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Document cover page

Official Title: Neural Correlates of Lidocaine Analgesia

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CONSENT TO ACT AS A Study Title: **Neural Correlates of Lidocaine Analgesia**
PARTICIPANT IN A RESEARCH STUDY

KEY INFORMATION

*1. You are being offered the opportunity to participate in a research study. One of the investigators will explain the study to you and will answer any questions you might have. You should take your time to make your decisio*n, which is completely voluntary.

2A. Summary of the research

Purpose of the research: The purpose of this study is to better understand how IV lidocaine acts in the brain to affect pain perception.

Duration, number of study visits: There is one visit associated with participation in this study. This visit will last approximately 3 hours.

Overview of study procedures:

- urine pregnancy screen (for females)
- nerve stimulator calibration to a pain intensity of 7/10
- brief physical exam including listening to your lungs and heart and looking at/in your neck and mouth; you will be weighed.
- questions about medical conditions, past surgeries, medications, allergies, any symptoms that you have during physical activity, and your weight. If you do not have a scale and are unable to locate one to use, give us your best estimate of your weight and we will weigh you on arrival to confirm.
- Two intravenous (IV) catheter placements (using needles)
- IV lidocaine infusion
- Blood draw through IV catheter (two 5mL tubes collected)
- MRI safety screening questions
- enter the high magnetic field environment of the MRI scanner
- connection to monitor that measures your heart rate, blood pressure, and breathing
- placement inside the MRI scanner
- experience painful stimulation while being scanned by the MRI
- Recovery from the drug, until thinking and feeling normally

3. Reasonable, foreseeable risks or discomforts

Risks and side effects related to the MRI scanning include those which are:
Likely: Discomfort from loud noise, positional discomfort
Rare but serious: claustrophobia, risk of interaction with undetected/undisclosed metal in/on subject's body that could cause physical injury; hearing damage/loss

Risks and side effects related to the collection & storage of personal health information include those which are:
Rare but serious: Breach of confidentiality

Risks and side effects related to the electric nerve stimulation include those which are:
Likely: Pain due to electric shock
Rare but serious: Theoretical risk of burns due to an interaction with MRI scanner

Risks and side effects related to the lidocaine administration include those which are:
Likely: sedation, abnormal taste
Less Likely: burning on injection, confusion, hearing abnormal sounds (ringing in ears)
Rare but serious: allergic reaction, seizures, abnormal heart rhythm

Risks and side effects related to IV access include those which are:
Likely: Discomfort or pain, bleeding or bruising, skin sensitivity
Less likely: possibility of multiple needle punctures
Rare but serious: infection, blood clot

Risks and side effects related to blood draw include those which are:
Likely: Discomfort or pain, bleeding or bruising, skin sensitivity
Rare but serious: infection

Risks and side effects related to the pre-visit restrictions include those which are:
Less Likely: Discomfort from hunger or strong urge to urinate

4. Reasonable, expected benefits
You will be compensated $150 for participation. There are otherwise no direct benefits to you from participating in the study. However, this study will help the researchers learn more about how the commonly-used mediation lidocaine changes the experience of pain.

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: **Neural Correlates of Lidocaine Analgesia**

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Why is this research being done?
You are being offered the opportunity to take part in a research study. Research Studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision. The purpose of this study is to better understand what happens in the brain when people receiving intravenous (IV) lidocaine and experiencing pain.

Who is being asked to take part in this research study?
Any adult under 70 years old who is not pregnant, free from any serious chronic medical condition, has never had a history of psychological or neurological disease, and who has never had a reaction to lidocaine may be able to participate in this study.

To re-iterate, specific exclusion criteria include:
- being pregnant or attempting to conceive
- having a body mass index (BMI) greater than 40
- being older than 70 years old
- having moderate to severe sleep apnea
- having chronic pain requiring the use of pain medicine 3 or more times per week
- having neurologic or psychiatric disease, including benign tremor, anxiety, and depression
- having history of cardiac rhythm disturbance (such as heart block, or atrial fibrillation)
- having history of seizures
- being severely claustrophobic
- have metal implants or non-removable metal piercings

- having metal-containing tattoos, particularly on the face
- having a history of adverse reaction to lidocaine or to any other local anesthetics of the amide type
- regularly taking: antiepileptics, antidepressants, anti-psychotics, anti-anxiety medication, stimulants, sleep-aids, or pain medication
- having Wolff-Parkinson-White syndrome
- having known renal or hepatic dysfunction
- having glucose-6-phosphate dehydrogenase deficiency or history of methemoglobinemia

We will recruit 30 people to participate. The total time for you to participate is 2-3 hours over 1 visit.

What procedures will be performed for research purposes?

There is one visit associated with participation in this study. This visit will last approximately 3 hours. The MRI scanners that will be used for this project are located within the two Magnetic Resonance Research Center facilities, either the 8th floor B-wing 3T scanners or the 7T scanner in the basement of the Biomedical Science Tower 3 (a research facility connected by bridge to UPMC Presbyterian/Montefiore). The scanner to be used would be determined in advance for a subject cohort, and you would be informed in advance of the research location.

If you decide to take part in this research study, you will undergo the following procedures:

Experimental Procedures:

If you qualify to take part in this research study, you will undergo the experimental procedures listed below,

1. We will ask you to abstain from solid food and caffeine for 8 hours prior to your scheduled visit, consume only clear liquids until 1 hour prior to your scheduled arrival time, and not urinate in the hour before the visit (if a urine sample is needed).

2. We will collect a urine sample to test for pregnancy from female subjects.

3. We will measure your weight.

4. A nerve stimulator will be connected to one or two of your fingers with two small electrodes. A small electrical current will then be delivered. Starting at zero, the intensity will slowly be increased until you report a pain of 7 out of 10, where 0 is no pain and 10 is intolerable pain. The nerve stimulator will then be turned off and then used periodically for a few seconds at a time during the rest of the experiment. Unless you request an adjustment, the level of current delivered (pain intensity) will not be changed after adjustment to the level you rate as 7 out

of 10 pain.

This study uses low doses of intravenous lidocaine. This drug is used routinely to relieve pain in patients, for example before, during, or after surgery. A physician anesthesiologist will interview you and do a brief physical exam to be sure you are safe to receive lidocaine. These will include (at least) questions about your medical conditions, past surgeries, medications, allergies, and any symptoms that you have during physical activity. The examination will consist of (at least) looking in your mouth, feeling your neck, and listening to your heart and lungs with a stethoscope.

Two intravenous needles (IV) will be placed, likely in your hand or arm and foot. The needles are removed, and small plastic catheters (tube) will remain in your body throughout the study. One IV will be used to give you fluid and the lidocaine used in the study. The other will be used to obtain a blood sample during the scan. This blood sample collection will consist of two 5mL tubes which is about ½ teaspoon of blood. You will also be connected to vital sign monitors, to measure your heart rate, blood pressure, and breathing. These procedures will take approximately 15 minutes.

You will receive both IV fluid (a saltwater solution) and lidocaine at the visit. For this study, the drug is administered by a physician anesthesiologist (a doctor with specialized training in the administration of these medications).

5. You will be asked additional screening questions to ensure that it is safe for you to undergo MRI scanning (no metal or electronic implants, no metal-containing tattoos, etc). Prior to entering the MRI environment, you will be asked to remove any jewelry or glasses and be asked to change into a hospital gown if your clothes contain any metal.

6. You will receive lidocaine and a medical saltwater solution (IV fluid) through your IV, which will take 10-15 minutes to reach effect. You will experience periodic brief painful stimulation, as described above. A qualified anesthesia provider will monitor your response to the medication at all times. This part of the study will take about 60 minutes, after this you will have completed the experiment for this visit.

7. You will then be monitored while you recover from the effects of sedation. Water will be available, and a limited selection of study-provided snacks may be available. But, you are encouraged to bring your own drink and snack to eat afterwards, if desired. Your IV line will be removed, and the study doctor will check with you to be sure you are feeling well. Once it is safe to do so, you will be discharged, typically 30 minutes later. You are not allowed to drive a vehicle or operate machinery after receiving lidocaine for the rest of the study visit day. You will need to arrange a way to get home or to your next destination (without driving) from the study visit. If you have any symptoms or concerns, please call

Dr. Vogt. You will be paid $150 for completing this study visit prior to your discharge.

What are the possible risks, side effects, and discomforts of this research study?
Performing the experimental tasks pose no risks to subjects. Other aspects of the study involve some risk, which are described below. As with any experimental procedure, there may be adverse events or side effects that are currently unknown and some of these unknown risks could be permanent, severe or life-threatening.

Risks of Pre-Visit Restrictions
There is a small risk of discomfort from the pre-visit restrictions, such as hunger and the urge to urinate.

Risks related to intravenous (IV) access

- Discomfort will occur in all subjects with needle insertion.
- There is a risk of a small bruise or soreness at the IV site, that may last for several days after the study.
- Individuals with sensitive skin may experience some temporary irritation or skin rash from the adhesive dressing or tape used to cover the puncture site.
- Less than 1% risk of fainting (syncope), or nausea/vomiting with IV placement
- IV infiltration (leaking out of the vein), in which case fluid would temporarily accumulate in your arm. This would resolve spontaneously, though this situation poses a very small risk of blood clot or tissue damage as a result.
- Extremely small risk of serious bleeding or infection related to IV placement. Study personnel who are trained in IV access will implement precautionary measures including ensuring your physical comfort, proper disinfection of the needle insertion site, application of pressure after removal of the needle, and monitoring for any problems.
- Some individuals have veins that are unexpectedly difficult to access, and these subjects could experience multiple needle sticks in an attempt to obtain a functioning IV. As IV access is required for the study procedures, inability to obtain IV access could result in involuntarily withdrawal from the study.

Risks related to IV blood sample collection:

- Minor discomfort or bruising at the site of IV placement
- In rare cases, blood collection may lead to infection.

Known risks of Receiving lidocaine:

Common side effects include:
Sedation, abnormal taste, pain on injection

Uncommon possible side effects include:
Confusion, hearing abnormal sounds (ringing in ears), allergic reaction, seizures, abnormal heart rhythm

Other risks of lidocaine administration:
Anxiety, depression, lightheadedness, dizziness, restlessness, feeling sleepy, drowsiness, nausea, dry mouth, headache, blurred/double vision, numb or tingling mouth, out of body sensations, ringing or buzzing of the ears, slowed or rapid heart rate, low blood pressure, slowed breathing, tremors (where your hands or a part of your body is shaky), seizures

Risks related to painful electric nerve stimulation
Because the effects of lidocaine on pain are being studied, pain will be repeatedly experienced in this study. Each occurrence of the pain will be brief, and you can have the painful stimulus (and the entire experiment) stopped at any time by notifying any research team member. Once electrical stimulation is stopped, there will be immediate pain relief.

Risks of MRI scanning

- You may feel nervous and/or claustrophobic during the MRI scans.
- While the MRI is running, you will be asked to lie still on a narrow bed inside of the scanner and the scanner will make a loud knocking or beeping sound. The noise level is within safety limits, but you will be asked to wear earplugs, since this noise is uncomfortable for some people. You will be in verbal contact with the investigators and operator of the MRI machine, and you can request that the experiment (and scanning) be stopped at any time, and you would be immediately removed from the scanner.
- During the scanning process, you are lying on your back, and it is possible that you may feel some discomfort related to positioning.
- There are no known long-lasting side effects from MRI scanning.

If your clothing is uncomfortable, or contains metal, you will be asked to change (in a private dressing room) into a hospital gown prior to entering the MRI scanner.

Risks of Breach of Confidentiality
There is a potential risk of breach of confidentiality that is inherent in all research protocols. There is a possibility that if research data were to become known, this knowledge could potentially impact a subject's future or have a negative impact on family or social relationships.

With your permission, we will use text messaging and email to remind you of appointments and scheduling issues. No personal information will be transmitted; however, know that both email and text messages are NOT secure.

What are possible benefits from taking part in this study?
You will receive no direct benefit from taking part in this research study. Participation in this study will help further the understanding of how the brain forms memories when under sedation and experiencing pain.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Although unlikely, you would be promptly notified if any new information develops during the course of this research study which suggests that you were put at any increased risk as a result of your participation.

Will my insurance provider or I be charged for the costs of any procedures performed as part of this research study?
Neither you, nor your insurance provider, will be charged for the costs of any of the procedures performed for the purpose of this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above).

Will I be paid if I take part in this research study?
You will be paid a total of $150 for completing the in-person visit and all associated procedures in the study. This payment will be processed on a reloadable debit card. Since you are being compensated for your participation in this study, your name, address, date of birth, and social security number will be released to the Accounting Office. All compensation is taxable income to the participant regardless of the amount. If you receive $600 or more in a calendar year from one organization, that organization is required by law to file a Form 1099 – Miscellaneous with the IRS and provide a copy to the taxpayer. Individuals who do not provide a social security number may still participate in the research, but the IRS requires that 24% of the payment be sent by the institution to the IRS for 'backup withholding;' thus you would only receive 76% of the expected payment.

Commercialization statement
Your data from this research study may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may realize.

Who will pay if I am injured as a result of taking part in this study?
If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. You waive no legal rights by signing this consent form.

What information will be collected about me and who will know about my participation in this research study?

We will not be reviewing your medical record information for the purposes of this study. However, we will collect information directly from you including: demographic information such as age, weight, and height; and portions of your medical history (including substance use history) necessary to determine your ability to safely undergo receive lidocaine and undergo MRI scanning. Representatives from the National Institutes of Health or the University of Pittsburgh Office of Research Protections may access identifiable private information for purposes of monitoring the study.

To protect your privacy, we will store this collected information separately from personal identifiers such as your name and contact information. Thus, your research data will only be identified by a code and not linked to you personally. Although we will do everything in our power to protect your privacy and the confidentiality of your records, just as with your medical information for health care purposes, we cannot guarantee the confidentiality of your research records. The identifiable link between your personal formation and your data will be stored for a minimum of 7 years after final reporting of study results, and then this link (your personal information) will be destroyed. All de-identified data from this study will be kept securely for an indefinite period of time. No third party, including relatives, personal physicians, or insurance companies will be granted access to the identifiable information we collect. It is possible that we may share the information from this study, so that it may be combined with other data in larger future studies. However, your information would only be shared with other researchers without any personal identifiers, so no one would be able to learn your identity. For the purpose of monitoring the conduct of this study, authorized representatives from the University of Pittsburgh Office of Research Protections may review your research information.

For the purpose of monitoring the conduct of this study, authorized representatives from the University of Pittsburgh Office of Research Protections may review your research information. Additionally, an Independent Medical Monitor, Dr. Tetsuro Sakai, MD, PhD (who is a UPMC anesthesiologist not involved in conducting the study) will review the medical information (such as heart rate, blood pressure and reported adverse events) that are collected during the study. This data will be shared with the Independent Medical Monitor in de-identified format, such that your name and personal information is not linked to the medical information.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or

communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings; if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Is my participation in this research study voluntary?
Yes! Your participation in this research study is completely voluntary. Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the investigators, the University of Pittsburgh, or UPMC. Your participation will not affect your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with any healthcare insurance provider.

May I withdraw my consent for participation in this research study?
You may withdraw your consent for participation in this research study at any time. Any identifiable research information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

To withdraw your consent for participation in this research study, contact the principal investigator of this research study at the address/phone number listed on the first page of this form.

If I agree to take part in this research study, can I be removed from the study without my consent?
You may be removed from the study by the researchers if any practical considerations or safety concerns arise that do not allow you to participate.

Will clinically relevant results be available to me?
Any clinically-relevant abnormalities will be disclosed to you, at the discretion of one of the study physician investigators. The MRI scan is being done for research purposes. It may detect an unknown abnormality but cannot provide a diagnosis. The study team will advise you if follow-up care is recommended for any abnormal medical findings.

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VOLUNTARY CONSENT

The above information has been explained to me and my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator.

I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that have occurred during my participation. By signing this form, I agree to participate in this research study and allow the use of my private health information. A copy of this consent form will be given to me.

_____	_____	_____
Participant's Signature	Printed Name of Participant	Date

CERTIFICATION of INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions as they arise.

I further certify that no research component of this protocol was begun until after this consent form was signed.

_____	_____
Printed Name of Person Obtaining Consent	Role in Research Study
_____	_____
Signature of Person Obtaining Consent	Date