CONSENT TO TAKE PART IN RESEARCH

Dartmouth College

Treatments for Temperature Responses and Reactivity

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You are being asked to take part in a research study on the effects of a known analgesic treatment cream. Taking part in research is voluntary.

We are inviting you to take part in this research study because you are an adult aged 18-55 with no pain conditions, pieces of metal in your body, implants or devices, and are not pregnant. Your decision whether or not to take part will have no effect on your academic standing. Please ask questions if there is anything about this study you do not understand.

What is the purpose of this study?

The purpose of the study how individuals' brains respond to aversive stimuli and how that may be treated.

Will I benefit from taking part in this study?

There are no direct benefits to you in participating in an fMRI study of brain function. Other than the monetary (or course credit) compensation and the possible psychological reward of participating in research, this paradigm provides no direct benefit to the subject.

What does this study involve?

This experiment is a drug treatment study on the effects of a known analgesic cream on various stimuli, and will be conducted in our laboratory in the Department for Psychological and Brain Sciences at Dartmouth College. Your participation in this study may last up to four hours, taking place over one online questionnaire session and two laboratory visits (Visit 1: ~1 hour, Visit 2: ~2 hours). After scheduling your first laboratory visit, you will also be sent a link to a series of surveys that pertain to your demographic information, values, personality, experiences, emotion control strategies, any emotional problems you may have experienced, questions regarding your use of alcohol, tobacco, and substances, questions regarding previous traumatic experiences, and mental health questions. These surveys are to be completed before you come in for your first session, and will take roughly an hour.

In the first visit, we will be calibrating your temperature sensitivity along various body sites, including left and right cheek, midline chest, midline trunk, left and right forearm, and left and right upper-calf. Calibration will entail stimulating each body site four times. You will be exposed to a thermode (Medoc Ltd), which is a machine that quickly heats up then cools down a small metal plate, placed on each of these body sites that will deliver heat and cold stimulations at a temperature range of 14ºF/-10ºC to 122ºF/50ºC a total of 32 times. You will be asked to make ratings to these stimulations.

This is likely to cause you some physical discomfort, though the stimulation will always be kept within limits that are tolerable to you. The heat stimulation would be similar to holding a cup of hot coffee. You may discontinue at any time if it becomes too uncomfortable.

The second visit will test the effects of analgesic cream, and involve MRI scanning. The coordinator will bring you to the MRI scanning room. While in the scanner, you will be exposed to the same thermode along with autonomic response recording equipment (Biopac MP160). During the first hour you will simply be tasked to periodically follow written instructions as they appear on the computer screen, and otherwise passively experience incoming sensations. Periodically, the coordinator will be entering the room to resituate the thermodes along various body sites. In the second hour a similar task will be presented to you, but the research coordinator will be applying one of two treatment creams at the site of the thermode. Again, you will be asked to answer various questions regarding your responses to the various stimuli. There will be time for you to ask questions regarding the instructions prior to the start of the experiment.

Once you are done with the scanning portion of the session, you will be brought to a behavioral testing room where you will be given a debriefing form regarding the study you participated in. You will receive your payment and be thanked for your participation.

While you are in the MRI scanner, we will be collecting a number of physiological autonomic measurements (e.g., heart rate, skin conductance, respiration). We will do so by using non-invasive sensors, which are not associated with any uncomfortable, harmful or painful sensations. The sensors will be placed, by the research coordinator and the MRI technician, on your hands, feet, and torso in order to record the physiological responses throughout the experiment. During the experiment it is very important for participants to remain as still a possible since the brain imaging technique is very sensitive to movement. You will be given specific instructions at the start of each task. Please ask the experimenter any questions that may arise while you are doing the task(s).

The magnetic field of the MR environment has the potential to cause burns or bodily injury if ferrous metal objects are implanted in the body or if personal articles containing ferrous material are brought into the environment. Prior to going into the MRI scanner, the study personnel and the MRI technologist on duty will ask that you remove all jewelry and metal objects from your pockets and may ask you to change into scrubs. You will be asked to complete a screening form to ensure it is safe for you to go into the MR environment. Because the effects of MRI on fetuses has not been determined, if you are female there are pregnancy tests available should you wish to take a pregnancy test before you go into the scanner.

When you go into the scanner, you will lie down on a padded table and will be placed into a long donut-shaped tube that is only slightly larger than your body. Your head and waist will be enclosed in the tube. If you are uncomfortable being in small or confined places (e.g., suffer from claustrophobia), please tell the research team.

A specially designed coil will be placed around your head to provide better images (as is done with standard clinical examinations). As the MRI scan is performed, you will hear loud rapping and knocking noises that are normal for an MRI scan. We will give you headphones to block out some of the noise. You will still be able to hear the researchers and the MRI technician through an intercom and will be able to squeeze a ball to get their attention and stop the scan at any point.

Temperature values are controlled to within .1 degrees Celsius by a computer, with a safety shutoff at a level tolerable to participants, and non-damaging to skin (the hardware will not allow stimulation at 50 degrees Celsius for longer than 6 seconds). The thermode is minimal risk. It is widely used in pain and clinical research and is approved by the U.S. Food and Drug Administration. We have used it safely in over 1,000 participants over the last 15 years. Nonetheless, because some people respond differently to thermal stimulation, there is a small risk (0.1%) of skin irritation or blistering (described below).

You will not be charged for any of the experimental study procedures, including the MRI scan. If incidental findings from study result in the need for further evaluation/treatment, then you or your insurance will be responsible for additional clinical evaluation/treatment that may be needed.

What activities will be done only for research purposes?

If you participate in this study all activities and data collected will be for research purposes. However, all your data will be anonymously stored and analyzed in such a way that there will be no identifying information available to link the responses you made back to your identity.

What are the risks involved with being enrolled in this study?

There are some potential risks if you take part in this study. These may include:

> **Thermal Pain:** You will be exposed to experimental pain induced by applying various temperatures to your skin. This is likely to cause you some physical discomfort, though the pain will always be kept within limits that are tolerable to you. Additionally, because some people respond differently to thermal stimulation, there is a slight risk (less than 0.1%) of irritation and/or blistering to the stimulated skin site. Several factors, including dryness of skin, dehydration, and possibly skin pigmentation, may influence a person's response to thermal pain stimulation. Skin irritation and/or blistering could also result from a malfunction of the equipment used in this study. However, the probability of a machinery malfunction is extremely low, as thousands of individuals are safely tested each year on this equipment, and we carefully monitor the equipment regularly to ensure its proper functioning.
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> Should you experience any skin irritation or blistering at any point during the experiment or shortly after, please let the experimenter know immediately. In the event of a burn, run the affected skin site under cool water for several minutes, and seek medical attention. Safety guidelines for the design and administration of this study are strictly followed in order to minimize any such risk. If at any point during the experiment, the thermode temperature

becomes intolerable to you, manually remove the thermode from your arm immediately and alert the experimenter. You may abort your participation without giving up credit or payment. **To be clear: you may immediately end your participation if any aspect of the research procedure makes you too uncomfortable to continue.**

Psychological Discomfort: The pre-session surveys online include questions regarding activities that may be illegal (e.g., substance use) as well as possible traumatic experiences. These questions may cause some psychological discomfort. You are not required to answer any questions if you don't want to, and we will protect the confidentiality of your information to the highest degree possible.

- **MRI Scanning - Physical Risks and Discomforts:** MR studies are among the safest of all non-invasive medical procedures, but certain hazards exist. To minimize these hazards, only trained technicians are in the immediate area and all participants are screened prior to entering the MR scanner. However:
  - Your participation in this research study is voluntary. Please think about the information below carefully. Feel free to ask questions before making your decision whether or not to participate. If you decide to participate, you will be asked to sign this form and will receive a copy of the form.
  - **Metal and MRI safety**. The MRI machine produces a constant, strong magnetic field (3 Tesla), so if you have metal implants and clips within your body they may be influenced by the magnetic field and shift in position. Thus, if you have such implants you must inform us and withdraw from the study. Metal earrings and necklaces also must be removed prior to the study. If you have shrapnel, surgical implants, or other pieces of metal in your body that cannot be removed, you may not be able to participate in studies involving the MRI scanner. In many cases, people having dental appliances in their mouths can participate but should notify the investigator to be certain.
  - **Pregnancy**. The risks of an MRI scan to the unborn fetus are unknown. We strongly recommend pregnant women do not take part in this research study. By signing this form you are indicating to the best of your knowledge that you are not pregnant. If you are uncertain then the study can be rescheduled to a later date.
  - **Hearing.** The functional MRI scanning produces a loud (92 dB) high frequency tone that can cause hearing damage if appropriate hearing protection is not used. Adequate hearing protection in the form of foam ear-plugs will be provided and required.
  - **Claustrophobia**. The functional scanning coil fits closely around your head, so if you feel anxious in confined spaces, you may not want to participate. If you decide to participate, and then at a later time decide to discontinue, just let us know and we will stop the experiment..
  - **Incidental Findings**. **MRI is commonly used in medicine for the purpose of diagnosing abnormalities of the brain. The procedures that are to be used in this study are different**

from clinical MRI scanning. As researchers, we do not intend to make any medical diagnosis with the MRI as used in this research project, and we are not trained in medical diagnosis. The MRI may not be reviewed in a timely way. However, if in the course of this research study we observe an anomaly in one or more of the MRI images, we feel ethically obligated to inform you of the observation. We believe it is important to inform you of such observations, because we cannot rule out the possibility that an anomaly may require medical attention. In this event, all information collected as part of this study will be made available to you for further examination by a medical professional. You will be fully responsible for the costs associated with a radiological examination and any further examinations or treatments that may be required for medical purposes. If you prefer not to be informed of an image anomaly, you must choose not to participate in the study.

If you are a Dartmouth Student, depending on the results of the medical review, we will also contact Dick's House or your parents to continue follow up.

Important items to know:

- **Leaving the study:** Whether or not you take part in this research is your choice. You can leave the research at any time and it will not be held against you. You have the right to refuse to answer any question(s) or refuse to participate in any procedure for any reason. Refusing to participate in this study will not result in any penalty or loss of benefits to which you are otherwise entitled. If you choose to discontinue the study early, you will be paid a prorated rate based upon the amount of time you participated in the study, with no penalty for discontinuing. The experimental data collected up until the time you decide to withdraw will be destroyed if you choose to do so. If you are a Dartmouth College student or employee, taking part in this research is not part of your class work or duties. You can refuse to enroll, or withdraw after enrolling at any time, with no effect on your class standing, grades, or job at Dartmouth College. You will not be offered or receive any special consideration if you take part in this research.
- **Number of people in this study:** We expect 150 people to enroll in this study.
- **Funding:** This research is funded by a grant from the National Institutes of Health, administered through the department of Psychological and Brain Sciences at Dartmouth College.

How will my privacy be protected?

All information you provide will be kept confidential except as required by law. Your name will not be used in any publication that may result from this study. The Office of the Committee for the Protection of Human Subjects may request access to this form to ensure procedures designed to protect research participants are being properly followed. The manufacturer of the MRI scanner

(Siemens) may request the use of images acquired in this study, although they will not have access to the names of any subjects.

For the MRI scan, basic identifying information will be collected from you (e.g., name, address, phone number) for scheduling visits. This is "identifying information" because it can be used to ascertain your identity. This information will be stored separately from other study data in a password-protected file available only to the PI and research coordinator. No identifying information will be linked to the data from the study except by this master list.

Your study data will be stored on restricted access/password protected servers and/or in locked filing cabinets in a locked room, to which only the PIs and members of the research team have access. These procedures will minimize the risk of identifying information being divulged to non-members of the research team. Strict standards of confidentiality are maintained. MRI data will be electronically stored and analyzed using ID codes. If the data are published, you will remain anonymous in all publications. Identifiable data will be stored indefinitely and will not be shared with other investigators or with the public without your explicit permission.

De-identified data may be published and shared in public repositories for scientific purposes, as required by our funding agencies and scientific journals. In such cases, every reasonable effort will be made to remove identifiers from the data that would indicate any connection to you (e.g. the removal of your name, address, SSN, etc.).

At the end of the study, we will discard personally identifying information, unless you have given us explicit consent to be re-contacted. Your other study data will be retained indefinitely in a de-identified form using a coded identification number and will be stored on password-protected computers accessible only to the research team.

Your Right to Revoke Consent to Participate in this fMRI Study: At any time now or in the future you feel that your data should no longer be used for research purposes, you have the right to revoke the consent you gave in signing this document. Please communicate your desire to have your data removed from the investigator's database by contacting the investigator(s) or person(s) listed below. Keep in mind that if your anonymized brain image data have been shared with other researchers or placed in a centralized archive, then it may be impossible to have these copies deleted.

This study has been issued a Certificate of Confidentiality from the federal government to help protect your privacy. This certification means that the researchers cannot be forced to tell people who are not connected with the study, such as the court system, about your participation in this study. But, if you request that we do so, we will release information that is unique to you.

There are three exceptions to this promise of confidentiality:

- If we see or are told information that makes us reasonably suspect that a child or at-risk adult is being or has been abused, mistreated, or neglected, we will immediately report that information to the county department of social services or a local law enforcement agency.
- If we learn of a serious threat of imminent physical violence against a person, we will report that information to the appropriate legal authorities and make reasonable and timely efforts to notify the potential victim.
- This promise of confidentiality does not include information we may learn about future criminal conduct.

Will I be paid to take part in this study?

You will be compensated 1 T-point/hr for your participation if you are an eligible student. Alternatively, you may select to be paid monetarily. If so, you will be compensated $12 for each of the behavioral and survey components of the study, $24/hr for the MRI portion and a $50 bonus for completion of all components of the study. Payment for research participation is taxable income.

Research Related Injury. If you are injured as a result taking part in this research study, seek medical attention immediately (if it is a medical emergency, first call 911). This care will be billed to you, your insurance, or another third party. Dartmouth College has no program to pay for medical care for research-related injury. Please contact the investigator as soon as possible to report the event.

Whom should you call with questions about this study?

If you have questions about this study or concerns about a research related injury, you can contact the research director for this study: Dr. Tor Wager at Tor.D.Wager@dartmouth.edu (303) 895 8739 or the postdoctoral PI: Dr. Michael Sun msun@dartmouth.edu during normal business hours.

If you have questions, concerns, complaints, or suggestions about human research at Dartmouth, you may call the Office of the Committee for the Protection of Human Subjects at Dartmouth College (603) 646-6482 during normal business hours.

CONSENT

I have read the above information about the *Treatments for Temperature Reponses and Reactivity Study* and have been given time to ask questions. By signing the informed consent document, I

acknowledge that I am 18 years of age or older. I have been given a copy of this signed consent form and I hereby consent to participate in the study.

I understand I may be re-contacted for follow-up assessments or future studies. I understand that if contacted, I can freely choose to participate in future research or not.

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Participant's Signature and Date / PRINTED NAME

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Researcher or Designee Signature and Date / PRINTED NAME