Northwestern University
Physical Medicine & Rehabilitation and Internal Medicine

Consent Form and HIPAA Authorization for Research

TITLE OF RESEARCH STUDY:
Corticostriatal plasticity in the transition to chronic pain: Effect of L-dopa

INVESTIGATORS:

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Introduction

You are being asked to take part in a research study. This document has important information about the reason for the study, what you will do if you choose to be in this research study, and the way we at Northwestern University would like to use information about you and your health.

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 in this study.
- You can agree to take part in this study and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Conflict of Interest Disclosure

If your doctor is also a person involved in this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether or not to participate in the research.

Financial Interest Disclosure

The following disclosures are made to give you an opportunity to decide if the following information will affect your willingness to participate in this research study: This research is being funded by The National Institute of Dental and Craniofacial Research (NIDCR) and The National Institute of Health (NIH).

Why am I being asked to take part in this research study?

You are being asked to participate because you currently have new lower back pain that began 4–20 weeks ago.

Why is this research being done?

The transition from acute low back pain to chronic low back pain has been shown to be a result of changes in brain activity. Acute pain might be mild and last just a moment, or it might be severe and last for weeks or months. In most cases, acute pain does not last longer than six months, and it disappears when the underlying cause of pain has been treated or has healed. Unrelieved acute pain, however, might lead to chronic pain. Chronic pain persists despite the fact that the injury has healed. Pain signals remain active in the nervous system for weeks, months, or years.

These pain signals can be directly affected by a chemical in the brain called dopamine. Dopamine helps control the brain's reward and pleasure centers; it enables us not only to see rewards, but to take action towards obtaining them. Dopamine also helps regulate movement and emotional responses. The purpose of this study is to assess the efficacy and safety of early treatment with the drug Carbidopa/Levodopa when used in combination with Naproxen in preventing chronic low back pain in individuals who have sub-acute low back pain following an injury, or new back pain, which has persisted for less than 20 weeks.

The study drug, Carbidopa-Levodopa, is an FDA-approved medicine traditionally used for the treatment of Parkinson's disease. The study drug will be used for an un-approved or un-labeled use: potentially preventing chronic lower back pain in individuals who have acute back pain. Carbidopa/Levodopa is an artificially made version of a naturally occurring hormone that helps regulate brain activity (Levodopa), combined with an artificially made version of a naturally occurring molecule that inhibits the breakdown of Levodopa (Carbidopa).

This study is a 24-week, two-armed, double-blind, randomized, placebo-controlled trial of the pharmacological treatment Carbidopa/Levodopa for individuals with sub-acute back pain (SBP).

- This is a two-armed study. If you qualify for the study you will receive either the study drug or placebo and Naproxen for your low back pain. Naproxen is a non-steroidal anti-inflammatory drug (NSAID) approved by the FDA for treatment of pain. The first 12 participants who will be eligible and will agree to sign the consent form will enter this study in order to validate the brain parameters obtained with our updated MRI scanner. The participation of these subjects may be discontinued afterwards based on the MRI results.
- This is a double-blind study. If you are in this study, you, the doctors, and the study staff will not know which treatment you will get. You will get the medicines in a way that will not make it possible for you, the doctor, or the study staff to know which treatment it is. However, in an emergency, doctors can get this information.
- This is a randomized study. If you are in this study, you will either be given the study drug or an inactive substance (known as a placebo) by chance using a process similar to the flip of a coin. This process is called randomization. Neither you nor the study staff will know whether or not you are taking the study drug. However, if you have a medical emergency, we can get this information.
- This is a placebo-controlled study. The study compares the study drug, Carbidopa/Levodopa, to a placebo. A placebo looks like the study drug, but is an inactive substance that has no medication. Researchers use a placebo to see if the study drug works better or is safer than not taking anything. Regardless of which treatment arm participants are in, everyone will receive Naproxen.

How many people will be studied?

The study investigators hope to screen 200 individuals and enroll 126 participants at Northwestern University.

How long will this research last?

The study duration is approximately 28 weeks and will consist of 8 visits. There will be a Screening Visit, Baseline Visit, and 6 Study Visits, which are outlined below. The schedule for the 6 Study Visits after your Baseline Visit will be referred to as Week 0, Week 1, Week 4, Week 8, Week 12, and Week 24. If you receive the study drugs, treatment will be terminated after Week 12, but your back pain will continue to be evaluated by monthly questionnaires until the end of the study (Week 24). Follow-up telephone calls at Week 16 and Week 20 will be made to continue evaluation of your back pain.

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

If you consent to participate, you will be asked to come to Abbott Hall located at 710 N. Lake Shore Drive, 10th floor, Chicago, IL 60611. Some of the study procedures will take place in nearby buildings and the study coordinator will direct you to those locations.

In this study, all subjects will continue their clinical care as needed with their primary care physician and/or specialist. If you are taking medication for your back pain upon entry into this study, you will be asked to discontinue your current treatment and take only the study medication for the first 12 weeks of this study. You will be allowed to take rescue pain medication (acetaminophen, up to 3 grams/day) as needed for the 12 week treatment period. You may not take other non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, naproxen, or other acetaminophen-containing medications during the 12-week treatment period. Additionally, the use of opioids (such as tramadol, codeine, oxycodone, and methadone) and tricyclic antidepressants (such as, Elavil, Silenor, Afafranil) except in low doses for sleep are prohibited during the study period. At each visit, we will record all medications that you are taking or have taken since the last visit. You will be allowed to resume former pain therapies for the follow-up period (Weeks 12-24) only after proper study medication discontinuation. Additionally, if you are interested, you will have an option to participate in other low back pain studies at Northwestern University.

- **Screening Visit (Visit 1: Week -4)**

The first visit will take 1.5 hours. You will be asked to complete the informed consent process and will be evaluated with inclusion/exclusion criteria. A medical/pain history and physical examination will be completed. You will be asked to assess your current back pain intensity and complete self-report questionnaires. Urine will be obtained for screening of illicit drugs; additionally, blood will be drawn for screening purposes (40 mL or 8 teaspoons) to check your kidney and liver functions, alcohol level, and blood cell counts (for problems like anemia). For women of child-bearing potential, blood will be collected for a pregnancy test. Temperature, weight, blood pressure and heart rate will be assessed. Orthostatic (standing) blood pressure measurements will be obtained if you are taking anti-hypertensive medications. You will return in 1 – 2 weeks for baseline fMRI scans unless you are not able to have, or meet the requirements for, brain imaging. Additionally, you will be trained on how to use an electronic application for a smart phone that will allow you to rate your pain 3 times per day for the 24-week duration of the study. You will be compensated for your responses. Failure to use the application to rate your pain will result in being dropped from the study.

- **Baseline Imaging Visit (Visit 2: Week -2)**

(Note: Those not eligible for brain imaging will go directly to Visit 3).

If you qualify for the study (based on the initial screening visit and your pain ratings on the smart phone app between visits 1 and 2) and are eligible for brain imaging, you will return for the baseline

imaging visit. This visit will take approximately 2 – 2.5 hours. You will be asked to rate your back pain and complete questionnaires. You will also undergo fMRI procedures. These scan data will be used to determine eligibility for entering the study.

This study uses functional magnetic resonance imaging (fMRI) to look at the brain at both the Baseline and the Final Visit. An fMRI is a type of brain scan that uses magnetic fields and radio waves to make an image of changes in blood flow in your brain while you perform certain tasks. In order to make sure the fMRI procedure will be safe, you will be asked to fill out a screening form before starting the study. It is important that you tell the researchers in this study if you have any history of:

- Metal fragments in your eyes or face.
- Implantation of any electronic devices such as (but not limited to) cardiac pacemakers, cardiac defibrillators, cochlea implants or nerve stimulators.
- Surgery on the blood vessels of your brain or the valves of the heart
- Claustrophobia (fear of enclosed places)
- Body piercing or tattoos
- Brain or skull abnormalities

You will be given instructions about the scanning prior to entering the MRI scanner. Next, you will be asked to lie still on the MRI patient table and your head will be placed in a specially-designed head holder. Your head will be cushioned by a firm foam pillow. The table will then slide into the enclosed space of the MRI scanner. Some people feel tired, uncomfortable or claustrophobic (afraid of small spaces) in the MRI scanner. The MRI scanning session will take about 50 minutes to an hour to complete once you are in the scanner.

The information from the MRI scanner is only useful if you are able to complete the whole imaging session, and hold your head very still the whole time; therefore, you will be encouraged to hold as still as possible and let the investigators know if you are uncomfortable in any way as soon as possible after the imaging session begins.

The front of the head-holder will be open, which lets you look through a special mirror and see the open end or a projection screen near your head. You will be asked to hold your head as still as possible and to respond to visual cues by pushing a button or thinking quietly to yourself.

The MRI scanner makes loud banging noises while taking a measurement, so either ear plugs or specially designed headphones will be used to reduce the noise. The researchers will be in communication with you through an intercom system to tell you how the study is going. The earplugs or headphones should not get in the way of communicating with the researchers.

- **Randomization Visit (Visit 3; Week 0)**

The randomization visit will take around 30 minutes. If you have not undergone a baseline MRI, you will receive treatment at this visit and you will be assumed to be at high risk for chronification of lower back pain. If you did receive brain imaging, we will inform you (also known as "debriefing") of the results from your first MRI screening that may indicate whether or not you are likely (~90%) to develop persistent low back pain with regular treatment (such as NSAIDs). If the results indicate that you are unlikely (~10%) to develop persistent low back pain, you will be given the option to participate in the observational substudy, which does not include medication.

Participants receiving treatment will be put on active study medication (carbidopa/levodopa plus naproxen) or a placebo plus naproxen; regardless, both of these groups will receive omeprazole and the rescue medication (acetaminophen). Omeprazole is prescribed one time per day as a preventative measure against possible gastric adverse effects of naproxen. Both the study

medication and the placebo will be identical in appearance and are suggested to be taken with food or a meal. If you are randomized to the group that receives the active carbidopa/levodopa capsules, you will begin treatment with 12.5/50mg, and over time you may be increased from the initial dose up to a total daily dose of 50/200 mg of carbidopa/levodopa. After a total of 12 weeks, you will be tapered off of treatment. You will take 2 capsules (one containing naproxen, and the other containing either placebo or carbidopa/levodopa) 3 times per day after the first week. Neither you nor the research team will know what treatment you will be receiving. You will be asked to report any changes in your health or medications, rate your current back pain, and complete the self-report questionnaires. Blood pressure and heart rate will be determined for all subjects. Orthostatic (standing) blood pressure measurements will be obtained for if you are taking anti-hypertensive medications. If you are a woman of child-bearing potential, you will have a urine pregnancy test done prior to receiving study medication.

- **Interim Treatment Visits (Visit 4 – Visit 7: Weeks 1, 4, 8, and 12)**

The interim treatment visits will take around 30 minutes. You will come to the study location and be asked to report any changes in your health or medications, rate your current back pain, and complete the self-report questionnaires. Blood pressure and heart rate will be determined for all subjects. Orthostatic (standing) blood pressure measurements will be obtained for all participants taking anti-hypertensive medications. You will be given enough medication at each visit to last until the next visit. You will also be asked to bring back your study medications in their vials so that we may count the number of pills remaining. You will also be asked about any side effects or adverse events experienced. During Visit 5, at which time you will have had 4 weeks of medication, blood will be obtained to determine that the medication is at safe levels in your body.

If, at the end of the initial 4-week period, you have had a significant improvement in your pain, you will be maintained on that initial dose for the duration of the treatment period (12 weeks total). If there has not been a response in your pain level, the dose of the active drug (if you have been randomized to this group) will be increased for 4 more weeks, after which the pain status will be re-evaluated. Again, if there has been significant improvement in your pain, that dose of study medication will be maintained for the following 4 weeks of treatment; if not, the dose will increase again for the final 4 weeks. If you experience any side effects at a higher dose, you will be given the next lower dose that you are able to tolerate and then be maintained on that dose for the remainder of the 12-week medication period. After completing 11 weeks of treatment, we will have you slowly reduce the dosage of the study drug over the course of one week, for a total of 12 weeks on study medication.

- **Final Visit (Visit 8: Week 24):**

The final visit will take about 2 – 2.5 hours. You will be asked to assess your current back pain intensity and complete self-report questionnaires. Blood pressure and heart rate will be determined for all subjects. Orthostatic (standing) blood pressure measurements will be obtained for all participants taking anti-hypertensive medications. If you attended the MRI scanning session at the baseline visit (Visit 2), you will also undergo fMRI procedures. A urine sample will be collected from female subjects that are of child-bearing potential. You will be asked to bring back the medication so that we may count the pills remaining. You will be asked about side effects experienced.

- **Interim Electronic Contact**

You will be contacted by telephone and/or internet access on a monthly basis for two months after you have completed 12 weeks of treatment. At each of these interactions you will be asked about

your back pain, changes in health/medications, side effects, and will be able to share any other information. At the end of this clinical trial, we will be able to inform you which medication treatment you received while on study and the dosage of these medications.

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.

What are my responsibilities if I take part in this research?
If you take part in this research, you will be responsible for the following:

- Attending all visits within the timeframe set by the study coordinator
- Taking study medications as directed
- Rating pain and mood on the study phone application (or computer)

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 if you do not follow the directions of the study doctor, you do not provide responses on the smart phone app, you develop a serious illness that is not related to taking part in the study, or the study doctor decides that the study is not in your best interest. You could also be asked to stop taking part if the study sponsor, the responsible regulatory authority, or Institutional Review Board/Independent Ethics Committee (IRB/IEC) decides to stop the study altogether. You may also be asked to stop taking part in the study if you become pregnant, intend to become pregnant or are nursing a child during the study period.

What do I need to know about reproductive health/sexual activity if I am in this study?

The effects of the study drug, Carbidopa-Levodopa, on human sperm, human eggs, and the developing fetus have not been studied. The risk of birth defects is also unknown or may be unforeseeable. No effects on fertility were seen in rats receiving doses of approximately two times the maximum human dose and four times the maximum human dose of Carbidopa and Levodopa, respectively. No malformations of the embryo or fetus were seen in mice receiving up to 20 times the maximum recommended human dose of Carbidopa/Levodopa.

The effects of Carbidopa-Levodopa in pregnant women have also not been adequately studied. However, it is known that Levodopa crosses the placental barrier, enters the fetus, is metabolized, and trace amounts can be seen in fetal tissue. Therefore, both men and women should not attempt pregnancy, and women should not be pregnant or breast-feeding while taking part in this study.

If sexually active, both men and women should use an effective method of birth control while taking the study drug. Barrier contraceptives (condoms or diaphragm) with spermicide, intrauterine devices (IUDs), hormonal contraceptives, oral contraceptive pills, surgical sterilization, and complete abstinence are examples of effective methods. If you or your partner become pregnant while taking the study drug, it is important that you tell your study doctor immediately. You will need to discontinue the study drug and will be withdrawn from the study. Additionally, we will ask your permission to notify your physician of your participation in this clinical trial and will ask to monitor you or your partner throughout the pregnancy and delivery or termination of pregnancy. Unbinding may occur by a member of the research staff if requested by your physician and/or obstetrician. All pregnancies occurring during the course of the study will be reported to the FDA, our sponsor (NIDCR) and the Institutional Review Board at Northwestern University.

Naproxen has been shown to be harmful to developing fetuses and should only be taken by pregnant women when there is no other alternative and their health care providers have determined that the benefits of naproxen outweigh the risks. Other treatment options will be discussed with you if you stop the study drug.

If you are considered to be postmenopausal, you are not required to use contraception while in this study. Rarely, women considered to be postmenopausal become pregnant. If you suspect that you become pregnant while taking the study drug, it is important that you tell the study doctor immediately. You may have to stop the study drug. Other treatment options will be discussed with you if you stop the study drug.

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

Risks from being in this study may include the following: possible side effects from the study medications or blood draw; feeling uncomfortable answering the questionnaires, participating in a MRI test. Here we describe some of these potential effects:

Study Medications

1) Carbidopa-Levodopa: A drug therapy that combines the dopamine agonists Levodopa and Carbidopa. The combination aims at increasing the levels of dopamine in the brain while preventing any similar increase in the rest of the body, hence minimizing side effects. To reduce the incidence of side effects, the dose of medication will be increased slowly and your health will be monitored closely. After completing 12 weeks of treatment, we will have you slowly taper off of the study drug.

The risks involved in using Carbidopa-Levodopa are as follows:

- Dyskinesia (involuntary movements)
- Nausea
- Mental disturbances (hallucinations, depression)
- Confusion
- Dizziness
- Urinary tract infection
- Headache
- Vomiting
- Constipation
- Impulse control symptoms (failure to resist a temptation, urge or impulse that may harm oneself or others such as excessive gambling, excessive shopping or binge eating)
- Fatigue
- Drowsiness
- Abdominal pain and distress
- Vivid dreams

2) Naproxen: All NSAIDs, including Naproxen, may cause serious cardiovascular side effects such as heart attack (myocardial infarction) or stroke (cerebrovascular accident), which may result in hospitalization and even death. Although serious cardiovascular events can occur without warning symptoms, you should be alert for the signs and symptoms of chest pain, shortness of breath, weakness, or slurring of speech, and should ask for medical advice if you observe any of these signs or symptoms.

Naproxen, as all other NSAIDs, can cause gastrointestinal (abdominal) discomfort, and, rarely, more serious side effects such as ulcers and bleeding, which may result in hospitalization and even death. Although serious gastrointestinal events can occur without warning symptoms, you should be alert for the signs and symptoms of ulcerations and bleeding, and should ask for medical advice when you observe any signs or symptoms that are indicative of these disorders, including epigastric pain (stomach pain), dyspepsia (upset stomach), melena (black stools) and hematemesis (vomiting blood). Older people are at higher risk for ulcers caused by these medications.

Other side effects that you may have after taking Naproxen include: constipation, diarrhea, heartburn, abdominal pain, nausea, headache, feeling dizzy, itching, hives, rash, ringing in the ears, feeling sleepy, shortness of breath and swelling of hands, feet and/or face.

Long-term use of Naproxen may result in abnormal liver tests or impaired kidney function. The cardiovascular (heart and blood vessel) safety of Naproxen in comparison to placebo has not been studied in a long-term research study.

3) Acetaminophen: The rescue medication for this study, acetaminophen, may cause liver damage and rarely death due to overdosing and/or mixing with alcohol. Early symptoms of liver damage include, but are not limited to, nausea, vomiting, sweating, and general malaise (not feeling well). Subjects should not take more than four 500 mg tablets during a 24-hour period. If you drink 3 or more alcoholic beverages per day you should tell the study doctor. Regular use of acetaminophen may increase the risk of chronic kidney failure, but only in those individuals with pre-existing kidney disease. Acetaminophen has no significant side effects on the kidney if your kidney function is normal and the dosing instructions are followed. Prior to receiving study treatment, your blood will be tested to see if your kidneys and liver are functioning well.

4) Placebo:
There is the risk that you will not get the study drug or your normal medication, and you may see no improvement in your condition or your symptoms may get worse.

This is not a complete list of side effects and others may occur. Tell your doctor about any unusual or bothersome side effects. If you have an allergic reaction to the study drugs seek emergency help and contact the study doctor as soon as possible. Signs of an allergic reaction include hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

5) Omeprazole
Omeprazole is a proton pump inhibitor that is prescribed to prevent any gastrointestinal upset due to intake of naproxen.

The side effects for omeprazole (given with a capsule of naproxen) include common and less serious symptoms such as headache, diarrhea, nausea, stomach pain, vomiting, and gas. Less common but serious side effects include: rash, face swelling, throat tightness, and difficulty breathing.

A number of drugs should not be taken while receiving omeprazole; these include atazanavir, nelfinavir,and saquinavir. Omeprazole may interfere with ketoconazole, iron salts, erlotinib, ampicillin esters, digoxin, and mycophenolate mofetil, clopidogrel, and cilostazol so please tell the study staff if you are taking any of these medications. In addition, drugs such as diazepam, warfarin, phenytoin, cyclosporine, disulfiram, benzodiazepines can be prolonged in their

elimination when taking in conjunction with omeprazole. Please make sure the study staff knows if you are taking any of these medications during the study so you can be monitored appropriately. In case such interactions would result in any clinically meaningful increase in risk you will be excluded for safety reasons.

Blood Draw
The risks of taking blood include pain, a bruise at the point where the blood is taken, redness and swelling of the vein and infection, and a rare risk of fainting.

Self-Report Questionnaires
Some of the questions asked may be upsetting or you may feel uncomfortable answering them. If you do not wish to answer a question, you may skip it and go to the next question.

Functional Magnetic Resonance Imaging
For the fMRI test, you will lie in a small closed area inside a large magnetic tube for up to 60 minutes at a time. Some people are scared or anxious in small places (otherwise known as claustrophobic). Because the test requires that participants lie as still as possible with only minimal movements, back pain may worsen during the test. During the test, study staff will continuously ask you about your level of pain and will discontinue the scan at any time requested. You will be asked about any concerns you may have prior to testing. If you cannot tolerate being in the MRI scanner, you will not be able to participate in the study.

The MRI pictures from this study will not be in a form readable by either you or your doctor; therefore, a copy of the MRI pictures and/or the results of your individual study will neither be available to you nor your doctor. While the MRI pictures in this study are not formally reviewed by a radiologist, if in the course of processing the images we notice any abnormality that would be possibly important to your health, we will tell you and a doctor you name.

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 decreased low back pain and the potential to avoid being in a chronic pain state. It is also possible that you will receive no benefit from taking part in this study.

Taking part in this study may help scientists to better understand how chemical interactions in the brain determine the type of pain, chronic or acute, in an individual following an injury. It will also help scientists to determine if early treatment with Carbidopa/Levodopa and Naproxen may benefit patients with sub-acute low back pain. This study may also help inform future research studies involving individuals with sub-acute low back pain.

What other procedures or courses of treatment might be available to me?

You do not have to take part in this research study. Instead of being in this study, you can consult a physician about your lower back pain and obtain other FDA-approved methods of treatment. Physical therapy may be of additional benefit. Your physician can tell you about what medication might be available to you.

Will it cost me anything to participate in this research study?

There will be no costs to you for being in this study. You will be provided with all study drugs and all procedures will be done free of charge for this study.

What should I do if I am injured as a result of being in this study?

If you become ill or get an injury or illness as a result of study medications or procedures you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury. Payment for this treatment will be your responsibility.

The hospital [university, researchers] will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back for care required because of a bad outcome.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, you can contact the research team. The Study Coordinator can be reached at 312-503-2886 Monday through Friday, 9a.m. to 5 p.m. Dr. Apkar V. Apkarian is the person in charge of this research study and can be reached at 312-503-0404 Monday through Friday, 9 a.m. to 5 p.m. For questions arising during the evenings or weekends, you may call 312-649-2964 and ask for Dr. Schnitzer to be paged.

This research has been reviewed and approved by an Institutional Review Board ("IRB"). You may talk to them at (312) 503-9338 or irb@northwestern.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 participant.
- You want to get information or provide input about this research.

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.

If you choose to be in this study, you have the right to be treated with respect, including respect for your decision whether or not you wish to continue or stop being in the study. You are free to choose to stop being in the study at any time.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice to not be in this study will not negatively affect your right to any present or future medical treatment.

Any new findings developed during the course of this research that may affect your willingness to continue in this study will be shared with you.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution. The sponsor, monitors, auditors, the IRB, the US Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov (ClinicalTrials.gov Identifier: NCT01951105) as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What else do I need to know?

- If you need medical care because of taking part in this research study, contact the investigator and medical care will be made available. Generally, this care will be billed to you, your insurance, or other third party. Northwestern University has no program to pay for medical care for research-related injury.
- If you complete all visits, you will get up to $410 for taking part in this research study. If you withdraw from the study, you will be paid for the portions that you completed. Compensation will be paid to you according to the following schedule:

Visit	Amount	Payment Type
Screening Visit 1	$25, up to $20 for transportation and validation for free parking	Cash
Baseline Imaging Visit 2	$50, up to $20 for transportation and validation for free parking	Cash
Treatment Visits 3 – 7	$25, up to $20 for transportation and validation for free parking, per visit	Check, Cash
Visit 8	*Final Imaging*:$50, up to $20 for transportation and validation for free parking *No Final Imaging*: $25, up to $20 for transportation and validation for free parking	Check, Cash

- Study payments will be given to you in cash at the time of your study visit. For Visit 2 and Visit 8 you will be mailed a $50 check to your home in addition to the $20 you receive for travel expenses. If you choose to drive and are given a parking validation for free parking $5 will be subtracted from the $20 cash for transportation. The Accounting Services at Northwestern University will be given your name, address, and Social Security Number in order to issue payment for your participation. Study payments are considered taxable income and reportable to the IRS. A Form 1099 will be sent to you if your total payments for research participation are $600 or more in a calendar year.
- You will also receive financial compensation when you rate your back pain. You will be asked to rate your pain 3 times a day. In doing so you may earn 75 cents/day (25 cents/response, 3 times per day maximum) and $147 over the course of the entire study. At the end of the study, you will receive the total amount of money earned from this application in check form. Study payments are considered taxable income and reportable to the IRS. A Form 1099 will be sent to you if your total payments for research participation are $600 or more in a calendar year.

HIPAA Authorization

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Health information that we may collect and use for this research includes:

- Results of physical examinations
- Medical history including back pain history and family history of back pain

- Lab tests, or certain health information indicating or relating to a particular condition as well as diaries and questionnaires
- Records about study medication or drugs
- Records about MRI scans
- Substance abuse information: current recreational drug use or history of alcohol or drug abuse

Once we have your health information listed above, we may share some of this information with the following people. Please note that any research information shared with people outside of Northwestern University and its clinical partners (or affiliates) will not contain your name, address, telephone or social security number or any other direct personal identifier unless disclosure of the direct identifier is required by law [except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigator's office]**.**

- Authorized members of the Northwestern University workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board (a committee which is responsible for the ethical oversight of the study),
- Clinical affiliates, including but not limited to the Northwestern Medical Faculty Foundation (NMFF), Northwestern Memorial Hospital (NMH), and Northwestern Memorial Physicians Group (NMPG). Your participation in this clinical trial will be tracked in an electronic database and may be seen by investigators running other trials that you are enrolled in and by your healthcare providers.
- Other University research centers and University contractors who are also working on the study,
- Study monitors and auditors who make sure that the study is being done properly,
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS).

Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission.

The results of this study may also be used for teaching, publications, or presentation at scientific meetings. However, your name and personal information will not be used.

Although you may revoke consent to participation in this research at any time and in any format, you must revoke authorization for use or disclosure of your health information in writing. To revoke your authorization, write to:

Dr. Apkar Vania Apkarian, PhD
Department of Physiology
300 E. Superior Street, Room 7-705
Chicago, Illinois 60611
tel. (312) 503-0404

You do not have to authorize the use or disclosure of your health information; however, you will not be allowed to take part in this research study. If you do not authorize the use or disclosure of your health information, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits.

Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

_____ The researcher may contact me in the future to see whether I am interested in participating in other research studies such as saliva collection.

Consent Summary:

I have read this consent form and the research study has been explained to me. I have been given time to ask questions, and have been told whom to contact if I have more questions. I agree to be in the research study described above. A copy of the consent form will be provided to me after I sign it.

A copy of this signed consent document, information about this study and the results of any test or procedure done may be included in my medical record and may be seen by my insurance company.

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

Signature of participant	Date
Printed name of participant	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

Time of consent: _____