Informed Consent Document for Study "A Phase II Randomized Controlled Double-Blind Clinical Trial of Sphenopalatine Ganglion Blocks for Headache after Concussion"

PI: Dr. Michael Popovich, University of Michigan

Approval Date: 12/3/2020

ClinicalTrials.gov ID: NCT04650282

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title: A Phase II Randomized Controlled Double-Blind Clinical Trial of Sphenopalatine Ganglion Blocks for Headache after Concussion

Company or agency sponsoring the study: National Institute of Neurological Disorders and Stroke

Names, degrees, and affiliations of the principal investigator and study coordinator (if applicable):

Principal Investigator: Michael Popovich, MD, MPH, Department of Neurology, University of Michigan
Study Coordinator: Lea Franco, Clinical Research Project Manager, Department of Physical Medicine and Rehabilitation, University of Michigan

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains important information that will help you decide whether to join the study. Take the time to carefully review this information. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your family, friends, or other doctors about joining this study. If you decide to join the study, you will be asked to sign this form before you can start study-related activities. Before you do, be sure you understand what the research study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find child care, or make other plans. In your decision to participate in this study, consider all of these matters carefully.

This research is studying a new treatment in small numbers of people to learn about its safety and its effect on your body as a treatment for headaches after concussion. This study will investigate if sphenopalatine ganglion blocks improve headaches after concussion. Your health-related information will be collected for this research study.

This study involves a process called randomization. This means that the treatment you receive in the study is not chosen by you or the researcher. The study design divides study participants into separate groups, based on chance (like the flip of a coin), to compare different treatments or procedures. There is a 50/50 chance that you will receive a sphenopalatine ganglion block with lidocaine (the treatment we are studying) or a block with a placebo medication. If you decide to be in the study, you need to be comfortable not knowing which study group you will be in.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include no improvement in your current headaches or other concussion symptoms, temporary pain including in the nose or increase in headache, temporary numbness of the nose and throat after the procedure, and nose bleeding. More detailed information will be provided later in this document.

This study may offer some benefit to you now or others in the future by improving headaches due to concussion. This study may not offer any benefit to you now but may benefit others in the future by furthering or understanding of potential treatments for headaches due to concussion and concussion in general. More information will be provided later in this document.

We expect the amount of time you will participate in the study will be two weeks.

You can decide not to be in this study. Alternatives to joining this study include the standard medical care as directed by your concussion doctor.

Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues in Section 2 of this document.

2. PURPOSE OF THIS STUDY

2.1 Study purpose: Headache is a common symptom after concussion and can contribute to a longer recovery from concussion. A procedure called a sphenopalatine ganglion block has been shown to be helpful for other types of headache, such as migraine. It is not known if this procedure is helpful for headaches caused by concussion. This research study is being done to learn if a sphenopalatine ganglion block improves headaches due to concussion.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study? You may be eligible for this study if you are between 18 and 60 years of age, have been diagnosed with a concussion, and are having headaches after your concussion at least two weeks from the date of your injury. You may not be eligible for this study if there are any concerns about your ability to safely undergo the sphenopalatine ganglion block procedure, such as allergies to the medication (lidocaine), conditions that increase your risk of bleeding, or structural abnormalities of your nose or face. You also will not be eligible for this study if you begin another treatment for headache (such as a medication) at the same time as you enroll in this study.

3.2 How many people are expected to take part in this study? 24 total subjects are expected to participate in this study; 12 will receive a lidocaine treatment, and 12 will receive a saline placebo.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

If you choose to participate in this study, you will provide information about the headaches that you are having since your concussion. We will ask you to fill out a short online survey every 24 hours for the two-week study period. In this survey, we will ask you to report on information pertaining to the last 24 hours, including: whether or not you have had a headache, how many headaches you had, how many hours of the day you have experienced headache, and if you have taken medications to treat your headache. We also will ask you to rate the severity of 22 different symptoms which are common after concussion, including headache.

In addition to the online surveys, we will ask you to attend a research study visit, which will occur at the middle of the two-week study period. This visit may coincide with a follow-up appointment at the concussion clinic, or it may be scheduled at as a separate visit. During this visit, we will perform a procedure called a sphenopalatine ganglion block. A sphenopalatine ganglion block is a procedure that is used to treat other patients with headaches, such as migraine headaches. We are doing this research study because we are hoping to learn if this procedure is beneficial for headaches after concussion. For the procedure, we will have you lay flat on an examination table. We will use a device called a SphenoCath, which is a soft rubber catheter that will be coated with a lubricating gel and inserted into each nostril. Using this device, we will direct a small amount of fluid into the nasal passage to an area near a bundle of nerves called the sphenopalatine ganglion, which is an important structure in the transmission of pain signals related to headache. After the procedure has been completed, you will be asked to remain flat for five minutes. After this five-minute period, we will sit you up and monitor you for another ten minutes.

Both before and after the sphenopalatine ganglion block procedure, we will collect some additional medical information during the research study visit. We will ask you to complete the same 22 item symptom checklist that you will complete as part of the daily online survey. We also will ask you to wear a heart rate monitor that is fitted around the chest, so that we can record your heart beat. We will record your heart beat while you are laying flat, and then we will record your heart beat immediately after you stand up and after you have been standing up for two minutes.

All participants in this study will receive a sphenopalatine ganglion block procedure. Importantly, because we are unsure if treatment with a sphenopalatine ganglion block is helpful for headaches after concussion, we will compare two groups of participants: one group will receive a medication called lidocaine, which is a numbing medication that is often used as part of sphenopalatine ganglion blocks; and one group will receive a placebo saline solution, which is not expected to have any direct medical benefit. As used in this study, lidocaine is not FDA-approved. To determine which participants receive lidocaine and which participants receive placebo, this research study will include a process called “randomization.” This means that you will be randomly assigned to the study groups (such as with a flip of a coin). You may either receive lidocaine or the placebo solution. There is a 50/50 chance that you will receive either the lidocaine treatment or the placebo solution. Because knowing if you have received one or the other solution may change your behaviors and influence study results, you will not be told which treatment you have received.

In addition to your direct participation in this study, which includes completion of daily online surveys and administration of the sphenopalatine ganglion block procedure, we may view your medical record to collect additional data that is pertinent to your concussion care.

As a subject participating in this research study, you have certain responsibilities that may apply to this study, such as ensuring that you arrive at all of your scheduled appointments, take your study medication as directed, and report any adverse reactions you may have during the study.

For some research studies, such as the one you are being asked to join, it is important that you do not learn the results of certain tests. Whether you intend it or not, sometimes learning this information may make you change your actions and behaviors in ways that could impact the outcome of the study.

Besides the information about the main study, the following information is specific to unspecified future use of identifiable data and/or biospecimens. We would also like your permission to keep some of your medical information collected in the main study, so that we may study it in future research. The future research may be similar to this study or may be completely different.

You can take part in the main study even if you decide not to let us keep your medical information for future research.

If you give us your permission, we will use your medical information for future research. Even if you give us permission now to keep some of your medical information, you can change your mind later and ask us to destroy it. Keep in mind, however, that once we have analyzed your medical information, we may not be able to take the information out of our research.

We may share your medical information with other researchers, so that they can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your medical information with other researchers, we will not be able to get it back.

Future use of your identifiable data will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of future research on your medical information. Allowing us to do future research on your medical information will not benefit you directly.

With appropriate permissions, your collected information may also be shared with other researchers here, around the world, and with companies.

Your identifiable private information may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

4.2 How much of my time will be needed to take part in this study?
Participation in this study will occur over two weeks. You will be asked to fill out an online survey every 24 hours during these two weeks. Completing this survey should take about five minutes each day. You will also be asked to present for one research visit, during which the sphenopalatine ganglion block procedure will be performed. This research visit is expected to last about one hour.

4.3 When will my participation in the study be over?
Your direct participation in this study will take two weeks, as described in section 4.2. In addition to this time, we will collect information from your medical records related to your concussion care after your direct participation is over. Information from your medical records could be collected through the end of your care at the concussion clinic. Most subjects will complete their care within about three months, but you could be seen in the clinic for a longer period of time.

After this study has been completed, your access to the intervention being tested may not be available.

4.4 What will happen with my information and/or biospecimens used in this study?
With appropriate permissions, your collected non-identifiable information may also be shared with other researchers, here, around the world, and with companies. We will not share any identifiable information with others.

Your identifiable private information may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

5. INFORMATION ABOUT STUDY RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The most common side effects (occurring in more than 10% of patients) are: bad taste of the medication, tearing from the eyes, and numbness of the mouth or throat. Because numbness may occur, participants should not eat or drink until the numbness has resolved, which may take a few hours.

Less common side effects (1% - 10% of patients) are: coughing, sore throat, dizziness, light-headedness, nose bleeding, other drainage from the nose, face or nose discomfort, and nausea.

Rare side effects (less than 1% of patients) are: blurred vision, infection of the ear, nose, or eyes.

The researchers will try to minimize these risks by: screening potential participants for any known conditions that would increase the risk of the sphenopalatine ganglion block procedure; using a lubricant gel in the nostril to reduce discomfort; only unused, sterilized medical supplies and medications will be used.

Additionally, there may be a risk of loss to confidentiality or privacy. See Section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors.

We have taken steps to reduce the risks associated with this study. We are screening for conditions that may make the sphenopalatine ganglion block procedure riskier (as discussed in section 3.1) and excluding potential participants from the study if they have a condition that may put them at greater risk of having the procedure.

After completion of the sphenopalatine ganglion block procedure, we will monitor you for 15 minutes to determine if any immediate complications or adverse effects from the procedure have occurred. If any immediate complications or adverse effects have occurred, we will provide first aid if necessary and will direct you to the appropriate medical care if needed.

The use of local anesthetics (such as lidocaine) may cause methemobloginemia, a serious condition that must be treated promptly. You or your caregiver should seek immediate medical attention if you or someone in your care experiences the following signs or symptoms following the procedure: pale, grey, or blue-colored skin (cyanosis); headache, rapid heart rate, shortness of breath, light-headedness, or fatigue.

5.3 If I take part in this study, can I also participate in other studies?
Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
You may not receive any personal benefits from being in this study. However, others may benefit from the knowledge gained from this study. Also, some subjects may experience improvements in headache after concussion or overall recovery from concussion. In the future, the results of this research could help to establish new treatments for headache after concussion and concussion in general.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?

If you decide not to take part in this study, you will still receive standard medical care from your doctor. There may be other ways to treat your headaches, including treatment with over-the-counter medications, prescription medications, physical therapy, and exercise. Your doctor can tell you more about these other treatments, their risks and their possible benefits. You should have this discussion about the risks and benefits or other alternatives prior to making your decision about whether or not you wish to take part in this research study.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information".

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
We do not expect that there will be any harm to you if you decide to leave the study before it is finished. If you decide to leave the study early, we may ask you questions about your decision to leave the study so that we better understand your decision.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researcher's telephone number listed in Section 10.1.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services.

If you are injured or in the event of a medical emergency, dial 911 or visit your nearest Emergency Room. If you believe the study has made you sick or caused you injury, contact one of the people listed in section 10 of this document (Contact Information). If taking part in the study makes you sick or causes you injury, you or your insurance provider will be billed for all costs of treatment as the study does not provide compensation for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?

Participants will receive up to a total of $100 for participation in this study. Participants will receive a pro-rated amount for meeting certain requirements of the study, as follows:

1. For completion of at least five of the seven daily online surveys prior to the sphenopalatine ganglion block procedure, participants will receive $25.

2. For attending the research study visit at which the sphenopalatine ganglion block is performed, participants will receive $50.
3. For completion of at least five of the seven daily online surveys following the sphenopalatine ganglion block procedure, participants will receive $25.

8.3 Who could profit or financially benefit from the study results?

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my information?
Research records will be kept in a separate research file that does not include names, registration numbers, or other information that is likely to allow someone other than the researchers to link the information to you.

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.

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?
Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study.

Medical information and billing records are protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA). This type of information is called protected health information (PHI). PHI about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Demographic information
- Personal identifiers
- Other information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
  - Make sure the study is done safely and properly
  - Learn more about side effects
  - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, Social Security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission to use my PHI?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities. (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission to use my PHI expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Michael Popovich, MD, MPH
Mailing Address: 2301 Commonwealth Blvd, Ann Arbor, MI 48105
Telephone: 734-936-1808
Study Coordinator: Lea Franco
Mailing Address: 325 E Eisenhower Pkwy, Ann Arbor, MI 48108
Telephone: 734-763-2200

You may also express a question or concern about a study by contacting the Institutional Review Board listed below:

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies, include the appropriate calling codes.)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

You will receive a copy of the signed and dated informed consent document. Your signature in the next section means that you have received copies of all of the following documents:

- You will receive a copy of this "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Sig-A

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with [NAME OF STUDY TEAM MEMBER OBTAINING CONSENT] ________________________. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: ____

Signature: ____

Date of Signature (mm/dd/yy): __________________________

Sig-D

Consent/Assent to Collect for Unspecified Future Research

This project involves the option to allow the study team to keep your identifiable specimens/data for use in future research. I understand that it is my choice whether or not to allow future use of my specimens. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

______ Yes, I agree to let the study team keep my specimens for future research.

______ No, I do not agree to let the study team keep my specimens for future research.

Print Legal Name: ____

Signature: ____

Date of Signature (mm/dd/yy): _________________________________

Sig-E

Legally Authorized Representative or Parent Permission

Subject Name:

____

Parent/Legally Authorized Representative:

Printed Legal Name:
____

Signature: ____

Address: ____

Date of Signature (mm/dd/yy): _______________________

Relationship to subject: Parent Spouse Child Sibling Legal guardian Other

If "Other," explain: ____

Reason subject is unable to consent: ____

If this consent is for a child who is a ward of the state (for example, a foster child), please tell the study team immediately. The researchers may need to contact IRBMED.

Sig-G

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: ____

Title: ____

Signature: ____

Date of Signature (mm/dd/yy): _________________________