University of Colorado Boulder

Permission to Take Part in a Human Research Study

Title of research study: Mind-body treatments for chronic back pain (NCT03294148)

Investigator: Tor D. Wager

Why am I being invited to take part in a research study?

We invite you to take part in a research study because have back pain for more than 3 months and meet all other inclusion criteria (e.g., fMRI safety criteria).

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at ***canlab@colorado.edu or tor.wager@colorado.edu***

This research has been reviewed and approved by an Institutional Review Board ("IRB"). You may talk to them at (303) 735-3702 or irbadmin@colorado.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Why is this research being done?

The purpose of this study is to test the efficacy of a subcutaneous injection of saline solution into the back as a treatment for back pain. Placebo treatments in randomized controlled trials are associated with significant symptom relief. In rigorous randomized controlled trials, placebo injections have been shown to be as effective as true epidural steroid injections. The reasons receiving a placebo may help ease pain are still largely unknown, but a placebo injection may cause the release of pain-relieving chemicals called opioids in the brain. Opioids are associated with pain relief, and also with relief from depression in some studies. Recent research suggests that placebos can still work even when patients

know they are receiving a placebo, possibly due to automatically triggered placebo responses. In this study, we want to understand the brain mechanisms of how placebo treatments can relieve back pain.

How long will the research last?

This study consists of 4 - 5 visits over 1.5 – 3 months, depending on which group you are randomized to. These visits will all take place here at the Center for Innovation and Creativity (CINC) at the University of Colorado Boulder, except for the placebo treatment, which will be administered at the Panorama Orthopedics and Spine Center in Golden, CO or at the at the Wardenburg Clinical Translational Research Center (CTRC) on the CU Boulder Main Campus. We will share your contact and demographic information with this clinic so they can schedule you for treatment (see the HIPPA form, attached).

Additionally, at 1, 2, 3, 6, and 12 months after your last session here, we will ask you to complete a brief (~10 minute) online questionnaire from home.

In total, this study will require 8 – 10.5 hours over 3 months, plus 1 – 2 hours over the entire study completing online questionnaires from home.

How many people will be studied?

We expect about 240 people will be in this research study.

What happens if I say yes, I want to be in this research?

We will ask you to **continue your normal treatment schedule and not to add, stop, or change any treatment-related activities** and **not to make any large lifestyle changes (i.e., diet, exercise)** for the time between the two brain scans (about 1 month). This is important to help us have a cleaner comparison of changes in the treatment vs. wait-list groups.

If you need to change, add, or remove any of your current treatments during course of study we ask that you inform the study team as soon as possible. In cases of medical emergency (e.g., emergency medical care in a hospital) follow the recommendations of your physician and inform the study investigator about any changes as soon as possible. In these cases, your participation in the study may be stopped and you will be compensated for the portions of the protocol that you completed. It is also possible that you could complete the study at a later date.

The study involves the following procedures:

Session 1: Eligibility Assessment (All participants, 1.5 – 2.5 hours)

First, we will test whether inflating and deflating a bladder under your back elicits back pain for you. This will feel similar to laying with a rolled-up towel placed under your low back and may elicit mild to moderately high intensity pain. While the bladder is inflating and deflating, we will ask you to rate how much pain you are in.

During this session, you will also have the option of completing an electroencephalogram (EEG). For this, we will place a cap with electrodes in it for measuring electrical signals on your scalp. We will also apply some conductive gel under the electrodes, to get better measure electrical signals. Then, we will ask you to sit still with your eyes closed for 20 minutes while we collect EEG measurements. If you choose to do the EEG, we will also collect EEG while the bladder is inflating and deflating under you. Additionally, we will ask you to listen to a tone that varies in volume and to rate how loud it is while we collect EEG. EEG collection is optional, and declining EEG will not impact any other aspect of your participation in the study.

We also apply several painful pressure stimulations to your thumbnail, to confirm that these stimulations are painful but tolerable for you. We want to confirm this because later in the study we will apply more pressure stimulations to your thumbnail.

The pressure pain device uses a computer-controlled pressure regulator and compressed air to push a small soft piston into your thumbnail for a few seconds. This feels like someone squeezing your thumbnail. Depicted in the image to the right is a picture of a thumb in the device.

We will then ask you to fill out several forms, including questions about your mood, personality, and MRI safety questionnaires. One of these forms will be on a smartphone application that we will ask you to download on to your phone. If you are eligible to participate in this study, we will schedule the next sessions with you. If you are not eligible, we will pay you for your time today.

Session 2: MRI 1 (All participants, 3 hours)

First, you will be asked to complete some questionnaires. We will then prepare you for the MRI scan. During fMRI scanning we ask you to complete the following tasks:

1. Ratings of ongoing back pain. We will elicit back pain of moderate intensity in the scanner by inflating the bladder under your back in the scanner, and ask you to rate your back pain every 30 – 60 seconds.

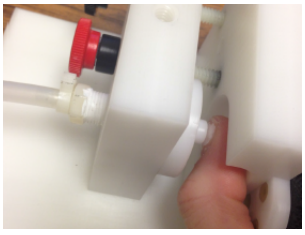
2. Pressure and sound pain task. We will apply pressure stimulations to your fingernail of varying intensities, and play unpleasant sounds through earbuds that will be in your ears. These stimulations will be mildly to moderately painful or unpleasant but tolerable. Before each stimulation, we will also tell you how other people rated the stimulation. After each stimulation, we'll ask how painful it was for you.

Then you will be asked to complete a task in which you can earn small amounts of money (~$1-$3) for a number of button presses, and another task where you will be given a $10 endowment that you can auction to not experience any pain or keep and experience up to 10 minutes of pain.

A blood sample will also be collected at this session. The blood sample will be collected with standard venipuncture (blood draw) technique of an upper extremity vein. You will have 8 ml of blood taken two times over the course of the entire study (16 ml of blood total), which is about the amount of blood in 3 teaspoons. If there is a contraindication to the blood draw, we will collect a blood spot instead. The blood spot uses a finger stick collection device. The device draws 2 -3 drops of blood from the fingertip, is mildly painful, and has minimal associated risks.

At the end of this session you will be randomized (like flipping a coin) into either the treatment group or the waitlist group. If you are randomized to treatment, we will schedule the treatment with you (see below). If you are randomized to waitlist, you will be asked not to start any other treatments until after your second fMRI session. Then we will offer you the treatment (optional).

We will also email or text you a brief daily survey for 3 days before and after this session.



Session 3: Treatment (30 minutes, treatment group only, offered to waitlist group later)

The placebo treatment is an injection of 1mL saline into the low back. It will be administered at the Panorama Orthopedics and Spine Center by a medical professional, just like a visit to a doctor's office. We will schedule the treatment for as soon as possible after Session 2.

Session 4: MRI 2 (all participants, 3 hours)

This session will be the same as Session 2 (see above) and will happen about 4 weeks after Session 3. You will again complete questionnaires, perform the same tasks inside and outside the scanner as before, and collect another blood sample. We will again email or text you surveys for three days before and after this visit.

Session 5: Treatment for waitlist group (30 minutes, optional)

Waitlisted participants will be offered the study treatment described in Session 3 above. Receiving this treatment is optional. It will be scheduled at your earliest convenience.

Brief weekly surveys:

Between sessions 2 and 4, we will email or text you a brief (~10 minute) survey once per week.

Online follow-up surveys (all participants)

1, 2, 3, 6, and 12 months after you completed your last visit, we will send you questionnaires to complete from home.

What happens if I do not want to be in this research?

You can leave the research at any time and it will not be held against you.

What happens if I say yes, but I change my mind later?

You can leave the research at any time and it will not be held against you. We will still use the data we have collected so far, unless you explicitly withdraw your consent in writing. However, it may not be possible to delete all your data because we de-identify them and may not be able to link you to all the data we have collected from you.

Is there any way being in this study could be bad for me?

The placebo treatment: You may experience mild pain during the injection. The risks for adverse events associated with the injection are minimal. We will not inject any drugs.

The pressure stimulations: The pressure stimulations will 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 pressure, there is a slight risk of lingering tenderness or discomfort on the thumb. In addition, risks could also result from a malfunction of the pressure equipment used in this study. However, the probability of a machinery malfunction is extremely low: we extensively tested the equipment and carefully monitor it regularly to ensure its proper functioning. If at any point during the experiment the pressure is intolerable, please remove your thumb from the device immediately and alert the experimenter. If you experience severe tenderness or discomfort at any point during the experiment or after, please contact the experimenter immediately. Tenderness or discomfort normally disappears

within 24 hours. In the event of injury, please seek medical attention immediately. Safety guidelines for the design and administration of this study are strictly followed in order to minimize any such risk.

Back pain elicitation: The inflating bladder will be painful but cannot damage your back. It may cause psychological discomfort by temporarily exacerbating your back pain. There is also the possibility of unforeseen risks with the bladder device, such as some lingering pain, even though the device cannot injure the back.

Blood sample: The risks of taking blood include pain, bruising, redness, swelling, or infection at the puncture site, and a rare risk of fainting. The risks will be minimized by using standard protocols for blood sampling, including techniques to minimize the risk of infection/adverse events.

Data: There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.

MRI risks: MRI studies are among the safest of all non-invasive medical procedures, but certain hazards exist, including:

1) If a piece of metal, a device made of metal, or an electronic device were on or in your body, especially in the eye, heart, or brain, you could be injured by the magnetic field.

2) If you were to be pregnant, it is possible that this protocol could injure the fetus (there is no good data to predict a percentage), but many pregnant women have been safely studied with MRI without injury to the fetus. However, you will be screened prior to the procedure and specifically asked whether you could be pregnant. You will only be studied if you record "No."

3) If you were not to wear earplugs, the noise could potentially injure hearing. Earplugs will be offered prior to the examination.

4) You may have some discomfort due to lying in one position for a long time. The discomfort should subside once the scan is complete, but some participants may be sore for longer.

5) At sufficient exposure levels, peripheral nerve stimulation (PNS) is perceptible as "tingling" or "tapping" sensations. PNS symptoms will usually subside shortly after the scan is completed.

6) You may experience nervousness and/or feelings of claustrophobia. You will be screened for claustrophobia prior to entering the scanner, but should you feel any psychological discomfort upon entering the scanner, you will be able to communicate with the MRI technician and you may stop the scan at any time.

EEG risks: EEG is considered safe. There is no risk of shock. There may be some discomfort when putting on the cap.

What are the possible benefits of the study?

You may not benefit directly by participating in this study. This study is designed for the researcher to learn more about the effectiveness of open-label placebo treatments. If this works well, this procedure could offer an alternative treatment with minimal risks for patients suffering from back pain, and could influence how back pain is conceptualized and treated by the medical community.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include a reduction or relief from your back pain following the injection.

What happens to the information collected for the research?

Only the research team will have access to your personal information collected during this study. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

The investigator (or staff acting on behalf of the investigator) will use your information for the research outlined in this consent form. They will also send blood samples to Dr. Michael Irwin, UCLA. Data sent to him will be completely de-identified (i.e., tagged only with a random ID, not with any identifying information). Only measures of immune system function will be extracted from these samples, and then they will be destroyed. EEG and select questionnaire data will also be shared with our collaborators at PainQX. This data will be also be completely de-identified (i.e., tagged only with a random ID, not with any identifying information). The data about your mood and feelings that you enter into the smartphone application will also be shared with the application developers, Cliexa. This data will be also be completely de-identified (i.e., tagged only with a random ID, not with any identifying information).

The data, blood and specimens collected from you during this study are important to this study and to future research. Data will be de-identified and then maintained indefinitely, and blood samples will be destroyed after analyses are completed.

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include MRI safety reasons or if the study doctor thinks that being in the study may cause you harm, you are not following study procedures, or any other reason.

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

What else do I need to know?

This research is being funded by the Foundation for the Study of the Therapeutic Encounter.

You may be able to serve as a scheduled back-up participant. Serving as a back-up is optional and has no bearing on any other aspects of their participation in the study. If you do this, you will be asked to arrive at the same time as another scheduled participant (the "primary" participant). If the primary participant fails to show, or is unable to be scanned for an unexpected reason, then you will be scanned instead. If the primary participant does show and is able to be scanned as expected, you will be paid $25 and sent home. This determination will be made approximately 1 hour and 10 minutes after the you are asked to arrive, once the scan for the primary participant is successfully underway. If you are a back-up, you may also have a "primary" scan scheduled at a future date (after which you can no longer serve as back-ups), or, you may continue serving as a back-up indefinitely and have your primary scan scheduled only when enrollment nears its end.

We do not expect any harm to you as part of this study, but if you feel you need medical care because of taking part in this research study, seek medical attention immediately (if it is a medical emergency, first call 911). Generally, this care will be billed to you, your insurance, or another third party. The University of Colorado has no program to pay for medical care for research-related injury.

It is important that you tell the Principal Investigator Tor Wager if you think you have been injured as a result of taking part in this study. You can call him at *303-492-7487* or contact him via email at Tor.Wager@Colorado.edu.

How much will I be paid for participating in this study?

All participants will be paid $50 for the eligibility session if completing EEG or $25 if not, $75 for each MRI session, and $5 for each follow-up survey completed (follow-up payments to be disbursed after the 12-month follow-up survey). You also have the option to receive a 3D print-out of your brain instead of a $75 payment for one of the MRI sessions. The market cost of a 3D brain print-out is over $250 for people who already have a brain image, which we will give you freely. You will thus be paid up to $225 for completing this study, or a 3D brain printout plus $150.

If you leave the study early, or if we have to take you out of the study, you will be paid only for the visits you have completed. If a visit is partially completed, your compensation will be prorated per hour of involvement. All payment will be given at your last assessment session, in cash. Payment for the follow up surveys will be in the form of an Amazon.com gift card sent to you electronically or through the mail, depending on your preference, after the final 12-month follow-up survey.

You can also earn several dollars at each assessment session from the progressive ratio button pressing task and from the willingness to experience pain task. The exact amount will vary depending on your choices, but is estimated to be $0 - $15 at each of the pre- and post-treatment assessment sessions.

If you are a back-up participant, you will be paid $25 for each visit.

Payments for participation in a study is taxable income.

May we have permission to contact you in the future regarding other studies?
____ Yes, you my you may contact me regarding future studies.
____ No, you may not contact me regarding future studies.

Would you like to do EEG today?
____ Yes
____ No

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

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	07.23.2018 IRB Approval Date