Protocol Title: Vasopressin and pain in the brain

Study No.: HP-00076723

NCT03446456

Informed Consent Form

Last Approval Date: 10-28-2021

RESEARCH CONSENT FORM
fMRI

Protocol Title: Vasopressin and pain in the brain

Study No.: HP-00076723

Principal Investigator:
Luana Colloca, MD, PhD
410-706-8244 (office)
301-364-8089 (cell)

We are asking you to take part in a study being led by Luana Colloca, MD, PhD at the University of Maryland School of Nursing (UMSON). Taking part in this study is voluntary. You can stop taking part in the study at any time. This form explains the details of the study and will help you decide if you want to take part. After reading this form carefully, please ask any questions you have. You will be tested to see if you understand the form.

PURPOSE OF STUDY

The purpose of this study is see how vasopressin changes the way that the brain perceives pain. Vasopressin is a hormone produced in the brain that is used to treat some forms of diabetes. For this study, we will assess the effects of vasopressin given as a nasal spray. 244 healthy participants will take part in this study. The study will take place at the UMSON and University of Maryland School of Medicine (UMSOM), Core for Translational Research in Imaging (C-TRIM). The participants in this study will be assigned to either Electro-encephalogram (EEG) or Magnetic Resonance Imaging (MRI) part of the study. You are participating to the fMRI part.

PROCEDURES

The study procedures will take place over two days. On the first day, the visit will take about 2-3 hours at the School of Nursing Clinical Testing Suites. On the second day, the visit will take about 2-3 hours at the C-TRIM. Day 2 will take place within 14 days of Day 1. The procedure described below will only happen once. All participants from this study will go through the procedure outlined below.

<u>Day 1:</u>

1. *Drug and Pregnancy Testing (~5 minutes)* - You will be asked to take a urine drug screening test and (if you are a woman) a pregnancy test. The experiment will stop if you test positive for any drug use or for pregnancy. We will test you for opiates, cocaine, methamphetamines,

amphetamines, and THC (a primary component of cannabis). The test may be positive for up to 40 days after exposure to one of these drugs.

2. *Pain Sensitivity Measurements and Additional Instructions (~20 minutes)* - The next step will be pain sensitivity measurements. You will have precisely controlled non-painful and painful heat stimulations to your forearm to test your sensitivity to pain. A probe will be placed on your skin to give the heat stimulations. The temperature of the stimulations will change so that you feel warm and hot sensations. You will get instructions about when to show that you feel warmth or heat by pressing a button. You will also learn how to report your pain on a scale from no pain to maximally tolerable pain.

3. *Saliva Samples (~10 minutes)* - We will collect 2-3 tablespoon of saliva to extract DNA and analyze how genes contribute to pain perception. We will give you a container, like a small cup, and ask you to spit into it. We will ask you to rinse your mouth out with water 10 minutes before the sample collection.

   These samples will not be used to see if you have any conditions or diseases and there will be no test of ancestry. These samples will be completely de-identified and will be coded so that your identity is protected. Any information gained from this sample will not be given to you or anyone else. There is no limit for the amount of time we may store your sample. We may continue to use it for future research purposes unless you give the PI a written request to stop taking part in the study or we stop the research study. You can ask for the sample to be destroyed at any time. If you decide to stop taking part in the study, no further information from that sample will be taken. Already collected information may be saved. Saliva samples will be stored for possible future use. If these future uses are for purposes unrelated to this study's goals, we will ask our ethical board for the institution's approval. You may choose to not have your saliva sample stored. If you choose to have the sample stored, you can contact the principal investigator at any time to have them destroyed. In order to analyze the information taken from your sample, your information may be shared with researchers from the University of Maryland, other universities, and the National Institutes of Health. The investigator will abide by the federal privacy rules that are in place to safeguard your privacy and confidentiality. Your name and personally identifiable information will never be shared.

_____ I consent to giving a saliva sample

_____ I do not consent to giving a saliva sample

_____ I consent to indefinite storage of my saliva sample for future studies

_____ I do not consent to indefinite storage of my saliva sample for future studies

4. *Psychological Testing (~1 hour 30 minutes)* - You will then be asked to complete an implicit association task (IAT). The IAT will be done on a computer that has tests for automatic thoughts about social groups. You will also take a series of questionnaires that measure personality traits. The experimenter will help you if you have any questions about these questionnaires. There will be several questionnaires about psychological traits that each take roughly 1-5 minutes on average to finish.

   We may need to get back in touch with you for additional data collection, such as another sample of saliva or completion of additional questionnaires. We may ask you to come in person or we may mail you the data collection tools.

   _____ I consent to be re-contacted for additional data collection

   _____ I do not consent to be re-contacted for additional data collection

Day 2:

1. *Pregnancy Testing (~5 minutes)* - If you are a woman, you will be asked to take an additional urine pregnancy test if the Day 1 pregnancy test is more than 24 hours ago. The experiment will stop if the test is positive for pregnancy.

2. *Magnetic Resonance Imaging (MRI) Preparation (~30 minutes)* - You will be given information about MRI safety and the task that you will be doing while in the MRI scanner. MRI uses a strong magnetic field and radio waves to take pictures of your brain while you perform a task. During the MRI, you will lie on a table that slides in and out of a cylinder and a device called a "coil" will be placed over your head. We will use some devices to measure your blood pressure, skin response from your hand, and both breathing and heart rate from your chest. During the MRI measurements, you will hear loud knocking noises, but you will be given earplugs or earmuffs to muffle the sound. There is a computer screen that you can see when you are inside the MRI. The screen will show you information needed to do the study task.

3. *Application of Vasopressin or Saline (~30 minutes)* – You will get a vasopressin or a saline nasal spray. Saline refers to salt water that is commonly used as fluid replacement in medicine. The treatment you get will be chosen by chance, like flipping a coin. You will have an equal chance of being given each treatment. Neither you nor the study doctor will know which treatment you are getting. You will be carefully watched to be sure that the drug is well tolerated.

4. *Pain Sensitivity Measurements (~10 minutes)* - Before the MRI measurements, we will make sure that the temperature settings, based on Day 1, are still okay for you. The maximum level

of pain will never be reached. You will not have more pain than you previously said was okay.

5. *MRI experiment (~1 hour)* - Before the MRI experiment, we will take measurements while you lie in the scanner but do not do any tasks. During the MRI experiment, you will see video clips of another person having heat pain on their forearm after two different creams were applied. One of the creams is a painkiller, while the other cream is a control and does not have any effect on pain. You will be asked to rate the pain experience of the person you are observing. During the second part of the MRI experiment, you will do the same task as the person you have just watched on the video clips. Before getting heat stimulations on your forearm, we will apply the same two creams as we used with the person in the video clips. You will be asked to rate your pain. You will have a safety button so that you can stop the MRI experiment at any time.

6. *Additional Questionnaires (~10 minutes)* – After leaving the MRI scanner, we will ask you to complete a few questionnaires about your feelings and emotions.

7. *Monitoring* – We will monitor your well-being for up to 2-3 hours after the administration of the medication (vasopressin or saline). You will be required to stay at our facilities until the 2-3 hours are over. You do not have to do any tasks during this time.

8. *Use of Deception* - At some point during the study, we will give you misleading information. After the study is over, we will give you a written explanation of how the information was not true and why. We will also answer any questions that you have about the procedure and explain the reasons we used misleading information.

POTENTIAL RISKS/DISCOMFORTS

1. *Risks Associated with medication:* Vasopressin is a hormone produced in the brain. It is usually given for a disease called diabetes insipidus, in which this hormone is not made by the body. In our study we use a nasal spray of arginine vasopressin at a high dose. You may have some side effects which last for a short time. Possible side effects are increased heart rate, tiredness, and weakness. Side effects of vasopressin, when given at a higher dose than you will get in this study, include headache, tremor, nausea, nasal congestion, a runny nose, flushing, stomach cramps, palpitations, increased blood pressure, nosebleeds, sore throat, cough, and upper respiratory infections. There are also possible side effects of water intoxication (excess of water in the body); symptoms of this include headache, loss of appetite, nausea, vomiting, and sleepiness. Vasopressin may increase fear and agitation. Other side effects that were observed in a previous study about vasopressin include dizziness, nasal congestion, drowsiness, anxiety, and self-reported increased feelings of aggression in men. These side effects are less likely at the dose you will be given, but they could happen. The effects of vasopressin are usually mild and last only a short time. Finally, there is a very small chance for allergic reaction. Please notify us right away if you have any side effects.

You cannot take part if you have a history of angioedema, high blood pressure (above 140 mmHg), symptomatic low blood pressure, or a history of fainting. There are no known side effects of saline nasal spray.

2. *Risks Associated with MRI:* People are at risk for injury from the MRI magnet if they have pacemakers or other implanted electrical devices, brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metallic prostheses (including metal pins and rods, heart valves, and cochlear implants), permanent eyeliner, implanted delivery pump, or shrapnel fragments. Welders and metal workers are also at risk for injury because of possible small metal pieces in the eye that they do not know about. You will be screened for these conditions and, if you have any, you will not have an MRI scan. If you think you may have any metal pieces in your body, you should tell the staff. All magnetic objects must be removed before entering the MRI scan room. For example, watches, coins, jewelry, and credit cards.

   It is not known if MRI is completely safe for a developing fetus. All women of childbearing potential will have a pregnancy test done no more than 24 hours before the MRI scan. The scan will not be done if the pregnancy test is positive.

   People with fear of small spaces may become anxious during an MRI. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss. Everyone having a MRI scan for this research will be fitted with hearing protection. If the hearing protection comes loose during the scan, you should let us know right away. Please tell the investigators if you have hearing or ear problems. You will be asked to fill out an MRI screening form for each MRI scan you have. There are no known long-term risks of MRI scans.

3. *Risks Associated with Heat Stimulations:* The heat stimulations on your forearm are moderately painful. They last less than 15 seconds and they may cause an uncomfortable and unpleasant feeling. Your skin may become red from multiple stimulations. You will take part in choosing a level of painful stimulation that is acceptable and tolerable for you. We will never use a higher level intensity than the one agreed upon. Please remember that you can stop the experiment at any time and withdraw from the study.

4. *Loss of Confidentiality:* There is always a risk for a loss of confidentiality when taking part in a research study. Every step will be taken to make sure of the confidentiality and anonymity of your results and identity. Steps will include using only an assigned code number for your personally identifiable information, including your contact information and name, on any documentation from this study. Electronic data will be password-protected and all paper copies of data will be stored in a locked cabinet. You will not be given the results of your questionnaires unless you score positively on the Mood and Anxiety Symptom Questionnaire (MASQ) or Beck Depression Inventory (BDI), because this information is used for

experimental and not clinical purposes. In case of a positive answer, you will be referred to your healthcare provider for follow-up. You have the right to access and disclose your records. Your healthcare provider will not get the results of your questionnaires since these answers are not collected for clinical purposes. You are required to take a drug test in order to take part in this study so that we can decide eligibility. Only designated research personnel will have access to your drug test results. The results of these drug tests will not be kept and will not be a part of any medical records.

5. *Breach of Privacy:* There is a minimal risk for a breach of privacy. To help keep your privacy you will be taken to a secured room to be screened. This will give you a private space to read the consent and HIPAA forms, and do the questionnaires. Only designated research personnel will have access to the rooms where you will be taking part in research activities. We will make every effort to minimize you interacting with people who are not a part of this research study.

6. *Risks Associated with Saliva Collection:* There are no known risks linked with the collection of saliva. You may have some discomfort from being asked to salivate.

7. *Risks Associated with Psychological Questionnaires:* You may have some discomfort while answering questions on the psychological questionnaires. You do not have to answer any questions that make you feel uncomfortable.

8. *Unknown Risks:* There may be risks or discomforts involved with taking part in this study that we do not know about yet. Research study staff will tell you right away if there is any new information that may affect your health, welfare, and decision to remain in the study.

POTENTIAL BENEFITS

You will not benefit directly by taking part in this study. If there are any incidental findings found on your MRI results, we will tell you about them and refer you to your primary care physician. Findings from this study could add to research on how the pain experience is generated in the brain.

ALTERNATIVES TO PARTICIPATION

This is not a treatment study. Your alternative is to not take part. If you choose not to take part, your healthcare at the University of Maryland, Baltimore will not be affected.

COSTS TO PARTICIPANTS

Injuries related to this research are unlikely. If medical issues happen as a result of this study, we will help you find medical care. All costs will be yours and/or your insurance company's responsibility.

PAYMENT TO PARTICIPANTS
You will be given $25 for Day 1 and $125 for Day 2 of the study. The money will come as a check that will be mailed to the mailing address you give. Also, a $150 gift card can be given to you based on your expressed preference. You will also be given 2 parking vouchers as thanks for taking part in this study. You can expect to get the checks in the mail within about 4-6 weeks of taking part in the study. If you decide to withdraw your data after taking part, you will still be paid. We will ask you to give your name, address and social security number to process the payment. If you do not have a social security number because of your current visa status, your compensation will be given in another form namely a $150 gift card. If you are invited to come back for additional sample collection, we will compensate an additional $25. If you fail the drug or the pregnancy test on Day 1, you will be considered ineligible for taking part in the study and you will not receive compensation. However, a parking voucher will still be given to you.

CONFIDENTIALITY AND ACCESS TO RECORDS
Only Dr. Luana Colloca and her trained and designated research personnel will have access to confidential information. All confidential information that includes personally identifiable information will be coded with a code number. The principle investigator will be the only person with access to the key to the assigned code numbers. All confidential information will be locked in a cabinet in a secured location at the University of Maryland, School of Nursing. Your personally identifiable information will not be used for this study's analyses, but it will be kept on file if federal agencies, such as the Intuitional Review Board (IRB), are required to review any information.

All study records will be considered confidential. Participants' names and personally identifiable information will not be used in reports or publications. Efforts will be made to limit access to your personal information, including research study records, to people who have a need to see this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

Those designated from the University of Maryland will be allowed to see certain research records of this study. Anyone looking at this information will do their best to keep this personal information confidential. Your personal information will not be released unless mandated by law.

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.

RIGHT TO WITHDRAW
Taking part in this study is voluntary. You do not have to take part in this research study. You are free to withdraw your consent at any time. Refusing to take part or stopping your participation in the study will cause no penalty or loss of benefits. If you decide to stop taking part, you have questions, concerns, or complaints, or if you need to report a medical injury

related to the research, please contact the investigator Dr. Luana Colloca at 410-706-8244 (office) or 301-364-8089 (cell). There are no negative consequences (physical, social, economic, legal, or psychological) for deciding to withdraw from this research study. If you withdraw from this study, already collected data may not be removed from the study database.

If you wish to withdraw from this study at any time, a written withdrawal request is required and should be sent to Dr. Luana Colloca at *colloca@umaryland.edu or* University of Maryland Baltimore School of Nursing, 655 W Lombard Street, Baltimore, MD, 21201. You will be told of any findings from this study that may affect your willingness to continue taking part. If you are an employee or student, your employment status or academic standing at UMB will not be affected by taking part or not taking part in this study.

CAN I BE REMOVED FROM THE RESEARCH?

The investigator, Dr. Luana Colloca, can remove you from the research study without your approval. Possible reasons for removal include incomplete data, abnormal pain sensitivity responses, and non-compliance with completing tasks. The entire study can be stopped at any time by the university, investigator, Institutional Review Board (IRB), or the facility where the study takes place.

UNIVERSITY STATEMENT CONCERNING RESEARCH RISKS

The University of Maryland, Baltimore (UMB) is committed to providing participants in its research the rights due them under State and federal law. You give up none of your legal rights by signing this consent form or by participating in the research project. This research has been reviewed and approved by the Institutional Review Board (IRB). Please call the Institutional Review Board (IRB) if you have questions about your rights as a research subject.

Participating in research may result in an injury, as explained above. If you suffer an injury directly related to your participation in this project, UMB and/or one of its affiliated institutions or health care groups will help you obtain medical treatment for the specific injury and provide referrals to other health care facilities, as appropriate. UMB and/or its affiliated institutions or health care groups will not provide you with financial compensation or reimbursement for the cost of care provided to treat a research-related injury or for other expenses arising from a research-related injury. The institution or group providing medical treatment will charge your insurance carrier, you, or any other party responsible for your treatment costs. If you incur uninsured medical costs, they are your responsibility. The study staff can give you more information about this if you have a study injury.

By signing this Consent Form, you are not giving up any legal rights. If this research project is conducted in a negligent manner and you are injured as a direct result, you may be able to

recover the costs of care and other damages from the individuals or organizations responsible for your injury.

If you have questions, concerns, complaints, or believe you have been harmed through participation in this research study as a result of researcher negligence, you can contact members of the IRB or the Human Research Protections Office (HRPO) to ask questions, discuss problems or concerns, obtain information, or offer input about your rights as a research participant. The contact information for the IRB and the HRPO is:

University of Maryland Baltimore
Human Research Protections Office
620 W. Lexington Street, Second Floor
Baltimore, MD 21201
410-706-5037

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

If you agree to participate in this study, please sign your name and date below:

_____
Participant's Signature

Date:_____

_____
Investigator or Designee Obtaining Consent Signature

Date:_____

If we can contact you for future research studies, please sign your name below:

_____
Participant's Signature