development, and Emotions: Phenotyping and Therapeutics (ADEPT) Study

Phase 2: Therapeutic Activities
Adults (age 18+ years)

PRINCIPAL INVESTIGATOR:

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To reach the research staff, please call 412-354-9297 or e-mail {TMS_Study@pitt.edu}

If you have any questions about your rights as a research subject or wish to talk to someone other the research team, please call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668. You may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during your participation. You may request a copy of this consent script.

SOURCE OF SUPPORT: Wellcome Leap MC Psych

Summary of Key Points:

- The ADEPT study involves two phases. All participants will complete procedures for Phase 1, and some participants, if qualified and interested, will also complete procedures for Phase 2.
- In Phase 2 of the Study, participants are asked to go through a series of therapeutic, or treatment, activities involving brain stimulation, training to build positive emotions. These activities could improve depression and anhedonia.
- The Phase 2 activities will help us to understand and treat anhedonia and depression because they are focused on the brain circuitry thought to influence those problems.
- Information from Phase 2 will be combined with information from Phase 1 to provide knowledge on how these activities change anhedonia and depression for who responds to them.

Introduction

Before agreeing to take part in this research study, it is important that you read and understand the following information. This consent document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternatives that are available to you and your right to withdraw from the study at any time. No guarantees or promises can be made as to the results of the study.

If you are not completely truthful with study team members regarding your health history, you may harm yourself by taking part in this study. You must think about the information in this consent document for yourself. You must then decide if you want to take part in the study.

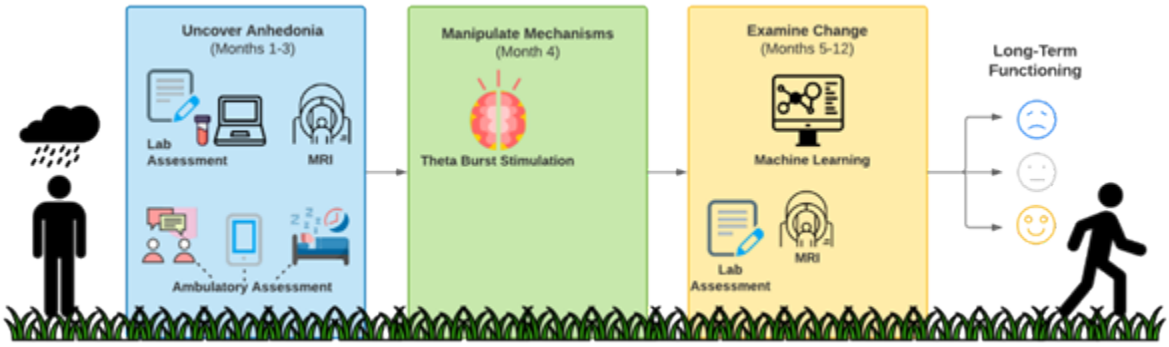
Why is this research being done?

In this research study, we are trying to understand and change anhedonia in young people with depression. Anhedonia is experienced by many people who have depression, and it involves difficulty with motivation, energy, and anticipation of pleasant events. We want to understand anhedonia early in life so that we can find ways to help young people develop along healthy pathways and avoid chronic illness. Anhedonia is related to function in the brain's reward circuit, inflammation in the body, and people's experiences and behaviors, and will measure all of these. We also want to see whether we can understand anhedonia by trying to disrupt or improve it. To do that, we are using activities that are based on treatments for depression and seem to target the brain's reward circuit., Finally, we will measure anhedonia over 1 year to see how it changes with time, development, or treatments. Eventually, the findings of this study might be useful for treating depression and improving people's quality of life.

What will happen in this study?

We are asking 300 adolescents and young adults (aged 15-25) who are currently experiencing depression to participate in our research study. Phase 2 of this study involves procedures that are therapeutic, meaning they can treat depression and anhedonia. These include transcranial

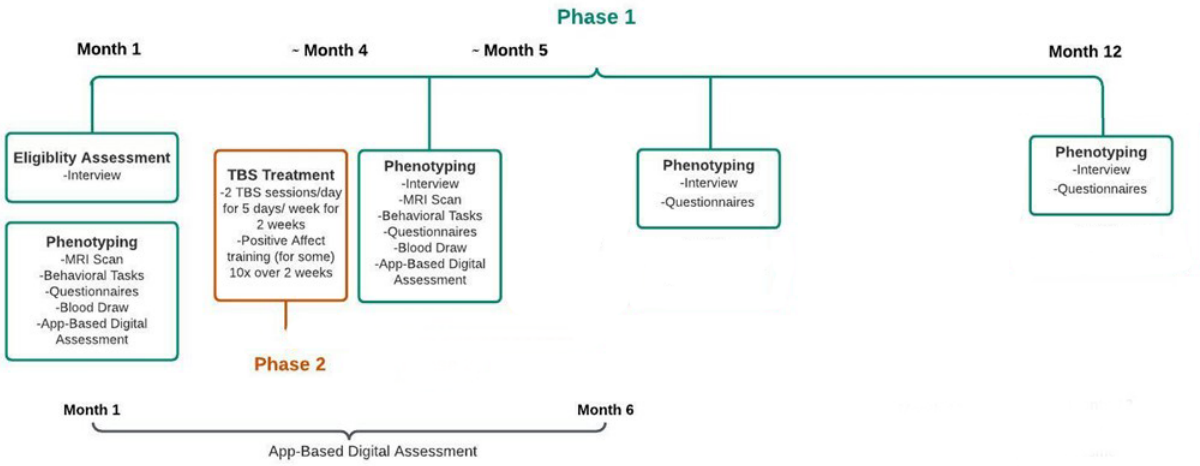
magnetic stimulation (TMS), which is a noninvasive procedure to treat depression that uses magnetic fields to stimulate nerve cells in the brain. Visits with TMS will include Positive Affect Training, which involves changing behaviors and thoughts to build positive emotions.



*At the current time, there are no plans for new participants to do ketamine.

In order for you to be eligible for Phase 2 of this study, you need to have tried at least one antidepressant medication trial without an improvement in your depression severity.

If you are eligible and interested, you will be asked to complete TMS (10 visits, 1 per weekday, over 2 weeks), and PA Training. If you do Phase 2, you will also continue the activities of Phase 1, which include (after Phase 2 starts) a phenotyping visit (blood draw, MRI, interview, computer tasks, and questionnaires) that occurs after TMS, after approximately 4-6 months, and at approximately 1 year after you begin the study. You will also continue the phone app-based assessment during months 1-6 and 10-12 of your participation.



Positive Affect (PA) Training

The exercises to improve positive emotions are called Positive Affect (PA) Training. You will receive positive affect training, which will be 30-minute trainings on most days, with 45-minute trainings on the first and last days. During these sessions, you will learn

about increasing PA by using behavioral and cognitive techniques.

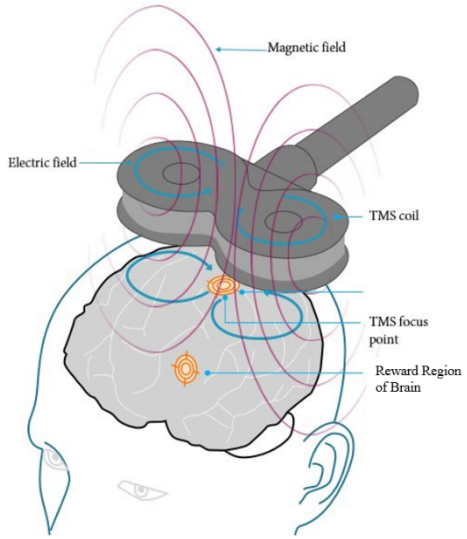
Each TMS visit will take approximately 1.5 hours.

Total Time Commitment: 15 hours in a 2-week period plus 3 follow-up visits within one year of completing the study

What is Theta Burst Stimulation (TBS)?

Theta Burst Stimulation (TBS) is a shorter version of TMS and is the type of brain stimulation we are using in the study. The TMS device, called the MagPro X100 TMS system, is approved by the FDA for treatment of Major Depressive Disorder in adult patients who have not received satisfactory improvement from prior antidepressant medications. Thus, the device is acceptable for studying how people with depression respond to treatments. We expect TBS to have potential value in improving depression, anhedonia, and mood in young people.

TBS is a technique to briefly change function in a region of your brain using a magnetic field that passes through the scalp and the skull safely. We will use the MRI brain images from Phase 1 of the study to guide the TBS so that the stimulation is in the right place for our study.



The study staff will be available to talk to you before you start the procedure, and they will give you a chance to see the device that will be used and to ask any questions that you have before beginning the TBS process. The staff will also be standing by while you are receiving TBS and you should tell the research team if anything is uncomfortable. You can also choose to stop the procedure at any time.

What are the risks in this study?

The brain stimulation in this study comes with the risk of experiencing scalp discomfort and/or a mild headache during or immediately after the TMS procedure due to the activation of the scalp muscle near the device. There is also a less common risk with the TMS of a delayed onset headache (which can be helped with ibuprofen), and the very unlikely possibility of a seizure. There have been no reported seizures in anyone that has received the procedure that is used in this study. There is also the rare chance that an unusually high-energy (hypomanic) temporary mood could result from the TMS procedure. Lastly, there is also a possibility that a TMS session will produce worsening of depression symptoms (a rare side effect). However, we do not anticipate this occurring.

For your safety during this study, call the study before you take any of the following so we can consult with one of our study MDs:

- new medications prescribed by your own doctor
- other medications sold over-the-counter without a prescription
- dietary or herbal supplements

What are the benefits of being in this study?

You may experience an improvement in your depression symptoms or mood. You may learn strategies for enhancing positive emotions in your daily life. You will receive information on crisis and treatment resources, which could help you to regulate your emotions and behavior.

What is the compensation?

You will be compensated for parking or bus fare that is needed to get to and from all visits to the laboratory. You will also receive payments for the Phase 2 study activities, as follows:

- **Up to $350 for TBS Week 1** ($70/visit x 5 visits)
- **Up to $400 for TBS Week 2** ($80/visit x 5 visits)

Payment to participants is considered taxable income regardless of the amount. If a participant receives $600 or more in a calendar year from one organization, that organization is required by law to file a “Form 1099 – Miscellaneous” with the IRS and provide a copy to the taxpayer. We are required to give your name and social security number to the Accounting Office. Participants who do not provide a social security number may still participate in the research, but the IRS requires that 24% of the payment be sent by the institution to the IRS for ‘backup withholding;’ thus you would only receive 76% of the expected payment.

You will have access to the University of Pittsburgh paid transportation services such as private car service or ride-share app (e.g. Uber) within a 50-mile radius if needed for any study procedures or appointments. Additionally, beverages and snacks may be offered to you.

Will I be billed for study procedures?

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical

care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. You do not waive any rights by signing this form.

Neither you, nor your insurance provider will be charged for the costs performed only for the purposes of this research study. You will be charged in the usual manner for any procedures performed as part of your standard medical care (care you would receive even if you were not participating in this research study).

Will I learn about new information that researchers learn?

We will tell you about any new information that we learn that may cause you to change your mind about staying in the study. We will also share some of our findings on depression and anhedonia in young people.

HIPAA Authorization
We are asking permission to use your medical records. For this study an entry for your CTRC visit will made in your UPMC medical record and the study team will record information from it. Your permission does not expire nor does the study team's ability to access the record. Individuals that will have access to your medical record identifiable information is detailed below. We will protect your privacy and the confidentiality of your records, as described in this document, but cannot guarantee the confidentiality of your research records, including information obtained from your medical records once your personal information is disclosed to others outside UPMC or the University (such as to the FDA or the sponsor).

Will this be confidential?

To protect your privacy and maintain the confidentiality of information we obtain, we will keep all information we obtain in a secure location and use a number rather than your name as identification. All paper records that could identify you will be kept in a locked filing cabinet, and all electronic records will be stored in password-protected files. Although we will do everything in our power to protect your privacy and the confidentiality of research records, we cannot guarantee the confidentiality of research records. However, no third party, including relatives, personal physicians, employers, insurance companies or other researchers will be provided with names or other identifying information.

There are 4 exceptions to your confidentiality in this study where individuals may have access to research records, which may include medical records. First, staff at the medical facilities where the study procedures will take place (BRIDGE Center, MUH CTRC, WPH Phlebotomy Lab) will have access to your identifiable information related to the eligibility screening for participants and for handling internal hospital operations. Second, authorized representatives of the University of Pittsburgh Office of Research Protections may review your identifiable research information for the purpose of

ensuring the appropriate conduct of this research study. Third, if the study staff learn that you or someone with whom you are involved is in serious danger of harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies. In rare cases, identifiable records may be released in response to an order by a court of law. Lastly, the FDA may access identifiable information for the purpose of monitoring the study.

What else is important to know?

Information from this study may be shared with other researchers here and at other research institutions, but those researchers will never be provided with any personal identifiers that would allow them to learn who you are. We will be sharing data with Wellcome Leap, the sponsor of our study and of the 11 other related studies on depression and anhedonia. Shared information will be labeled with an ID number, not with any personal identifiers.

We may send blood and related samples to Mt Sinai School of Medicine, where Dr. Scott Russo's lab will perform assays. Additionally, we may send related samples to Dr. Walt's lab with the Massachusetts General Hospital at Harvard University. The samples will only be labeled with IDs, site if appropriate (University of Pittsburgh), and the date of sample, not with identifying information.

Your data and specimens used in this research study may contribute to a new discovery or treatment. There are no current plans for whole genome sequencing, but it is possible for future use of blood samples. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights, nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may realize. No individual results will be disclosed, but the research team will communicate study findings to participants as they emerge.

Per University of Pittsburgh policy, all research records must be maintained for at least 7 years following the final reporting or publication of a project. However, these records may be kept indefinitely by the research team.

A description of this study will be available on http://www.clinicaltrials.gov, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Your participation in this study is completely voluntary, at all times.

Withdrawal from study participation

Your decision to participate, or later withdraw, from this study will not affect your current

or future relationship with the University of Pittsburgh, current or future medical care at a UPMC Health System hospital or affiliated health care provider, and current or future relationship with a health care insurance provider. If you decide you no longer want to continue to participate after you have signed the consent form, you should contact Dr. Forbes or her research staff with the information on the front of this form. You may withdraw from the study at any time. If you choose to withdraw, we will typically continue to use information already collected. However, if you prefer that we no longer use any information from your participation, including from your medical record, you should provide a written and dated notice to Dr. Erika Forbes. The FDA may always access identifiable information regarding drug safety.

If a participant decides to withdraw from the study: You can withdraw from this research study at any time. Any identifiable research information obtained as part of this study prior to the date that you withdrew your consent will continue to be used by the investigators for the purposes described above. If you want to withdraw, notify the study team. Your decision to withdraw will have no effect on your current or future relationship with the University of Pittsburgh or UPMC.

If the investigator removes a participant from the study: It is possible that you may be removed from the research study by the researchers for failing to follow study procedures. You may also be removed from the study by the study staff if you no longer meet the eligibility criteria (for example, if you are not safe to undergo an MRI scan or are found ineligible during the interview) or if you are unwilling or unable to follow study procedures.

VOLUNTARY CONSENT

By signing below, I agree to have my interview audio- or videotaped. Recordings are for training, supervision, and quality purposes.

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions and voice concerns about any aspect of this research study during this study, and any future questions I ask will be answered by the researchers listed on the first page of this form at the telephone number(s) given. By signing this form, I agree to participate in this research study and authorize the use and sharing of my medical records.

_____
Participant's Printed Name

_____ _____
Participant's Signature Date

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____
Printed Name of Person Obtaining Consent Role in Research Study

_____ _____
Signature of Person Obtaining Consent Date