STUDY TITLE: SUPRASPINAL PROCESSING OF SENSORY ASPECTS OF PAIN

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Key Information:

The following is a short summary of this study to help you decide whether to be a participant in it. More detailed information about the study is listed later in this form. This document does not replace the discussion you should have with the research team about this study, including having any questions or concerns answered.

Combined Parental Permission/Assent: If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When we say "you" in this form, we mean you or your child; "we" means the study doctor and other staff.

We are asking you to be in a research study so that we can learn new information about the brain that may help others with chronic pain. If you decide not to be in the study, we will still take really good care of you. If you decide to be in the study, you may change your mind at any time and stop being in the study. You may take all the time you need to make your choice. Please ask us any questions that you may have. You may also ask questions after you have decided to be in the study. We will be happy to answer them.

WHY ARE WE DOING THIS RESEARCH?

The purpose of this study is to learn more about how chronic pain changes the brain and how different types of chronic pain can affect the brain differently. This may help us identify new ways of better diagnosing chronic pain. Also, we want to be able to better predict how people with chronic pain will respond to treatments.

We are asking you and up to 500 people your age to be in this study because you have either migraine, complex regional pain syndrome, functional abdominal pain, or musculoskeletal pain.

We are also asking people who do not have chronic pain to participate.

WHO IS IN CHARGE OF THIS RESEARCH?

Robert Coghill, Ph.D., is the researcher at Cincinnati Children's Hospital Medical Center (CCHMC) who is in charge of this study. This study is paid for by the National Institutes of Health/National Institute of Neurological Disorders and Stroke.

WHO SHOULD BE IN THIS STUDY

You can be in this study if you are between the ages of 10 and 17 and have migraine, CRPS, functional abdominal pain, and/or musculoskeletal pain. You can also participate if you do not have chronic pain and are in good general health.

WHO SHOULD NOT BE IN THIS STUDY

You should not be in this study if you have one or more of the following conditions:

- Certain types of neurological or psychiatric disorders that are not related to chronic pain
- diabetes
- pregnant
- older than 17 years old or younger than 10 years old at start of study
- any metallic implant or other conditions that are not safe in the MRI

HOW LONG WILL YOU BE IN THIS STUDY?

You will be in the study for one year. You will have one or two in-person visits at the beginning of the study (baseline), 3 remote online assessments, and one in-person visit after one year at the end of the study. On rare occasions, technical difficulties may cause us to invite you back on an additional visit.

WHAT WILL HAPPEN IN THIS STUDY?

This study will be started with a sensory testing session and an MRI scanning session (baseline). These may be done in one or two visits to Cincinnati Children's Hospital. Each session will last approximately 3 hours.

If you are a sexually active person of childbearing potential a negative pregnancy test may be required. We encourage you to discuss this issue further with our study staff if you have any questions. We will have to report positive pregnancy tests to your parents and your doctor. If you become pregnant after the baseline session, you may remain in the study.

We will take a urine sample to test for drugs. We will have to report positive drug tests to your parents.

Sensory Testing

In the sensory testing session, you will receive some stimuli, such as temperature, vibration or touch stimuli, and we will ask you to rate how intense and unpleasant these stimuli are. You will experience some pain while you receive these stimuli, however they will not harm you and are designed to be tolerated by most people. Importantly, you can stop stimulation at any time. In addition, we will take images of the temperature of your body with a special camera. You will also fill in questionnaires that ask about your feelings, your health, information about your chronic pain and the treatments you have tried so far. This will take about three hours. The questionnaires for these sessions may be filled out online.

MRI Scanning

In the MRI session, we will use and MRI scanner to look at your brain. This machine is a giant magnet that is open at both ends. You will be in the MRI scanner for about 1.5 hours. We will use pillows to keep your head still. When you are comfortable, we will take different types of images of your brain. Each type of image takes several minutes to get. You will have breaks of a few minutes between the collection of the different types of images. However, you we would like you to stay in the scanner during these breaks.

Some MRI images will be taken while you are not doing anything. Others will be recorded while you are doing some tasks. The tasks will involve some of the stimuli that you experienced in the sensory testing session. These would be heat stimuli and touch stimuli. You will also

experience a combination of visual, sound, and touch/movement stimuli in the scanner. You will also tell us what you felt about these stimuli while in the scanner. Just like in the sensory testing session, you will be free to stop stimuli at any time.

Please let us know if you are not comfortable in the MRI, as it is really important for the study that you are as comfortable as possible in there. If you feel uncomfortable, we will try to make you more comfortable or take you out of the machine. The MRI technologists are only a few feet away and we will be in constant communication with you via a microphone system.

We will ask your parents for information about your doctor during the first visit. A radiologist will look at the images we take to make sure that there are no concerns. If anything is found, we will get in touch with your doctor.

Remote Online Assessments

After you have completed the baseline visits, you will fill out questionnaires online once every three months for 9 months. During the online sessions, we will send you a link to complete questionnaires that ask about your feelings, your relationship with your parents, your health, information about your chronic pain and any new or worsening symptoms you might have. This will take you about 60 to 90 minutes to fill out.

1-Year Sensory Testing

About a year after your first visit, you will return to Cincinnati Children's Hospital for another sensory testing session (3 hours).

WHAT ARE THE GOOD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

There are no benefits to you for taking part in this research. We hope the information learned from this study will help other children and teenagers with chronic pain in the future.

WHAT ARE THE BAD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

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

Questionnaires

You may be asked questions that make you uncomfortable or cause you to remember situations that were upsetting to you. You do not need to answer any questions that you do not wish to answer, and you can stop the answering questions at any time. If you become very upset, we will stop the study. We will also offer to have you speak to someone about what you are feeling. Rarely, these questionnaires can reveal emotional problems that would put you at risk of hurting yourself. If this is the case, we will refer you to a clinical psychologist for a full clinical evaluation and/or treatment.

Sensory Testing and Tasks

Many of the temperature and touch stimuli will cause brief pain, but do not cause a burn or other damage to your body. Also, some of the images, sounds, and movements we use might feel uncomfortable to you, but they will not harm you. The stimuli are chosen so that most people can tolerate them. If you are already experiencing pain, the sensory stimuli may increase it temporarily. These stimuli have been used for many years with no harmful physiological or psychological complications. However, the heat may cause redness of the skin for up to several

hours but does not cause any blistering. A computer-controlled device that touches your 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.

MRI Scanning

The MRI is not associated with any known biological risks to adults or children, but you may feel uncomfortable because you will be lying in a small space. If you cannot tolerate this, the scan will be stopped immediately. During the scanning, the MRI machine produces loud noises, so your ears will be protected by earplugs and special headphones. Persons with any electronic objects or certain metal objects in their head or body may not participate because these objects may malfunction, heat up, or move. Other objects, like braces and some permanent retainers, can cause a lot of problems with the MRI images. A checklist of excluded metal objects will be presented to you by the MRI technician or the study staff prior to the MRI scan.

Confidentiality

Taking part in this research study may involve providing information that you consider confidential or private. There is a slight risk that your private information will not remain confidential. We will do our best to protect your private information. We will de-identify research records, keep research records secure, and allow only authorized people to have access to research records.

Other Risks

There also may be other risks that we cannot predict. You should tell the study 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.

WHAT OTHER CHOICES ARE THERE?

At any time, instead of being in this study, you can choose not to be in it. At any time, if the study team thinks it is not good for you to be in this study, we will end your participation.

HOW WILL INFORMATION ABOUT YOU BE KEPT PRIVATE?

Making sure that information about you remains private is important to us. Any records with your name or other private information will be securely stored in locked file cabinets or on password-protected, encrypted computers.

Once we start to analyze the data, we will remove your name and other private information from all data and replace it with a code. The link between this code and your name will be kept in a locked file only accessible to study staff and, if requested, regulatory personnel from Cincinnati Children's Hospital or other regulatory agencies.

Anytime that we talk about the data in presentations or scientific papers, we will not present any information that could identify you.

Data Storage and Sharing:

Research gives us the best information and progresses more quickly when data is available from many studies and many individuals, and when many researchers can work with the data and analyze them in different ways. Because of this, the National Institutes of Health and many

scientific journals require that we store and share data. Your stored data will also be made available to other researchers. The shared data may be used indefinitely for research not related to this study, without asking you for additional consent.

If you withdraw from this research study before it is finished, we will keep and continue to use data that have already been collected.

Potential benefits of sharing of data

There is no direct benefit to you from the storage and sharing of your data. However, sharing may help researchers make new discoveries about chronic pain. Also, sharing data improves the openness, integrity, and reproducibility of scientific research.

Risks of sharing data

Even though we will protect your privacy as much as possible, there is a very small chance that the data could be identified as yours. The risk of this happening is very small, but may increase in the future as technology changes.

Research using data from this study may lead to new tests, drugs, or devices with commercial value. You will not receive any payment for any product developed from research using your data.

If you do not want your data used for other research, you should not participate in this study.

Future use of Private Information and/or Data

Research using private information and/or data is an important way to understand human disease. You are being given this information because the investigators want to save private information such as MRI data, sensory and psychological testing results for future research. Data collected for or generated from this study will be shared and used for future research. Data may be shared with other scientists at Cincinnati Children's and possibly with outside collaborators, who may be at another institution or for-profit company. This research will not include whole-genome sequencing.

Your name and other personal identifiers will be removed from private information and data, and, after such removal, the information and/or data will be used for future research studies or shared with other scientists for future research studies without additional informed consent from you.

WHAT IF WE LEARN NEW INFORMATION DURING THE RESEARCH?

The study doctor will tell you if they find out about new information from this or other studies that may affect your health, safety or willingness to stay in this study.

WILL IT COST YOU ANYTHING EXTRA TO BE IN THE RESEARCH STUDY?

There are no costs to you for being in this study. All study costs, including any 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 charged to you and your parents.

WILL YOU BE PAID TO BE IN THIS RESEARCH STUDY?

You will be paid for being in this research study. You will be paid a total of $410 if you participate in all sessions of the study. Specifically, you will be paid up to $225 for the baseline

session(s) (Questionnaires: $50, Sensory testing: $75, MRI: $100). You will be paid $20 for each of the 3 online sessions, and $125 for the 1-year sensory testing session and surveys.

You will receive payment for this study in the form of a reloadable debit card. We will give you a booklet that will explain how to use the card. Because you are being paid for your participation, CCHMC is required by the Internal Revenue Service (IRS) to collect and use your social security number (SSN) or taxpayer identification number (TIN) to track the amount of money that we pay you. You will need to complete a Federal W-9 form for this income tax reporting. This form requires your Social Security number. This form will be given to the CCHMC business office. It will not be kept as part of your study folder. If you move, you will need to complete another W-9 with an updated address.

Information collected for this research may result in the development of a product that could be officially registered and sold. You will not be paid if this happens.

WHAT HAPPENS IF YOU ARE INJURED FROM BEING IN THIS STUDY?

If you believe that you have been injured as a result of this study, you should contact **Dr. Robert Coghill** as soon as possible to discuss the concerns. Treatment for injuries is available at Cincinnati Children's Hospital. If you go to the Emergency Room or to another hospital or doctor it is important that you tell them that you are in a research study. If possible, you should give them a copy of this consent form. Cincinnati Children's Hospital follows a policy of making all decisions about compensation for the medical treatment of physical injuries that happened during or were caused by research on an individual basis.

WHO DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?

For questions, concerns, or complaints about this research study you can contact Dr. Robert Coghill listed on page 1 of this document.

If you would like to talk to someone that is not part of the research staff or if you have general comments or questions about your rights or about the study, you can call the Cincinnati Children's Hospital Institutional Review Board at 513-636-8039.

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

To be in this study you must also give your permission (or authorization) to use and disclose (or share) private information about you, called “protected health information” (called PHI for short).

What protected health information will be used and shared during this study?

Cincinnati Children's Hospital will need to use and share your PHI as part of this study. This PHI will come from:

- Your Cincinnati Children's Hospital medical records
- Your research records

The types of information that will be used and shared from these records include:

- Laboratory test results, diagnosis, and medications

- Reports and notes from clinical and research observations
- Imaging (like CT scans, MRI scans, x-rays, etc.) studies and reports
- If applicable, information concerning HIV testing or the treatment of AIDS or AIDS-related conditions, drug or alcohol abuse, drug-related conditions, alcoholism, and/or psychiatric/psychological conditions (but not psychotherapy notes).

Who will share, receive and/or use your PHI in this study?

- Staff at all the research study sites (including Cincinnati Children's Hospital)
- Staff who provides services to you as part of this study
- Other individuals and organizations that need to use your PHI in connection with the research, including people at the sponsor and organizations that the sponsor may use to oversee or conduct the study.
- The members of the Cincinnati Children's Hospital Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs.

How will you know that your PHI is not misused?

People that receive your PHI as part of the research are generally limited in how they can use your PHI. In addition, most people who receive your PHI are also required by federal privacy laws to protect your PHI. However, some people that may receive your PHI may not be required to protect it and may share the information with others without your permission, if permitted by the laws that apply to them.

Can you change your mind?

You may choose to stop allowing us to use and share your PHI at any time. This would also include stopping your participation in the research study. If you wish to stop allowing us to use and share your PHI you need to notify the study doctor, listed on the first page of this document, in writing. We will stop using and sharing your information right away and no new PHI about you will be used or shared. The only exceptions are:

(1) any use or sharing of PHI that has already occurred or was in process prior to you asking us to stop using and sharing your information

(2) any use or sharing that is needed to maintain the integrity of the research.

Will this permission expire?

Since this study involves the creation or maintenance of a research database, this permission will not expire.

Will your other medical care be impacted?

By signing this document, you agree to participate in this research study and give permission to Cincinnati Children's Hospital to use and share your PHI for the purpose of this research study. If you refuse to sign this document, you will not be able to participate in the study. However, your rights concerning treatment not related to this study, payment for services, participation in a health plan or receiving benefits will not be affected.

SIGNATURES

The research team has discussed this study with you and answered all of your questions. Like in any research, the researchers cannot predict exactly what will happen. Once you have had enough time to consider whether you should participate in this research you will document your consent by signature below. You will receive a copy of this signed document for your records.

☐ By checking this box, you are consenting to your contact information being shared with Pediatric Pain Research Center staff and being contacted about other research studies.

_____

Printed Name of Research Participant

_____ _____

Signature of Research Participant Indicating Assent/Consent — Date

_____ _____

Signature of Parent or Legally Authorized Representative* — Date

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* If signed by a legally authorized representative, a description of such representative's authority must be provided.

_____ _____

Signature of Individual Obtaining Consent — Date