

Department of Neurology

PAIN PERCEPTION AND STRESS REDUCTION FOR MIGRAINES

Informed Consent Form to Participate in Research

MIGRAINEURS – PARTS 1 AND 2

Rebecca Erwin Wells, MD, MPH Principal Investigator

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you suffer from migraines 4-20 days/month. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

While medications are first line therapy for migraines, $\leq 50\%$ of migraineurs respond to drug treatments and $>10\%$ discontinue due to adverse events. This research study has two purposes: 1) to assess the response to experimental heat pain (pain intensity, pain unpleasantness, and emotional reactivity) in migraineurs and healthy volunteers, and 2) to understand better ways to manage migraines without medications. You are being invited to participate in both parts of the study. If you wish, you may choose to only participate in Part 1 – the pain perception portion.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

At least 147 people at Wake Forest Baptist Health will take part in this study. Part 1 will involve at least 49 healthy volunteers and 49 migraineurs (many migraineurs may overlap with Part 2) and Part 2 will involve at least 98 migraineurs.

WHAT IS INVOLVED IN THE STUDY?

This study will be evaluating weekly educational classes about stress, headaches, and/or relaxation that could aid in migraine management. There will be two different classes that will be teaching these skills and you will be assigned by chance (like the flip of a coin) to one of the two groups. Neither you nor the investigator will know to which class you have been assigned. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency.

As part of this research study, you will be audiotaped/ videotaped/ photographed during the weekly classes and/or during the initial follow-up study visits. This is being done so that study investigators can review your experience in the weekly classes for educational, research and study related purposes. You understand that you may request the recording be stopped at any time during the course of the research study. You can also withdraw your consent to use and disclose the audiotapes/ videotapes before they are used. You should also understand that you will not be able to inspect, review, or approve the audiotapes/ videotapes before they are used in this study.

Please choose one of the following regarding the use and disclosure of the audiotapes/ videotapes used in this research study:

_____ I would like the audiotapes/ videotapes/ photographs of me to be destroyed once its use in this study is finished.

_____ The audiotapes/ videotapes/ photographs of me can be kept for use in future research and/or educational purposes provided they are kept secure and any future study will be reviewed by an Institutional Review Board (IRB). I understand that I will not be able to inspect, review or approve their future use.

Screening Visit:

First, a study investigator will confirm your migraine diagnosis with your medical history and a neurological exam. Socio-demographic and clinical information will be collected at this visit. You will also complete several questionnaires and quantitative sensory testing (QST). QST is experimental heat pain testing using a thermal probe. First you will be trained on how to rate your pain with the thermal probe being applied to your left arm. Then the thermal probe will be applied to your right arm for a pain threshold assessment, and you will be asked to let the study staff know when you feel pain as the temperature increases. Lastly, the thermal probe will be applied to your right calf. A series of temperatures will be randomly administered and you will be asked to rate your pain after each temperature. Each series will be repeated twice.

If you qualify for this study, you will need to track your migraines for the next 4 weeks to confirm eligibility, as well as throughout the entire study. You will be taught how to log daily migraine information into our electronic database, REDCap.

For the duration of the study, you may continue taking your current headache medicines, but we will ask you to keep your headache medications the same (by not starting a new medicine or changing the dose of your current medicines).

The data collected from this visit will be used for Part 1 and Part 2 of the study.

Randomization:

Once the 4-week migraine logs are reviewed by study team members, if you are eligible you will

be randomized to one of the two groups. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in each group. You will continue to track your migraine occurrences daily in the REDCap system during the 8 weeks of classes and until the 6 month follow-up visit. After the 8 weekly classes have concluded, study participants will be incentivized to keep daily headache logs as follows:

1. For each DAY that the participant keeps their headache log on time, their name is entered into a drawing up to 30 times per month.
2. At the end of each month, a name will be drawn and a winner will receive a \$50 gift card.

Weekly Classes

There will be a total of nine sessions – 8 weekly classes and a retreat day. You will begin attending 8 weekly 2 hour classes where you will learn about headaches, triggers, stress, general health, and/or relaxation/gentle stretching. You will discuss and learn drug-free ways to better handle your headaches. You may be asked to practice the skills you learn in class at home for 30-45 minutes/day. These home activities are very important to our study and are a way to help teach you healthy ways to engage in life. If assigned, we will ask you to keep a log of your home activities. Towards the end of the 8 weeks, there will be a “retreat” day where you will deepen your experiences with what you have been learning.

Initial Follow-up

At this visit, you will complete the same questionnaires from the screening visit. QST will also be repeated. You will also be interviewed for approximately 30 minutes in order to evaluate your experience with the weekly classes. Each interview will be audiotaped.

3-Month & 6-Month Follow-up

At both of these visits, you will complete the same questionnaires from the screening visit. QST will also be repeated.

The study doctor may take you out of the study without your permission. This may happen if:

- You no longer meet eligibility for the trial
- You are causing disruptions to the weekly classes
- You have started a new headache medication

If this happens, the study doctor will explain why you need to stop taking part in the study. We will ask you to come in for a final study visit as described above.

If you decide to stop taking part in the study for any reason, we will ask you to make a final study visit as described above.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for about 9 months. You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study

staff first to learn about any potential health or safety consequences.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the interventions we are studying include:

1. Experimental Heat Pain Assessments/QST – The quantitative sensory testing may cause brief pain, but all temperatures will be < 50°C and no stimulus as designed produces tissue damage. The thermal probe used for this experiment, MEDOC TSA-II, will deliver thermal stimuli with a 16 x 16 mm thermal probe. The pain stimuli are chosen so that most people can tolerate them. These stimuli have been used for many years with minimal harmful physiological or psychological complications. However, the heat may cause redness of the skin for up to several hours, but should not cause any blistering.

You can easily pull away from the device if the feeling is not tolerable. The laboratory staff are experts in conducting the heat-pain intervention and the temperature of the thermal heat probe will be monitored at all times. A computer controlled device that touches the skin is used to apply the heat used for sensory testing. In extremely rare cases, the computer controlled stimulator has been reported to malfunction and to cause a burn to the small skin region being tested. Since this device will not be strapped to your leg or arm, you can easily pull away from this device and stop stimulation at any time.

2. Weekly Classes – A risk to taking part in this study is the likelihood of receiving an intervention (that requires time and energy) that may not be effective in helping to treat migraines. The classes or other study-related procedures may cause some, all, or none of the side effects listed below.

Most Likely

Gentle stretching can cause muscle soreness if muscles have not been exercised in a long time. Sitting for extended periods of time can be uncomfortable. Chairs will be provided for comfort, and participants will be allowed to move as needed to relieve any discomfort.

Less Likely

With any activity, there is always a risk of injury. The instructor will advise the participants to avoid any posture that causes discomfort or pain. The instructor will be attuned to watching for any problems during each session.

Rare

There have been rare case reports of meditation or yoga causing a brief limited episode of psychiatric illness. However, most of these case reports are in individuals with a prior history of unstable psychiatric illness. Having a history of unstable psychiatric illness is an exclusion criteria for participating in this project so therefore we have in place an extra precaution to not encounter this risk.

3. Questionnaires – As part of this study, you will be asked questions about your thoughts and feelings. If we learn that you or someone else is in danger of harm, the study team is required to report that information to the proper authorities.

In addition, there is a slight risk of a breach of confidentiality. Taking part in this research study

may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Reproductive Risks and other Issues to Participating in Research

Pregnant women are excluded from participation in this study. The interventions and QST do not pose any risk to your fetus but may affect the results of the study. If you are a sexually active woman of childbearing potential and have not been using a reliable method of birth control and have a possibility of being pregnant, please inform the study staff. We will not be performing a test for confirmation of pregnancy status. If you are unsure of your pregnancy status we will request that you do not participate in the study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be: the opportunity to participate in a group program with other adults with migraines, learning ways to cope with stress, being educated about health topics, and/or learning relaxation/gentle stretching exercises.

WHAT OTHER CHOICES ARE THERE?

Your alternative is to not participate in this study or to refer to your personal physician for standard treatment.

What About My Health Information?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes: name, date of birth, diagnosis, and contact information.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

Based on your responses to the study questionnaires, if there is cause for concern about your mental state or that you may harm yourself or others, your confidentiality may be breached in order to provide you with appropriate care through the emergency department.

We will make every effort to keep your Protected Health Information private. We will store

records of your Protected Health Information in a cabinet in a locked office or on a password protected computer. Only the following people or organizations will be granted access to your Protected Health Information:

- 1) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research
- 2) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center
- 3) Representatives of the government agency sponsoring the study, National Institutes of Health (NIH) and the National Center for Complementary & Integrative Health (NCCIH)
- 4) Representatives of the American Pain Society
- 5) De-identified demographics and data from the Social Connectedness Scale will be provided to the questionnaire's author. Your name or any other identifying information will not be included.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

CERTIFICATE OF CONFIDENTIALITY

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, *[except as explained below]*.

The Certificate cannot be used to resist a demand for information from personnel of the United States federal or state government agency sponsoring the project and that will be used for auditing or program evaluation of agency funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not be used to prevent disclosure to state or local

authorities if there is cause for concern about your mental state or that you may harm yourself or others.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Rebecca Erwin Wells that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Rebecca Erwin Wells, Principal Investigator



However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

WHAT ARE THE COSTS?

There are no costs to you for taking part in this study. All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOU BE PAID FOR PARTICIPATING?

You will be paid a total of \$80 if you complete the weekly classes and all the scheduled study visits.

Screening Visit - \$10

Initial Follow-up Visit - \$15

3-Month Follow-up Visit - \$20

6-Month Follow-up Visit - \$35

To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the National Institutes of Health (NIH), the National Center for Complementary and Integrative Health (NCCIH), and the American Pain Society (APS). The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of \$25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of \$25,000 coverage for each claim and is limited to a total of \$250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [REDACTED].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. Rebecca Wells at [REDACTED].

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, your condition worsened, you failed to follow instructions, or because the entire study has been stopped.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

This study will be enrolling students from the Wake Forest University and Wake Forest University Medical Center campus. In addition to your rights as a research participant noted in the previous section, as a student, you are under no obligation to participate in this study. You may refuse to participate or withdraw from the study at any time and for any reason without affecting your grades, performance evaluations, or assignments. You will not be pressured into participating in this research study by any statements or implied statements that your grades, performance evaluations or assignments will be affected by your willingness to enroll in the study. Your medical records/information will not be used by the faculty, administration or study staff to make decisions regarding the status of your medical benefits. If you have questions regarding your enrollment in the study and your status as a medical student, please contact the Office of Student Services for additional information.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Rebecca Erwin Wells at [REDACTED].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [REDACTED].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed): _____

Subject Signature: _____ Date: _____ Time: _____ am pm

Person Obtaining Consent: _____ Date: _____ Time: _____ am pm