COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: Neurofeedback in individuals with substance use disorders

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Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to test whether individuals treated with methadone can learn to use neurofeedback in MRI, and whether neurofeedback training can help to prevent opioid relapse and reduce clinical features of opioid use disorder such as craving.
- Study procedures will include: A screening session that may be in-person or remote, weekly MRI sessions, and a final study visit one month after the MRI sessions that may be in-person or remote. At each study visit we will also ask you to complete surveys and provide a urine sample. We will also track your medication adherence across the study through your clinic records.
- Seven study sessions are required in total.
- These sessions will take up to 12.5 hours in total.
- There are some risks from participating in this study. These include risks to privacy and risks and inconveniences to participating in MRI scans, described below.
- The study may have no benefits to you. We expect that the results of the study may benefit science and others by increasing our knowledge about opioid use disorder and how to potentially treat opioid use disorder using neurofeedback.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand.

Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?
We are asking you to take part in a research study because **you are between the ages of 18-50 years and are on methadone treatment for opioid use disorder**. We are looking for **24** participants to be part of this research study.

Who is paying for the study?
Funding for this study is from the National Institutes of Health, National Institute on Drug Abuse.

What is the study about?
The purpose of this study is to test the effects of neurofeedback on opioid use, brain activation patterns, and clinical features of opioid use disorder. Neurofeedback is viewing a picture (such as a graph) of your brain activity in real time during an MRI scan.

What are you asking me to do and how long will it take?
If you agree to take part in this study, this is what will happen:

1. **Screening session:** To determine if you are eligible for this study, we will ask you questions about different aspects of your life including your health, smoking, substance use behaviors and attitudes, and the ways in which you view yourself. If you are determined to be eligible, we will ask you to complete additional questionnaires about similar topics. You will also be asked for a urine drug test. The screening session will take about 1 and ½ hours and will be completed in-person or by computer or telephone. If you are eligible, we will also schedule your MRI appointments during this visit.

2. **MRI sessions:** This study involves 5 MRI scans. Each MRI session will take about 1.5-2.5 hours and will include an MRI scan, a urine test and surveys (described below). All imaging will take place at the Magnetic Resonance Research Center (MRRC) in the Anlyan Center at the Yale Medical School. In this part of the study we will take pictures of your brain with a magnetic resonance imaging machine (also known as an “MRI”). The pictures of your brain will give us information about the structure and activity level of different parts of your brain, and information about how brain areas are connected. We are particularly interested in understanding how different parts of the brain work together to do different tasks and whether you can control the activity patterns in specific parts of your brain. The MRI scan will take about 60 minutes.

   MRI scans are painless, do not involve the use of radiation, and are used routinely to diagnose medical problems. You must inform the research staff if you have any metal objects in your body (for example: rods, pins, or surgical implants) because having an MRI could be harmful. Some surgical devices such as screws, rods, etc. are composed of non-metallic materials that would not be harmful during an MRI. Some people may feel nervous in the scanner, and if you find it is too difficult you may stop at any time. More information about the potential risks and inconveniences of the MRI scan are described below.

   For the MRI scan, you will lie on your back on a comfortable mattress, your head will be placed on a cushioned head rest, and you will wear earplugs to reduce the level of noise. Your upper body will be slid halfway into the scanner, which is a large tube. We will ask you lay still during the scan. You will be able to communicate with the research

staff with headphones and a microphone. We will tell you when we begin taking pictures of your brain and you will notice a series of knocking noises made by the machine when the pictures start. A member of the research team will accompany you to the MRRC and will stay with you for the duration of the MRI session.

During the MRI scan, you will be asked to either rest or do several different tasks:

Monetary Incentive Delay Task: In this task, you will be asked to press a button in response to a target stimulus, such as a box displayed on the screen, in order to win or avoid losing money.

Stroop Task: In this task, you will see color names presented in different "print" colors, and you will be asked to respond by pressing a button to indicate the print color, by ignoring the color name.

Intervention Task: In this task, you will lay still while we measure your brain activity, and you will be asked to try to change your brain activity pattern. To do this, we will provide you with a visual stimulus indicating how well you are producing the desired brain activity pattern, such as a line that updates over the course of the task. It is important for the study that you do your best during the interventions tasks. We will then ask you to try to change your brain activity without the visual feedback. This will take about 5 minutes, and you may take part in up to 6 intervention tasks at each MRI scan.

3. **Surveys and urine test:** At each MRI session, prior to the MRI scan, you will be asked to provide a urine sample for testing of substance use and complete both computer and paper and pencil surveys. The surveys will ask about your substance use behaviors and cognitive abilities.

4. **One month study visit:** One month after your MRI scans, you will be asked to attend a remote or in-person final study visit to complete the same computer and paper and pencil questionnaires and provide a urine sample. This study session should take about 30 minutes.

5. **Debriefing:** At the end of the one-month study visit, you will be fully debriefed by study personnel, who will explain more thoroughly the purpose of the study and answer any questions you may have.

What are the risks and discomforts of participating?

Common

1. **Surveys**: All of the surveys are noninvasive and should add no risk. The major disadvantages are the time taken to complete them, and possible breach of confidentiality. Careful efforts to maintain your confidentiality will be made.

Uncommon

2. **Urine collection:** A urine drug test will be performed at each study visit. The main risk to urine collection is possible breach of confidentiality. If you are uncomfortable with the urine test, we recommend that you do not participate.

3. **Pregnancy related risks:** If you are currently pregnant or planning to become pregnant, you will be ineligible for the study. If you become pregnant before your MRI sessions, please tell the study team immediately.
4. **MRI risks:** Magnetic resonance (MR) is a technique that uses magnetism and radio waves, not X-rays, to take pictures and measure chemicals of different parts of the body. The United States Food and Drug Administration (FDA) has set guidelines for magnet strength and exposure to radio waves, and we carefully observe those guidelines.

   You will be watched closely throughout the MR study. Some people may feel uncomfortable or anxious. If this happens to you, you may ask to stop the study at any time, and we will take you out of the MR scanner. On rare occasions, some people might feel dizzy, get an upset stomach, have a metallic taste or feel tingling sensations or muscle twitches. These sensations usually go away quickly but please tell the research staff if you have them.

   There are some risks with an MR study for certain people. If you have a pacemaker or some metal objects inside your body, you may not be in this study because the strong magnets in the MR scanner might harm you. Another risk is the possibility of metal objects being pulled into the magnet and hitting you. To lower this risk, all people involved with the study must remove all metal from their clothing and all metal objects from their pockets. We also ask all people involved with the study to walk through a detector designed to detect metal objects. It is important to know that no metal can be brought into the magnet room at any time. Also, once you are in the magnet, the door to the room will be closed so that no one from outside accidentally goes near the magnet.

   We want you to read and answer very carefully the questions on the MR Safety Questionnaire related to your personal safety. Take a moment now to be sure that you have read the MR Safety Questionnaire and be sure to tell us any information you think might be important.

   This MRI study is for research purposes only and is not in any way a complete health care imaging examination. The scans performed in this study are not designed to find abnormalities. The principal investigator, the lab, the MR technologist, and the Magnetic Resonance Research Center are not qualified to interpret the MR scans and are not responsible for providing a health care evaluation of the images. If a worrisome finding is seen on your scan, a radiologist or another physician will be asked to review the relevant images. Based on his or her recommendation (if any), the principal investigator or consulting physician will contact you, inform you of the finding, and recommend that you seek medical advice as a precautionary measure. The decision for additional examination or treatment would lie only with you and your physician. The investigators, the consulting physician, the Magnetic Resonance Research Center, and Yale University are not responsible for any examination or treatment that you receive based on these findings. The images collected in this study are not a health care MR exam and for that reason, they will not be routinely made available for health care purposes.

How will I know about new risks or important information about the study?

We will tell you if we learn any new information that could change your mind about taking part in this study.

How can the study possibly benefit me?

There are no direct benefits to you for participating in the study. You may gain some control over your symptoms by learning to control activity patterns in your brain. It is important to note, however, that you may be receiving either the true experimental intervention (that we hope can help improve symptoms) or a control intervention (that we do not believe has any potential to improve symptoms).

How can the study possibly benefit other people?
The benefits to science and other people may include a better understanding of opioid use disorder and potential new treatments for opioid use disorder.

Are there any costs to participation?
You will not have to pay for taking part in this study. The only cost is your time coming to the study visits.

Will I be paid for participation?
You will be paid for taking part in this study. All participants will receive $25 for the screening session, up to $50 per MRI session, $25 for the follow-up session and a $200 study completion bonus. For MRI sessions that include the MID task described above, you will receive up to $50 per session because this payment will depend on your performance on the MID task. You may earn a little more or a little less than $50, but in general it will be about $50 per MRI session. For MRI sessions that include the intervention task described above, you will receive an additional bonus payment based on your performance (how well you are able to change your brain activity) on a randomly selected intervention task run. This bonus will be up to $15 per training scan. Total payment for taking part in this study will be $545. You are responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments. You may be reimbursed up to $50 per study visit for travel expenses. If for some reason you attend an MRI session but are not able to complete the full session, you may still be paid for the session, at the discretion of the research team, and you may be asked to come back for an additional MRI session.

What are my choices if I decide not to take part in this study?
Instead of participating in this study, you have some other choices.

You could:

- Take part in another study.
- Not receive any additional treatment for your substance use disorder than your ongoing care.

You are free to choose not to participate, and if you do become a subject, you are free to withdraw from the study at any time. If you withdraw it will not adversely affect your relationship with this clinic or the clinicians or doctors here.

How will you keep my data safe and private?
We will keep information we collect about you confidential. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if you we learn that you are hurting a child or an older person.

Your name or other identifiers will not appear on the study assessments. Instead, you will be assigned a study number that will be used for all data. The document linking your name and

study number will be kept on a password protected secure computer that is only accessible to approved members of the study team.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission.

We will also share information about you with other researchers for future research, but we will not use your name or other identifiers. We will not ask you for any additional permission.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by NIDA which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of such as child abuse and neglect, or harm to self or others.

What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called “Protected Health Information.” It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- Research study records
- Medical and laboratory records of only those services provided in connection with this study.
- Records about your study visits
- Records from the APT Foundation regarding your treatment for opioid use and use of methadone
- Information obtained during this research regarding:

- Urine screening
- Clinical evaluation
- MRI scans
- Surveys

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- The funding agency: National Institute on Drug Abuse, National Institutes of Health
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- The PI: Kathleen Garrison, Ph.D.
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record. However, this is a blinded treatment study and if you sign this permission form, you will not be allowed to look at or copy your study related information until after the research is completed.

What if I change my mind?

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to Dr. Kathleen Garrison, 1 Church Street #730 at Yale University, New Haven, CT 06510.

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to ensure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able. Yale School of Medicine and Magnetic Resonance Research Center do not provide funds for the treatment of research-related injury. If you are injured as a result of your

participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not give up any of your legal rights by signing this form.

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the research if necessary. For example, if you are unable to lay still in the MRI scanner, or become pregnant during the study.

If you leave the study for any reason, the study team may ask if you wish to take part in the follow up portion of the study. If you agree to continue with the follow up portion of the study, information about your health will continue to be collected as described above. The study team will discuss with you the different withdrawal options.

What will happen with my data if I stop participating?

If you withdraw from the study, urine samples that have been collected from you can be withdrawn if they have not yet been analyzed or destroyed. If you want your samples withdrawn, you must tell the study team before or at the time you leave the study. Deidentified data derived as part of the research will be unable to be withdrawn.

Who should I contact if I have questions?

Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigator, Dr. Kathleen Garrison, at 203-737-6232
If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

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.

Authorization and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date