Protocol Title: Vasopressin and pain in the brain

Study No.: HP-00076723

NCT03446456

Study Protocol with Statistical Analysis Plan

Last Approval Date: 11-02-2021

UNIVERSITY of MARYLAND BALTIMORE

Date: Wednesday, November 3, 2021 9:39:07 AM Print Close

HP-00076723

View: v2_Introduction Page

Introduction Page

1 * Abbreviated Title:
Vasopressin and pain perception in the brain

2 * Full Title:
The influence of vasopressin on observational learning of placebo analgesia

3

* Select Type of Submission:

- (●) **IRB Application**
- ( ) Humanitarian Use Device (for FDA approved Indication & non-research purposes ONLY)
- ( ) Single Patient Expanded Access (pre-use)
- ( ) Single Patient Emergency Use (post-use)
- ( ) Unsure if this proposal requires IRB review (Not Human Subject Research)

Note: The Type of Submission cannot be changed after this application has been submitted for review.

4 Original Version #:

ID: VIEW4DF8709A33C00
Name: v2_Introduction Page

HP-00076723

View: v2_Research Team Information

Research Team Information

1 * Principal Investigator - Who is the PI for this study (person must have faculty status)? ***Faculty status is defined as being a full-time (>51% effort) faculty member holding one of the following titles at UM: Professor; Associate Professor; Assistant Professor.***
Luana Colloca

CITI Training: ID00009072

1.1 * Does the Principal Investigator have a potential conflict of interest, financial or otherwise, related to this research?
◯ Yes ● **No**

2 Point of Contact - Who is the alternative point of contact for the PI? This person can be a study coordinator or any other study team member. In case the IRB cannot contact the PI, this person is a secondary person to contact:
Nathaniel Haycock

CITI Training: ID00004399

2.1 Does the Point of Contact have a potential conflict of interest, financial or otherwise, related to this research?
◯ Yes ● **No**

3 Other Team Members - list all additional members of the research team for this study. DO NOT include the PI or POC in this list:

	Name	Edit Submission	cc on Email	Research Role	Has SFI?	CITI Training
View	Sarah Murthi	no	no	Research Team Member	no	ID00004433
View	Chika Okusogu	no	no	Research Team Member	no	ID00009720
View	Rachel Cundiff	no	no	Research Team Member	no	ID00011058
View	Titilola Akintola	no	no	Research Team Member	no	ID00005568
View	Kristina Park	no	no	Research Team Member	no	ID00008060
View	Sharon Thomas	no	no	Research Team Member	no	ID00002441
View	Christina Tricou	no	no	Research Team Member	no	ID00009152

	Name	Edit Submission	cc on Email	Research Role	Has SFI?	CITI Training
View	Yang Wang	yes	no	Research Team Member	no	
View	Elizabeth Olson	no	no	Research Team Member	no	ID00010083
View	Margaret Yin	no	no	Technician or Assistant	no	ID00010207
View	Alexis Saunders	no	no	Research Team Member	no	ID00010205
View	Se Eun Lee	no	no	Research Team Member	no	ID00009486
View	Rachel Massalee	yes	no	Research Team Member	no	ID00010242
View	Kathryn Smith	no	no	Research Team Member	no	ID00010059
View	Charlene Tugwete	no	no	Research Team Member	no	ID00010675
View	Nandini Raghuraman	no	no	Technician or Assistant	no	ID00002190

IMPORTANT NOTE: All research team members (including PI) must have current CITI and HIPAA training completed.

ID: VIEW4DF85C16F2800
Name: v2_Research Team Information

HP-00076723 View: v2_Resources

Resources

If this study is a collaborative UM/VA study, please clarify which resources are being used at each institution.

1 * Describe the time that the Principal Investigator will devote to conducting and completing the research:
The PI will devote 20% of her time conducting and completing the research.

2 * Describe the facilities where research procedures are conducted:
The first visit will be conducted on the 7th floor in the Clinical Laboratory Facilities at the School of Nursing and the second visit will be conducted at the Core for Translational Imaging at University of Maryland. The facilities are described below:

UMB School of Nursing (SON) Clinical Laboratory Facilities
The clinical laboratory facilities, under the direction of Prof. Luana Colloca, are located on the 7th floor of the School of Nursing. These laboratories provide state-of-the-art pain assessment and testing equipment for clinical studies. There is over 1700 square feet available for this study. This includes a spacious intake area, clinical exam suite, pain-testing suite, and office space for record retention and refrigerators for sample collection.
There is a clinical testing suite for participant visits. This facility has a waiting room area designated for waiting participants. Only designated research personnel in the SON have a key to these clinical suites. There is a quiet and secured room where participants can complete questionnaires and read documents (informed consent form) without distraction. In this same room, there is a telephone where participants can be contacted to be screened to participate in this study. In two of the other rooms in this suite, the equipment used for this experiment is housed (Medoc). All of these research designated rooms can be locked and secured to protect participant identity and privacy.

Core for Translational Imaging at University of Maryland (C-TRIM: Human Imaging):
The human imaging arm of C-TRIM houses a research dedicated 3.0 Tesla Siemens scanner and is equipped with a 32 channel body and head coil and state of the art pulse sequences are available for various neuro, body, musculoskeletal, cardiac, and breast applications. Special coils are available for pediatric and neonatal imaging. A strong research relationship exists between the C-TRIM and the scientists from Siemens Medical Solutions which strongly facilitates the progress on many ongoing research projects. The MR physics group is trained on the use of the IDEA pulse sequence environment and the ICE image reconstruction environment available on the Siemens scanner. Dedicated image processing workstations are available at the C-TRIM to facilitate various projects. Investigators are provided training on the use of the equipment and image processing techniques. For fMRI stimulus presentation and subject response collection, E-prime is available on the windows systems, and we also have the capability of collecting both cardiac and respiratory information digitally during MRI scans. In-house developed software is also available to control the triggers from or to the scanners. Matlab is available for the development of novel image processing algorithms, and other programming languages and packages are available for image processing and analysis (C++, Java, Perl, AFNI, FSL, MIPAV, TrackVis). Dedicated office space is provided for the MRI staff and additional carrels are available for researchers and guest faculty.

3 * Describe the availability of medical and/or psychological resources that subjects might need as a result of anticipated consequences of the human research:
All personnel interacting with participants will be adequately trained to handle unexpected medical emergencies. During the first visit, there will always be at least 2 trained personnel available on the floor. During the second visit (when the vasopressin (AVP) is administered), the PI (medical doctor by training) and a medical doctor from UMB will be available for medical advice. There will also always be a dedicated certified nurse or a medical doctor available who is part of our protocol within 5-10 minutes of the CTRIM center. In case of an urgent medical emergency, 911 will be called for immediate medical assistance. In case of serious adverse events (SAEs), the PI will also contact the pharmacy to know the drug allocation and report an SAE.

4 * Describe the process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions:

All research team members will be adequately trained prior to performing any study related procedures. The PI and co-investigators created a manual of procedures, which describes all of the research procedures and equipment. The PI will train the personnel before starting the experiments and will schedule regular meetings with the study team members to evaluate the progression of the study and the study conduct. This research team includes targeted expertise ranging from genetics, human pain, psychology, brain imaging to administrative roles.

ID: VIEW4DF83CB976400
Name: v2_Resources

HP-00076723

View: v2_Sites Where Research Activities Will Be Conducted

Sites Where Research Activities Will Be Conducted

1 * Is this study a:

- ○ Multi-Site
- ● **Single Site**

2 * Are you relying on an external IRB (not UM) to be the IRB of Record for this study?

○ Yes ● **No**

3 * Are any other institutions/organizations relying on UM to be the IRB of Record for this study?

○ Yes ● **No**

3.1 Attach the applicable regulatory documents here (i.e., IRB Authorization Agreement (IAA), FWA, local ethics approval, other IRB approvals, etc.). Final UM approval will be contingent upon final execution of all required regulatory approvals:

Name	Created	Modified Date

There are no items to display

4 * Is UM the Coordinating Center for this study? (Applicable for multi-site studies. A Coordinating Center is responsible for overall data management, monitoring and communication among all sites, and general oversight of conduct of the project.)

○ Yes ● **No**

5 Is VA the Coordinating Center for this study? (Applicable for Collaborative studies between the VA, UM and other sites. A Coordinating Center is responsible for overall data management, monitoring and communication among all sites, and general oversight of conduct of the project)

○ Yes ○ No

6 * Institution(s) where the research activities will be performed:

- [x] **University of Maryland, Baltimore**
- [ ] University of Maryland, Upper Chesapeake Kaufman Cancer Center
- [ ] VAMHCS
- [x] **UMB School of Medicine**
- [ ] Marlene and Stewart Greenebaum Cancer Center
- [ ] University Physicians Inc.
- [ ] Shock Trauma Center
- [ ] General Clinical Research Center (GCRC)
- [ ] Maryland Psychiatric Research Center (MPRC)
- [ ] Johns Hopkins
- [ ] International Sites
- [ ] UMB Dental Clinics
- [ ] Center for Vaccine Development
- [ ] Community Mental Health Centers
- [ ] Private Practice in the State of Maryland
- [ ] Institute of Human Virology (IHV) Clinical Research Unit
- [ ] Joslin Center
- [ ] UMB Student Classrooms
- [ ] National Institute of Drug Abuse (NIDA)
- [ ] National Study Center for Trauma and EMS
- [ ] Univ of MD Cardiology Physicians at Westminster
- [ ] Nursing Homes in Maryland
- [ ] University of Maryland Biotechnology Institute
- [ ] Maryland Department of Health
- [ ] Maryland Proton Treatment Center
- [ ] Mount Washington Pediatric Hospital
- [ ] Institute of Marine and Environmental Technology (IMET)

- [ ] Other Sites
- [ ] University of Maryland Medical System (Select below)

ID: VIEW4DF870DF2C000
Name: v2_Sites Where Research Activities Will Be Conducted

HP-00076723

View: v2_Funding Information

Funding Information

1 * Indicate who is funding the study:

- [ ] Federal
- [ ] Industry
- [x] **Department / Division / Internal**
- [ ] Foundation
- [ ] Private
- [ ] State Agency

2 * What portion of the research is being funded? (Choose all that apply)

- [x] **Drug**
- [ ] Device
- [x] **Staff**
- [x] **Participant Compensation**
- [x] **Procedures**
- [ ] Other

3 Please discuss any additional information regarding funding below:

Fund: Dr. Luana Colloca's UMBSON start up

ID: VIEW4DF85DF452400
Name: v2_Funding Information

HP-00076723

View: v2_Research Protocol

Research Protocol

1 * Do you have a research protocol to upload?

- ○ Yes
- ● **No, I do not have a research protocol and will use the CICERO application to enter my study information**

2 If Yes, upload the research protocol:

Name	Created	Modified Date

There are no items to display

ID: VIEW4E00563F8D000
Name: v2_Research Protocol

HP-00076723

View: v2_Risk Level

Risk Level

What is the risk level of your study? (Ultimately, the IRB will determine the appropriate risk level and your designation is subject to change.)

* Choose One:

- ○ Minimal - The probability & magnitude of harm/discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations/tests.
- ● **Greater Than Minimal - Does not meet the definition of Minimal Risk.**

ID: VIEW4E02805225800
Name: v2_Risk Level

HP-00076723

View: v2_Type of Research

Type of Research

1 * Indicate **ALL** of the types of research procedures involved in this study (Choose all that apply):

- [x] **Use of unapproved drug(s)/biologic(s) or approved drug(s)/biologic(s) whose use is specified in the protocol.**
- [ ] Evaluation of food(s) or dietary supplement(s) to diagnose, cure, treat, or mitigate a disease or condition.
- [ ] Use of device(s) whose use is specified in the protocol
- [x] **Psychological/Behavioral/Educational Method or Procedure (i.e., survey, questionnaires, interviews, focus groups, educational tests).**
- [x] **Sample (Specimen) Collection and/or Analysis (including genetic analysis).**
- [x] **Data Collection or Record Review (i.e., chart review, datasets, secondary data analysis).**
- [ ] None of the above.

2 * Is this study a clinical trial OR will this study be registered at ClinicalTrials.gov?
A clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

(●) **Yes** ( ) No

ID: VIEW4E0280569E000
Name: v2_Type of Research

HP-00076723

View: v2_Lay Summary

Lay Summary

1 * Provide a summary of the background and purpose of the study in language that can be understood by a person without a medical degree.

The feeling of pain is not just a sensory experience, but is also influenced by emotions, beliefs and expectations, making pain a highly subjective experience. This is evident in clinical practice, where the behavior of the physician and the treatment context can strongly influence the pain experience of patients. Research has shown that patients' expectation that a treatment will reduce their pain influences their perception of pain, even if the treatment has no active ingredient. The expectancy-induced analgesia emerges due to a modulation of the individual pain experience of patients by an engagement of endogenous (produced by our bodies) inhibitory systems in our central nervous system.

The development of expectancy-induced analgesia can be generated in several ways. We have previously demonstrated that social information and observational learning (e.g. the patient observes analgesia in another person receiving a treatment) can lead to expectancy-induced analgesia and pain reduction. However, the neural mechanisms (mechanisms in the brain) of how these expectancies are acquired and the neural mechanisms of analgesia induced by observational learning are unknown.

We recently establish a procedure to investigate neural mechanisms of observational learning in placebo analgesia. Here we propose to investigate the influence of vasopressin, a neurotransmitter that is important for social interaction, on observational learning.

We will use functional magnetic resonance imaging (fMRI), a non-invasive method, to investigate neural activity in humans. Participants will either receive vasopressin or saline with a nasal spray. During fMRI scanning, participants will then undergo an observational learning phase, where they will learn the experience of analgesia in another person through a video, and a testing phase, where they will perceive painful stimulations with the same cues as the observational phase. The comparison of the vasopressin group and the saline group will allow us to investigate how vasopressin influences behavioral effects of observational learning on pain perception as well as its effect on the neural processing of observational learning. We will also use electroencephalogram (EEG) that is a non-invasive method to investigate neural activity in humans with a higher temporal resolution than fMRI. Participants will undergo the same procedure as described above (observational learning phase, testing phase).

A better understanding of how the human brain processes observationally-induced analgesia would allow us to improve the therapeutic context of pain treatments by increasing the contextual factors which help patients cope with pain.

ID: VIEW4E02805CF7000
Name: v2_Lay Summary

HP-00076723

View: v2_Justification, Objective, & Research Design

Justification, Objective, & Research Design

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Describe the purpose, specific aims, or objectives of this research. State the hypothesis to be tested:

The purpose of this research is to investigate how vasopressin (AVP) influences the neural mechanisms associated with observationally-induced analgesia. More specifically, we will investigate how observing another person experiencing analgesia shapes subsequent behavioral and neural responses to painful stimulations.

Aim 1: To investigate how AVP influences the neural mechanisms associated with observationally-induced analgesia as assessed with fMRI or EEG approaches.

Hypothesis 1: We expect that AVP will boost activation in neural regions involved in social cognition.

Our overall objective is to determine the effect of AVP on neural mechanisms associated with observationally-induced analgesia.

2 * Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.:

This experiment has a between-subject study design. Participants will be randomized into an AVP group and a control group. The experimenter as well as the participant will be blinded regarding the allocation of the participant. Participants in the AVP group will receive intranasal AVP and the participants in the control group will receive intranasal saline before the fMRI experiment. Participants have 50%/50% chance of being placed in either group. The experiment in the fMRI scanner and the EEG is divided into two phases: an observational phase, in which participants will observe a video of a demonstrator experiencing analgesia, and a testing phase, in which study participants will receive heat pain to investigate how their pain perception was influenced. During both phases there will be a placebo condition (pain with the expectation of having received a treatment) and a control condition (pain without the expectation of having received a treatment). All participants will complete both phases, including the observational and testing phase. Neural processes are in many cases lateralized differently in left-handed people. Therefore, to increase homogeneity in analyzing pain processing signals, we exclude left-handed people to eliminate this potential source of error.

3 * Describe the relevant prior experience and gaps in current knowledge. Describe any relevant preliminary data:

Expectancy of analgesia related to the act of receiving a treatment (e.g. a painkiller) can reduce pain perception, even if this treatment is in fact an inert substance (e.g. placebo, Wager and Atlas, 2015). Expectancies about analgesic treatments can be acquired in several different ways, including direct experience of analgesia (i.e. the patient learns that after taking a specific drug, pain will decrease), verbal instructions (i.e. the doctor tells the patient that a specific drug will reduce pain) or social observation (i.e. the patient observes pain relief in another patient after this patient took a specific drug; Colagiuri et al., 2015).
The direct experience of pain relief in the context of treatment cues (i.e. conditioning) reduces subsequent pain perception when the same treatment cues are present. The neural underpinnings of how treatment expectancies are acquired during conditioning have been investigated previously. These studies indicate that the prefrontal cortex is involved in learning treatment expectations in the context of conditioned analgesic effects (Lui et al., 2010; Watson et al., 2009).
However, these expectancies can also be acquired by observing others. Our group was the first to demonstrate that analgesia can be triggered by observing another person that experiences analgesia (Colloca and Benedetti, 2009). This finding has been corroborated with additional studies by our group and other groups (Colloca and Benedetti, 2009; Egorova et al., 2015; Hunter et al., 2014; Swider and Bąbel, 2013; Vögtle et al., 2013). In these experiments, participants acquire expectancies of analgesia not by experiencing pain relief themselves, but rather by observing another person (the demonstrator) experiencing analgesia after receiving a certain analgesic treatment (actually a sham treatment). These placebo manipulations generate expectancies which lead to placebo effects of similar sizes that those shown through direct experience via conditioning paradigms (Colloca and Benedetti, 2009).
Even though previous research has focused on the direct experience of pain relief within a treatment context, social psychology suggests that most human behaviors are in fact modulated by sociality and learned by observing others (Bandura, 1977; Miller and Dollard, 1941). We recently established a paradigm to investigate neural mechanisms of observational learning in placebo analgesia. Our preliminary data analysis (unpublished data) suggests that while participants are observing someone else experiencing less pain due to an analgesic treatment, brain regions associated with mentalizing processes such as left and right temporoparietal junction (TPJ) and

medial prefrontal cortex (mPFC) show increased activation. However, the underlying neurotransmitter systems are unknown. Here, we aim to investigate how AVP modulates this network of brain regions. AVP is a likely candidate system, because recently it has been associated with placebo analgesia by my current mentor's lab (Colloca et al., 2016), is involved in controlling a wide variety of social behaviors (Meyer-Lindenberg et al., 2011), and has been shown to critically modulate TPJ activity (Zink et al., 2011). We expect that AVP will lead to increased activation of the mentalizing network during observational learning, and therefore, to increased placebo analgesia as a result of the observational learning. In order to investigate this, we will perform a similar observational learning study in a group receiving intranasal AVP and a control group receiving intranasal saline.

4 * Provide the scientific or scholarly background, rationale, and significance of the research and how it will add to existing knowledge:

Background: Clinical outcomes are not just related to pharmacological substances, but also to the context in which a treatment is given as well as expectancies, fears, desires and beliefs of the patient. The beneficial effects on health related outcome changes due to the treatment context and not due to specific actions of a drug are known as placebo effects (Benedetti, 2002; Wager and Atlas, 2015). In the field of pain, the reduction of pain perception due to placebo effects is called placebo analgesia or expectancy-induced analgesia.

Previous research shows that in placebo analgesia, informational cues of the treatment context generate the expectancy of pain relief due to a treatment (Montgomery and Kirsch, 1997). These expectations can be acquired through several ways (Colagiuri et al., 2015), including learning through direct experience (i.e. conditioning), verbal instruction or observation of others.

Several studies investigated the influence of direct experience of analgesia using conditioning paradigms on placebo effects. These studies show that conditioning creates more robust placebo effects than verbal suggestions alone (Colloca et al., 2008; Voudouris et al., 1990) and that the magnitude of experienced pain relief and the duration influence subsequent placebo effects (Colloca et al., 2010; Colloca and Benedetti, 2006; Geuter et al., 2013; Kessner et al., 2013).

On the neural level, placebo effects on pain perception are mediated by the descending pain modulatory system (Fields, 2004). Endogenous opioids are involved in the pain descending modulation systems, and placebo analgesia can be substantially reduced by opioid antagonists (Amanzio and Benedetti, 1999; Benedetti et al., 2007; Eippert et al., 2009; Levine et al., 1978). Several studies implicate functional connectivity between the rostral anterior cingulate and the periaqueductal gray, a region critical for descending pain modulation, and placebo analgesia (Bingel et al., 2006; Eippert et al., 2009; Wager et al., 2004). Additionally, there is considerable evidence that prefrontal regions, especially the dorsolateral prefrontal cortex (DLPFC), are critically involved in placebo analgesia (Krummenacher et al., 2010). The prefrontal cortex consistently shows higher activations related to the anticipation of analgesia and experience of pain relief induced by a placebo manipulation (Wager et al., 2004; Wager and Atlas, 2015), and is involved in the acquisition of expectancies during conditioning of placebo analgesia (Lui et al., 2010; Watson et al., 2009).

Therefore the current understanding is that the prefrontal cortex maintains and updates expectancies regarding pain (Lorenz et al., 2003), and that these prefrontal regions influence the experience of pain by activating the descending pain modulatory system (Wager and Atlas, 2015).

The influence of social learning on placebo analgesia has been investigated to a lesser degree. Recent research suggests that placebo analgesia can also be induced by observational learning (Colloca and Benedetti, 2009; Hunter et al., 2014; Swider and Bąbel, 2013; Vögtle et al., 2013), however, the neural neurotransmitter systems underpinning observationally-induced placebo analgesia have not yet been investigated.

Rationale: To harness the placebo effects in clinical contexts, it is important to understand how placebo effects arise and are maintained. Previous neuroscience research has primarily focused on conditioning paradigms, however human behaviors are affected by social learning (Bandura, 1977; Miller and Dollard, 1941). Social learning refers to learning about your environment due to information gained by observing others. Our overall hypothesis is that AVP will increase neural activation in regions related to social cognition during observational learning. Our objective is to determine the interplay of AVP and observationally-induced analgesia using an fMRI approach. fMRI is a noninvasive technique to measure changes in blood oxygenation in the brain enabling us to draw inferences about the localization and extend of neural activation associated with specific events and cues including the perception of experimental painful stimulations and their modulation. We designed an experiment to be performed behaviorally and with fMRI measurements in order to determine the interplay of AVP and observationally-induced analgesia.

Significance: This experiment will advance our understanding of endogenous processes associated with observationally-induced analgesia and the factors that influences pain processing. A better understanding of how treatment expectancies, formed through social observation, influence the individual experience of pain is significant in several ways. First, it will allow a better understanding of the contextual factors shaping pain and responses to treatments in clinical settings. Second, knowledge about the neural processes associated with endogenous pain relief might lead to novel developments in pain therapeutic strategies. Third, we anticipate generating findings that will advance our knowledge of how cognitive processes (i.e. expectancies) are represented in the brain and how they influence human social behaviors.

Exploratory genetic analysis: Previous research shows that pain perception and placebo analgesia is at least in part due to genetic factors (Colagiuri et al., 2015). Therefore, we would like to conduct exploratory analysis on the genetic basis of pain perception and placebo analgesia.

HP-00076723

View: v2_Supporting Literature

Supporting Literature

1 * Provide a summary of current literature related to the research: ***If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.***

Placebo effects are influenced by many factors including expectations about the treatment, previous experiences as well as other cognitive and emotional factors. Within these factors, previous experience via conditioning has been one of the most studied mechanisms of neurobiological investigation of placebo effects leading to the conclusion that these effects are primarily learned responses and that conditioning, instructional and observational cues in turn lead to expectancy of benefit and changes in clinical outcomes(Colloca and Miller, 2011).

Observationally-induced placebo analgesia has been investigated in settings in which study participants observed a demonstrator experiencing both electrical-like pain and analgesia (Colloca and Benedetti, 2009). The participant sat down close to the demonstrator receiving painful and non-painful electrical stimulations while a set of two cues (either red or green) were displayed on a monitor in front of them. The demonstrator repeatedly rated the pain stimulus higher after the red cue and lower after the green cue. Participants had to pay attention to the lights displayed on a monitor, with particular regard to their meaning. Therefore, the participant was made to believe that the green cue was followed by a non-painful stimulus while the red cue was followed by a painful stimulus. Afterwards, participants received painful electric stimulations after the red and green cues. However, the level of pain was surreptitiously set at the same intensity and any changes in pain reports was operationally defined as the results of learning and expectations formed via observation. Participants showed a strong placebo analgesic effect. Moreover, when compared to a conditioning group which experienced first-hand analgesia, the level of analgesia was similar. Thus, observation was strong enough to boost analgesia and expectancy of pain relief. Observationally-induced placebo analgesia has been replicated in several further studies with similar designs, showing that observation induced also nocebo hyperalgesic effects (Vögtle et al., 2013), larger observationally-induced placebo effects when the demonstrator is male (Swider and Bąbel, 2013). Interestingly, similar observationally-induced placebo analgesia was found when the participants observe a video instead of a live demonstrator (Hunter et al., 2014), indicating that video clips can be used in contexts such as fMRI settings.

On the neural level, although our results regarding observationally-induced placebo analgesia are not yet published, fMRI studies of social learning and fear have been performed (Olsson et al., 2007), in which participants observed another person receiving electrical fear-inducing shocks after one cue, but not after an alternative cue. During a subsequent test phase participants were exposed to the same cues but no electric shocks were given. The authors observed significant activation of the amygdala – a region linked to fear processing (Büchel et al., 1998; LaBar et al., 1998) - during the observational phase and the test phase. Additionally, the authors observed activation in brain regions related to empathy and mentalizing processes. This suggests that during observational learning, there is a potential overlap with brain regions implicated in the direct experience. Additionally, during observational learning, brain regions implicated in social cognition processes like empathy or mentalizing are involved (Olsson and Phelps, 2007). In placebo analgesia, the learning of treatment expectations during conditioning has been associated with the dorsolateral prefrontal cortex (Lui et al., 2010; Watson et al., 2009), a region which has been associated with maintaining and updating treatment expectations (Lorenz et al., 2003). Empathy for pain is mediated by affective pain processing regions such as the anterior insular cortex and the posterior anterior cingulate cortex (Bernhardt and Singer, 2012; Engen and Singer, 2013; Singer et al., 2004), while mentalizing is associated with brain regions such as the medial prefrontal cortex and the temporoparietal junction (Mahy et al., 2014).

AVP is a neuropeptide that is synthesized in the paraventricular and supraoptic nuclei of the hypothalamus and is released into peripheral as well as central circulation. AVP has been associated with emotion recognition, social affiliative and aggressive behavior, social memory, and social stress and anxiety (Meyer-Lindenberg et al., 2011). Due to the central role of social information in placebo analgesia and the importance of AVP in social behaviors, my current lab was the first to investigate the role of AVP in placebo analgesia (Colloca et al., 2016). Increased placebo analgesia after verbal suggestion in the group receiving intranasal AVP as compared to the saline was observed. Additionally, previous genetic studies observed an association between polymorphisms in the arginine AVP receptor 1a (AVPR1a) gene and mentalizing ability as assessed with a questionnaire (Uzefovsky et al., 2015), and AVP has also been shown to modulate brain regions associated with mentalizing (e.g. TPJ) in a social recognition paradigm (Zink et al., 2011). Therefore, AVP is a prime candidate system of interest for the understanding of how neurotransmitter systems influence observational learning of analgesia.

2 If available, upload your applicable literature search:

Name	Created	Modified Date
Vasopressin information(0.01)	11/20/2017 10:53 AM	11/20/2017 10:53 AM

Name	Created	Modified Date
Neuroimaging study performed by study staff(0.01)	8/31/2017 4:06 PM	8/31/2017 4:06 PM
Vasorpessin study performed by the PI(0.01)	8/31/2017 4:06 PM	8/31/2017 4:06 PM
social learning study performed by the PI(0.01)	8/31/2017 4:05 PM	8/31/2017 4:05 PM
review of placebo analgesia by the group(0.01)	8/31/2017 4:05 PM	8/31/2017 4:05 PM

ID: VIEW4E02805A7E400
Name: v2_Supporting Literature

HP-00076723

View: v2_Study Procedures

Study Procedures

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below. (If this study is a collaborative UM/VA study please list each procedure that is being conducted and the locations where it is being conducted.)

1 * Describe all procedures being performed for research purposes only (these procedures would not be done if individuals were not in the study) and when they are performed, including procedures being performed to monitor subjects for safety or to minimize risks:

The study will investigate the neural processes associated with AVP and observationally-induced analgesia using fMRI. The whole experiment consists of two experimental sessions on two days (the two sessions will take place not further apart than 14 days). On day 1, participants will be informed about the experiment, participate in a pain sensitivity assessment and fill out some psychological questionnaires.
On day 2, we will use an fMRI approach to investigate how AVP influences observationally acquired expectancy of pain relief and pain perception along with the associated neural mechanisms (see Table 1 for a study overview).

Experimental Day 1:
On day 1, participants will arrive to the UMSON clinical laboratories and will be informed about the nature and purpose of the research (see attached Consent form). A copy of the signed form will be given to the participant. First, participants will complete a drug test and, for female participants, a pregnancy test. We will test for opiates, cocaine, methamphetamines, amphetamines and THC (marihuana). The test may be positive for up to 40 days after exposure to one of these drugs. If the drug test or the pregnancy test will be positive, the experiment will be discontinued and the participant will not be paid. Afterwards, participants will familiarize with the heat stimulation and a pain calibration will be performed to identify the individual pain sensitivity as well as the level of pain to be used during the fMRI part of this study on day 2. Thermal stimulations will range from warm to heat intensities expressed in Fahrenheit delivered through the Medoc Pathway equipment. The calibration phase will include the delivery of thermal stimulations starting from a gentle warm sensation to a hot sensation. Importantly, the level of warm and hot will be based on the participants' sensitivity. To make them even more comfortable during this procedure, participants will be given a stopping device so that they can directly block the machine in case they feel distress during the stimulation. Participants will then learn how to rate pain perception using a visual analogue scale (VAS) ranging from 0=no pain to 100=maximum tolerable pain (See Testing measures). After the pain calibration, participants will be asked to perform an implicit association test (IAT, see Testing measures) and to complete some questionnaires for an exploratory approach. The IAT is a measure designed to detect implicit associations between mental representations, and can be used to measure implicit in- and out-group biases (Greenwald et al., 1998), which can be used as covariate in our analysis. Those participants who will not complete the questionnaires on day 1 will receive a Redcap link (HIPAA compliant tool) to finalize the questionnaires via email. A saliva sample will be collected for future genetic studies and data derived from this sample will not be used for the current study.

Experimental Day 2:
On day 2, before the experiment, study staff will get the intranasal AVP or saline from the pharmacy at UMB. Participants will be invited to the C-TRIM center for the fMRI part of the study. At the beginning of the second visit, participants will be asked to fill out the MRI screening before they can undergo the MRI scan. The C-TRIM MRI screening form will be signed by a MRI technician from the Imaging Center or the PI. The questionnaire must be completed prior to a scan as part of the C-TRIM policy to ensure participant safety. Additionally, a pregnancy test will be performed with any female participants who participated in Day 1 more than 24h ago, due to the fact that results will be considered valid for 24 hours only.
Then we will instruct the participant about safety issues related to the MRI scanner and the task he/she will complete during the fMRI session. The experimenter will tell participants that we investigate how AVP will influence pain processing in the brain when they observe pain in others via a video (observational phase) and during direct experience of pain (see Figure 1 and Participant instruction script under Additional files). Then the intranasal AVP or saline will be self-administered by the participant. The dose of AVP will be 40IU. This dose has been chosen based on the literature covering brain function and AVP in humans as well as our previously published trial (see attached, Colloca et al. Biol. Psychiatry, 2016). The quantity per unit (1mL) of Arg8-Vasopressin Synthetic. This amount will be diluted in 0.9% Sodium Chloride. 40 IU is used currently used in vasopressin research as it has been shown to reliably modulate brain activity while minimizing the occurrence of unwanted side effects. Safety was assessed in the last study by Colloca et al. 2016, observing the following side effects: dizziness (1/30), nasal congestion (7/30), drowsiness (5/30), anxiety (3/30), and self-reported propensity to act aggressively (4/30 (men)). The experimenter as well as the participant will be blinded regarding the allocation of the participant. Randomization will be performed/maintained by the UMMC Pharmacy. Blinding will only be broken in case of a potential medical emergency during the experiment. Based on the delay between application and maximum effect, we will have a time lag of approximately 30-60 min between the drug administration and the start of the

fMRI observational phase. The PI as well as a medical doctor will be reachable at all times during the experiment in case of unexpected emergencies. Participants will receive two creams on their forearm. Each cream corresponds to one of the conditions. The experimenter will inform the participant that one of the creams is an inert control cream (control condition), while the other is a painkiller cream (actually a sham cream, placebo condition). Since we use deception, we added in the consent a sentence informing participants about the use of misleading information (see attached Consent form). Actually, both creams are the same cream and are inert. The cream was chosen based on recommendations by the UMB pharmacy. A hypoallergenic cream routinely used as vehicle by pharmaceutical companies, will be used. The cream is free of dyes, fragrances, masking fragrances, lanolin, parabens and formaldehyde. FDA approved food colors will be used for the creams in either green or blue, respectively. The cream will be applied by the investigator wearing gloves.
The creams will be applied with the instruction that the cream will take a few minutes until it will have an effect.
Immediately before entering the MRI scanner, participants will fill out a few questionnaires regarding state anxiety and their mood. In the scanner, we will attach a pulsometer and electrodes for recoding respiratory and galvanic responses during the experiment (see Testing measures). These electrodes will be pasted on the hand and chest and the acquired measures will be used to optimize data analyses. Notably, these electrodes are part of the, MRI equipment and are not invasive. Participants will receive a device to provide pain ratings (see Testing measures) and the alarm pressure ball used in the MRI settings for safety issues. Participant will be instructed to press the alarm ball if he/she will feel discomfort and wishes to stop the experiment (details are provided in the Risks section and Safety file under Additional documents). Once in the MRI scanner, we will confirm pain sensitivity in order to account for possible changes in pain sensitivity due to the scanner environment. The experiment will start with a resting state acquisition and an anatomical T1 scan to allow participants to familiarize with the environment. A reverse cross will be displayed and participants will be invited to relax while looking at the symbol. The study paradigm will start with the observational phase (Figure 1), in which the participant will observe a demonstrator (Figure 2) while heat pain sensation are provided under the placebo and the control condition. The demonstrator will receive painful stimulations and the thermode will be switched to two distinct spots of the forearm. A computer screen in front of the demonstrator will show an anticipatory colored cue depending on the condition (either blue or green for control or placebo, respectively). The sequence of runs and the color presentation will be counterbalanced across participants. During each presentation of the demonstrator, a lightning signal will indicate that the demonstrator is going to receive heat pain. The demonstrator will show a relaxed neutral facial expression during the placebo runs and exhibit a painful grimace during the control run. Afterwards, the video clip will end and will be replaced by a fixation cross period. Then, the participant is asked to rate the pain of the demonstrator. The rating will be followed by a few seconds of fixation cross. This rating will help make sure that the participant pays attention to the video and is cognitively processing the contents of the video. Afterwards, the pain rating of the demonstrator will be presented. The demonstrator will provide a high pain rating in the control condition and a low pain rating in the placebo condition. Each trial will end with the presentation of a variable inter-trial interval (jitter). Afterwards, we will conduct the testing phase. Before starting the testing phase the participants will rate his expectancy of pain level. During the testing phase, participants will experience short heat pain stimulations. Participants will be informed that they will receive thermal stimulations on the site whereby the two creams have been applied and that the visual cues will let them know about the stimulation site similarly to the observational phase. Indeed, participants will see the same colored cues shown in the observational phase in association with analgesia and control level of thermal pain. After cue presentation, a heat pain stimulus corresponding to a previous calibrated pain intensity of approx. 50/100 VAS will be applied. Afterwards, a fixation cross will be displayed, followed by the pain rating using the VAS. After a short delay, participants will rate the unpleasantness of the pain stimulation using the VAS (pain unpleasantness rating, see Testing measures). A variable inter-trial interval with another fixation cross (to keep attention high) will be displayed at the end of each trial. The order of the placebo and control runs will be randomized across participants. The experimenter will move the thermode to the other site after the first run of the testing phase. During both phases, jittering (the inter-stimulus time changes randomly from trial to trial) will be included to improve data analysis. The specified trial duration is approximately 35±10 seconds. Afterwards, participants will be taken out of the MRI scanner and complete a few additional questionnaires, including the post experimental intrinsic motivation inventory (PEIMI) and a self-developed questionnaire (Experimenter Rating Scale, ERS, see attached questionnaires) regarding their experience with the experimenter, as previous research shows that experimenter personality can substantially influence placebo analgesia (Kelley et al., 2009). At the end of the experimental session, participants will be debriefed about the use of deceptive information and offered to withdraw their data if they feel any distress related to being deceived (see debriefing form). Participants will be monitored for 3 hours after the self-administration of the medication (vasopressin or saline) to make sure that assistance is available in case of unexpected side effects. If at the end of the experiment the 3 hours have not passed, participants will continue to be monitored until the 3 hours are over. If there is any case where participants were deceived but discontinued their participation before being informed about the deception, then they will be called over the telephone to be informed about the deception.

EEG experiment:
Participants will arrive to the UMSON clinical laboratories and will be informed about the nature and purpose of the research (see attached EEG Consent form). A copy of the signed form will be given to the participant. First, participants will complete a drug test. If the drug test will be positive, the experiment will be discontinued and the participant will not be enrolled and compensated. Afterwards, participants will familiarize with the heat stimulation and a pain calibration will be performed to identify the individual pain sensitivity as well as the level of pain to be used during the EEG part of this study.

The same pain calibration performed as described above (see fMRI experiment) will be done for the EEG experiment. Thermal stimulations will range from warm to heat intensities delivered through the Medoc Pathway equipment (see the Medoc Pathway Safety file). The calibration phase will include the delivery of thermal stimulations starting from a gentle warm sensation to a hot sensation. Importantly, participants will define the level of warm and hot based on their sensitivity. To make them even more comfort during this procedure, participants will be given a stopping safety button so that they can directly block the machine in case they feel distress during the stimulation (see Medoc Pathway Safety Guide). Participants will learn how to rate pain perception using a visual analogue scale (VAS) ranging from 0=no pain to

100=maximum tolerable pain (See Testing measures). After the pain calibration, participants will be asked to perform an implicit association test (IAT, see testing measures). The IAT is a measure designed to detect implicit associations between mental representations, and can be used to measure implicit in- and out-group biases (Greenwald et al., 1998), which will be used as covariate in our analysis. A saliva sample will be collected for future genetic studies and data derived from this sample will not be used for the current study.

We will then start the EEG part of the study. Then the intranasal AVP or saline will be self-administered by the participant. The dose of AVP will be 40IU. This dose has been chosen based on the literature covering brain function and AVP in humans as well as our previous published trial (see attached Colloca et al. Biol. Psychiatry, 2016). The quantity per unit (1mL) of Arg8-Vasopressin Synthetic. This amount will be diluted in 0.9% Sodium Chloride. 40 IU is used currently used in vasopressin research as it has been shown to reliably modulate brain activity while minimizing the occurrence of unwanted side effects. Safety was assessed in the last study by Colloca et al 2016, observing the following side effects: dizziness (1/30), nasal congestion (7/30), drowsiness (5/30), anxiety (3/30), and self-reported propensity to act aggressively (4/30 (men)).
The experimenter, as well as the participant, will be blinded regarding the allocation of the participant. Randomization will be performed/maintained by the UMMC Pharmacy. Blinding will only be broken in case of a potential medical emergency during the experiment. Based on the delay between application and maximum effect, we will have a time lag of approximately 30-60 min between the drug administration and the start of the EEG observational phase. The PI, as well as a medical doctor, will be reachable at all times during the experiment in case of unexpected emergencies. The experimenter will fill out a few questionnaires regarding state anxiety and their mood. Then the EEG montage will be placed. Once the EEG montage is completed, the experiment will start with recording an EEG resting state acquisition (4min eyes open and 4 min eyes closed).
Afterward, the observational phase will start which includes both a case and control condition. This part of the study for the fMRI and EEG experiments follow the same design. This will allow us to detect both EEG measures and explore both responses occurring at the level of electrical signals. In fact, participants will receive two creams on their forearm. Each cream corresponds to one of the conditions. The experimenter will inform the participant that one of the creams is an inert placebo cream, while the other is a painkiller cream. Since we use deception, we added in the consent a sentence informing participants about the use of misleading information (see attached EEG Consent form). Actually, both creams are the same cream and are inert. The cream was chosen based on recommendations by the UMB pharmacy. A hypoallergenic cream (VanicreamTM) routinely used as a vehicle by pharmaceutical companies, will be used. The cream is free of dyes, fragrances, masking fragrances, lanolin, parabens, and formaldehyde. FDA approved food colors will be used for the creams in either green or blue, respectively. The cream will be applied by the investigator wearing gloves. The creams will be applied with the instruction that the cream will take a few minutes until it will have an effect.
The paradigm will start with the observational phase (Figure 1), in which the participant will observe a demonstrator (Figure 2) while heat pain sensation is provided under two conditions: An active cream (actually a sham cream, case condition) and a control cream (control condition). The demonstrator will receive painful stimulations and the thermode will be switched to two distinct spots of the forearm. A computer screen in front of the demonstrator will show an anticipatory colored cue depending on the condition (either blue or green for control or case, respectively). The sequence of runs and the color presentation will be counterbalanced across participants. The demonstrator will show a relaxed neutral facial expression during the case runs and exhibit a painful grimace during the control run. The participant will sometimes be asked to rate the pain of the demonstrator.
The pain rating of the demonstrator will be presented briefly. The demonstrator will rate the pain in the case condition between VAS 70-90 and in the control condition between VAS 10-30. Each trial will end with the presentation of a variable inter-trial interval (jitter).
Afterward, we will conduct the testing phase. Before starting the testing phase the participants will rate his expectancy of pain level. During the testing phase, participants will experience mild heat pain. Participants will be informed that they will receive thermal stimulations on the site whereby the two creams have been applied and that the visual cues will let them know about the stimulation site similarly to the observational phase. Indeed, participants will see the same colored cues shown in the observational phase in association with analgesia and control level of thermal pain. A heat pain stimulus corresponding to a previously calibrated pain intensity of 50/100 VAS will be applied briefly, followed by the pain rating using the VAS.
A variable inter-trial interval (to keep attention high) will be displayed at the end of each trial. The order of the case and control runs will be randomized across participants.

Participants will also be asked to complete questionnaires for an exploratory approach. Those participants who will not complete the questionnaires will receive a Redcap link (HIPAA compliant tool) to finalize the questionnaires via email. At the end of the experimental session, participants will be debriefed about the use of deceptive information and offered to withdraw their data if they feel any distress related to being deceived (see debriefing form). Participants will be monitored for 3 hours after the self-administration of the vasopressin to make sure that assistance is available in case of unexpected side effects. If at the end of the experiment the 3 hours have not passed, participants will continue to be monitored until the 3 hours are over. If there is any case where participants were deceived but discontinued their participation before being informed about the deception, then they will be called over the telephone to be informed about the deception.

2 * Describe all procedures already being performed for diagnostic or treatment purposes (if not applicable to the study, enter "N/A"):

N/A

3 * Describe the duration of an individual participant's participation in the study:

We anticipate that this experiment will last approximately 2-3 hours for the first and 3-4 hours for the second visit. The whole experiment will last up to 5-7 hours. The EEG experiment will last for 4-5 hours and will be completed in a single session.

4 * Describe the amount of time it will take to complete the entire study:

We anticipate performing the study within one year after the approval by the IRB.

5 * Describe any additional participant requirements:

None.

ID: VIEW4E0280585B400
Name: v2_Study Procedures

HP-00076723

View: v2_Sample Size and Data Analysis

Sample Size and Data Analysis

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Provide the rationale and sample size calculations for the proposed target population:

Based on a previous relevant publication (Colloca et al., 2015), we expect a moderate effect size of d=0.45. To achieve the desired Power of 0.8 and an α-value of 0.05, a sample size of n=51 is required per group. Based on previous experience, we expect that around 20% (n=20) of the collected data cannot be used for analysis (i.e. due to drop-out or subject movement during the fMRI scan). Therefore we plan to include a total of 122 participants in our study. The power analysis was performed using G*Power 3. We expect a similar effect size for the EEG Experiment, therefore we will need up to an additional 122 participants, bringing the total number of participant involved to 244. Study participants who completed the fMRI Experiment will not be invited to participate in the EEG Experiment (and viceversa).

2 * Provide the plan for data analysis. Include in the description the types of comparisons that are planned (e.g., comparison of means, comparison of proportions, regressions, analysis of variance, etc.), which is the primary comparison/analysis, and how the analyses proposed will relate to the primary purposes of the study:

Behavioral analysis:
In the behavioral analysis, primary outcome measures are the pain and unpleasantness ratings during the test phase to investigate if we observe significant effects of AVP on observationally-induced placebo analgesia. We will use ANOVAS and mixed effect models to analyze the differences between the ratings in the placebo and control conditions. To investigate if measurements obtained from questionnaires are related to the behavioral effect, we will use Correlation coefficients between the questionnaire scores and the difference of the means of both conditions. Analysis will be performed in SPSS.

fMRI analyses:
Images will be pre-processed and analyzed using SPM12 (Wellcome Trust Center for Neuroimaging; http://www.fil.ion.ucl.ac.uk/spm/). Preprocessing consists of slice timing correction, within-subject realignment, coregistration, segmentation, normalization and smoothing. Slice timing correction will be performed to account for the measurement timing differences of the slices. Realignment and unwarping will be performed to correct for movement artefacts. The anatomical image will be coregistered to the mean functional image and then used for segmentation and normalization to MNI space using the DARTEL routine implemented in SPM. The same normalization parameters will be then used to normalize the functional images to MNI space and spatial smoothing will be performed.
Our primary outcome measures are the fMRI signal differences between the placebo and the control condition in the AVP group compared to the control group. At the first-level, stimulus outcome onsets will be entered separately for the placebo condition and the control condition. On the second level, we will use between-subject t-tests between the contrast estimates obtained from the first level analysis.
During the observational phase, we will investigate the influence of AVP on the neural mechanisms associated with observational learning in placebo analgesia (Aim 1). During the test phase we will investigate if we can replicate neural placebo analgesia effects similar to previous investigations (Bingel et al., 2006; Colagiuri et al., 2015; Wager et al., 2004).

EEG analysis:
Data will be re-referenced to the average of the two ear electrodes, band-pass filtered, removed of obvious non-brain (i.e. movement) artifacts, and epoched into 4 second segments. Following preprocessing, a fast fourier transform will be applied to each epoch. The resulting spectral information will then be averaged across epochs. This spectral information will then be exported to Matlab where it will be analyzed with custom scripts.

ID: VIEW4E02806052800
Name: v2_Sample Size and Data Analysis

HP-00076723

View: v2_Sharing of Results

Sharing of Results

1 * Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject's primary care physicians) and if so, describe how it will be shared:

As the results in this experiment are not directly relevant for the treatment of the participant, there no need for discussing the overall results of the investigation with the participant's doctor.

However, the BDI II has one question (#9) that asks the participant to rate their feelings of suicidal thoughts or wishes. We will review each participant's BDI form after completion at each study visit to assess whether the participant displays the potential for harm to self or others. Any participant who scores a 2 or 3 on that item will be referred to their provider for follow-up. Also, participants who have a total score of 29 or above on their BDI, will be referred to their provider for follow-up. In case of any problem during the experimental session, we will call 911 for any participant who experiences a medical or psychological emergency to ensure the safe transport of the participant to UMMC. Similarly, the MASQ – item 61 asks about "Thought about death or suicide". In case of a positive answer, participants will be referred to their provider for follow-up.

Moreover, the only information that will be shared with the participant is incidental findings from the MRI. They will be referred to their primary care physician for follow up. No additional information will be provided. A copy of the MRI scan on disk can be provided to the participant if they would like it.

ID: VIEW4E02808CBD800
Name: v2_Sharing of Results

HP-00076723 View: v2_Research with Drugs or Biologics

Research with Drugs or Biologics

You indicated on the "Type of Research" page that your study involves use of unapproved drug(s)/biologic(s) or approved drug(s)/biologic(s) whose use is specified in the protocol AND/OR evaluation of food(s) or dietary supplement(s) to diagnose, cure, treat, or mitigate a disease or condition.

1 * List all drugs/biologics to be administered in this study. Be sure to list each drug/biologic with its generic name only.

	Drug Name	FDA Approved	IND Number	PI IND Holder
View	arginine vasopressin	yes		no

2 * Attach the drug package insert or investigational drug brochure for the drugs being administered in this study:

AVP Insert(0.01) 9/1/2017 5:36 PM 9/1/2017 5:36 PM

3 If more than one drug is administered, discuss the risk implications of drug/therapy interactions:

4 * Will you be using Investigational Drug Services?

● **Yes** ○ No

ID: VIEW4E0916E6E1400
Name: v2_Research with Drugs or Biologics

HP-00076723

View: v2_Placebos

Placebos

1

* Is this study placebo controlled?

● **Yes** ○ No

ID: VIEW4E0514EECCC00
Name: v2_Placebos

HP-00076723

View: v2_Placebo Use

Placebo Use

You indicated that this study is placebo-controlled.

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.

1.1 * Justify the use of the placebo study design and how the benefit to society outweighs the risks to the participants:

This study investigates the influence of Arginine Vasopressin on observational learning of placebo analgesia in healthy participants. We need a control group receiving intranasal saline instead of intranasal vasopressin as the comparison between the groups will allow us to assess the effect of vasopressin on observational learning. The risk for the participants randomized into the control group is not larger than the risk of the participants randomized into the vasopressin group, as participants are not in need of medication. Therefore the gain in knowledge about the neural mechanisms of observational learning and the benefits to society outweigh the potential risks to the participants.

1.2 * Is the placebo being used in place of standard therapy?

○ Yes ● **No**

1.3 * Is the standard treatment considered effective?

● **Yes** ○ No

ID: VIEW4E0514D79B400
Name: v2_Placebo Use

HP-00076723

View: v2_Psychological/Behavioral/Educational Methods and Procedures

Psychological/Behavioral/Educational Methods & Procedures

You indicated on the "Type of Research" page that your study involves a psychological/behavioral/educational method or procedure such as a survey, questionnaire, interview, or focus group.

1 * Select all behavioral methods and procedures which apply to this study:

- [x] **Surveys/questionnaires**
- [ ] Key informant or semi-structured individual interviews
- [ ] Focus groups or semi-structured group discussions
- [ ] Audio or video recording/photographing
- [ ] Educational tests or normal educational practices (education instructional strategies, techniques, curricula, or classroom management methods)
- [ ] Individual or group behavioral observations
- [ ] Psychosocial or behavioral interventions
- [x] **Neuropsychological or psychophysiological testing**
- [x] **Deception**
- [ ] Other psychosocial or behavioral procedures

ID: VIEW4E09416F57800
Name: v2_Psychological/Behavioral/Educational Methods and Procedures

HP-00076723 View: v2_Surveys/Questionnaires

Surveys/Questionnaires

You indicated that this study involves surveys and/or questionnaires.

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * List all questionnaires/surveys to be used in the study, including both standardized and non-standardized assessments:

The pain vigilance and awareness questionnaire (PVAQ)
Pain Catastrophizing Scale (PCS)
Fear of Pain Questionnaire (FPQ)
Interpersonal Reactivity Index (IRI)
State and Trait Anxiety Inventory (STAI-Y1 & Y2)
Neuroticism – Extroversion - Openness Inventory (NEO)
Basic Empathy Scale (BES)
Life-Orientation Test-Revisited (Lot-R)
Tridimensional Personality Questionnaire (TPQ)
Sensation Seeking (SS)
Multidimensional Iowa Suggestibility Scale (MISS)
Behavioral Inhibition and Behavioral Activation Scale (BIS/BAS)
Positive and Negative Affective Schedule (PANAS)
Penn State Worry Questionnaire (PSWQ)
Anxiety Sensitivity Index (ASI)
Edinburgh Handedness Inventory (EHI)
Beck Depression Inventory (BDI)
Becks Anxiety Inventory (BAI)
Mood and Anxiety Symptom Questionnaire (MASQ) – short form
Social Desirability Scale (SDS)
Belief about Medicines Questionnaire (BMQ)
Multidimensional Mood State Questionnaire (MDMQ)
Post experimental intrinsic motivation inventory (PEIMI)
Experimenter Rating Scale (ERS)
Demographics questionnaire.
Last Night Sleep questionnaire.

2 * Upload a copy of all questionnaires/surveys:

Name	Created	Modified Date
QuestionnairesVASO.pdf(0.01)	8/31/2017 4:13 PM	8/31/2017 4:13 PM

3 * What is the total length of time that each survey is expected to take?

The pain vigilance and awareness questionnaire (PVAQ) - 2 minutes
Pain Catastrophizing Scale (PCS) - 3 minutes
Fear of Pain Questionnaire (FPQ) - 2 minutes
Interpersonal Reactivity Index (IRI) - 3 minutes
State and Trait Anxiety Inventory (STAI-Y1 & Y2) trait - 2 minutes

Neuroticism – Extroversion - Openness Inventory (NEO) - 4 minutes
Basic Empathy Scale (BES) - 2 minutes
Life-Orientation Test-Revisited (Lot-R) - 1minute
Tridimensional Personality Questionnaire (TPQ) - 5 minutes
Sensation Seeking (SS) - 5 minutes
Multidimensional Iowa Suggestibility Scale (MISS) - 6 minutes
Behavioral Inhibition and Behavioral Activation Scale (BIS/BAS) - 3 minutes
Positive and Negative Affective Schedule (PANAS) - 2 minutes
Penn State Worry Questionnaire (PSWQ) - 2 minutes
Anxiety Sensitivity Index (ASI) - 2 minutes
Edinburgh Handedness Inventory (EHI) - 1 minute
Beck Depression Inventory (BDI) - 4 minutes
Becks Anxiety Inventory (BAI) - 3 minutes
Mood and Anxiety Symptom Questionnaire (MASQ) short - 4 minutes
Social Desirability Scale (SDS) - 4 minutes
Belief about Medicines Questionnaire (BMQ) - 3 minutes
Multidimensional Mood State Questionnaire (MDMQ) - 1 minute
Post experimental intrinsic motivation inventory (PEIMI) - 4 minutes
Experimenter Rating Scale (ERS) – 2 minutes
Demographics questionnaire – 1 minute.
Last Night Sleep questionnaire – 2 minutes.

4 * Are any of the questions likely to cause discomfort in participants or cause harm if their confidentiality were breached? (i.e., Illegal activities)

○ Yes ● **No**

5 * Do any questions elicit information related to the potential for harm to self or others?

● **Yes** ○ No

5.1 If Yes, what procedures are in place to assure safety?

We have 2 questions in our questionnaires which ask for suicidal thoughts:
The BDI II has one question (#9) that asks the participant to rate their feelings of suicidal thoughts or wishes. We will review each participant's BDI form after completion at each study visit to assess whether the participant displays the potential for harm to self or others. Any participant who scores a 2 or 3 on that item will be referred to their provider for follow-up. Also, participants who have a total score of 29 or above on any BDI administration will be referred to their provider for follow-up.

The MASQ – item 61 asks about “Thought about death or suicide”. In case of positive answer, participants will be referred to their provider for follow-up.

If a psychiatric emergency arises because of a verbalization of suicidal idealizations or thoughts, research personal will call 911 to ensure that the participant will safely arrive at a hospital for medical evaluation.

ID: VIEW4E09460F5EC00
Name: v2_Surveys/Questionnaires

HP-00076723 View: v2_Testing

Testing

You indicated that this study involves neuropsychological or psychophysiological testing.

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * List all of the tests to be used in the study, including both standardized and non-standardized assessments:

1. Pain calibration
2. Pain modulation assessment

2 * Describe procedures related to all testing:

1. Pain calibration

The Pain sensitivity assessment will be performed to account for the large variability in pain perception, sensitivity and nociception signaling. An ascending series of stimuli will be delivered.

We will determine a warm perception threshold, a pain perception threshold and a pain tolerance threshold. Each threshold will be determined through a total of four measurements.

An ascending series of stimuli will be delivered starting at a sub-warm threshold, until painful sensations will be induced. Initially stimuli at a very low and usually imperceptible level will be delivered. Next, the trained investigator will increase the intensity of the stimuli in steps until the study participant reaches a threshold, indicated by a level that they felt was "definitely painful, but tolerable". To minimize floor effects by ensuring that this level of stimulation is at least somewhat painful, when this threshold level is reached, the participant will be asked to report their pain sensation on a VAS from 0 ("no pain") to 100 ("worst pain tolerable"). If their reported pain is less than 50 out of 100, then the subject is asked if he would feel comfortable trying a higher intensity, such that the participant pain ratings at the end of calibration is at least 50 out of 100 on a VAS. This procedure has been used several times by the PI and many other labs (Colloca & Benedetti 2006, Colloca & Benedetti 2009, Colloca et al 2010, Colloca et al 2015, Colloca et al 2008, Lui et al 2010).

Thermal pain stimuli are delivered using the Medoc Pathway CHEPS/ATS system, with a 27-mm diameter CHEPS/ATS thermode. There are maximum and minimum temperatures set (heat = 50 degrees Celsius) on the Medoc PATHWAY ATS machine to prevent any tissue damage.

2. Pain modulation assessment

We will use the individually calibrated temperature at VAS 50/100 during the test phase of the experiment. Participants will rate their pain on a VAS from 0 ("no pain") to 100 ("worst pain tolerable"). The distance between the 0 and the middle of the patients mark will be measured and quantified as pain rating. Participant's pain rating will be provided with an fMRI compatible VAS device (see Testing measures, Celeritas® Fiber Optic Response System).

Thermal pain stimuli are delivered using the Medoc Pathway CHEPS/ATS system, with a 27-mm diameter CHEPS/ATS thermode. There are maximum and minimum temperatures set (heat = 50 degrees Celsius) on the Medoc PATHWAY ATS machine to prevent any tissue damage. The PATHWAY system has been used extensively in many research groups in pain research in the MRI, including by one of the co-investigators (Schenk et al., 2014).

3 * Upload relevant testing materials:

Name	Created	Modified Date
Medoc certificate(0.01)	8/31/2017 4:15 PM	8/31/2017 4:15 PM
testing measures(0.01)	8/31/2017 4:15 PM	8/31/2017 4:15 PM

4 * What is the individual duration of each test and what is the entire duration of all tests?

Pain calibration – 20 minutes

Pain perception assessment – 20 minutes

5 * Are any of the questions likely to cause discomfort in participants or cause harm if their confidentiality were breached? (i.e., Illegal activities)

○ Yes ● **No**

6 * Do any questions elicit information related to the potential for harm to self or others?

○ Yes ● **No**

6.1 If Yes, what procedures are in place to assure safety?

ID: VIEW4E0BC1E3C2800
Name: v2_Testing

HP-00076723

View: v2_Deception

Deception

You indicated that this study involves deception.

1 * Indicate why deception is the only feasible means of conducting the research. Include information about the likely characteristics and cultural values of the participants that contribute to the justification for using deception:

Placebo research involves elements of deception (Miller et al., 2005; Miller, 2008; Miller and Kaptchuk, 2008; O'Neil and Miller, 2009). It consists of deliberately communicating misleading information about the goal of the research study and the nature of experimental procedures. Deception in placebo research is adopted to create expectations of pain intensity increases and decreases. Thus, the present study complies with the American Psychological Association (APA, 2010 par. 8.07 ref. 39) guidelines for the use of deception in research. It should also be noted that this study goes beyond the APA guidelines in using an "authorized deception" approach as detailed below.

2 * Describe the manner in which the participants are being deceived. Specify the information that will be withheld from the participants or the misinformation that will be provided to them:

Specifically, we use deception to make participants believe that a certain cream is an analgesic treatment. During the observational phase, a demonstrator rates the pain low after heat pain stimulation on one of the sites where cream was applied (placebo run) while he rates the pain high after heat pain stimulation on the other site where cream was applied (control run). Therefore the participants are made to believe that one of the creams has an analgesic effect, while the other has no effect. However, both creams are inert and have no analgesic properties. The effect of their expectation is then tested in the test phase.
Participants will be informed about this surreptitious change at the end of their participation in the debriefing and they will complete an exit form (see below) which will provide them the opportunity to withdraw their data from the study.

3 * Provide the rationale/justification for the deception:

Deception is needed for creating expectations of benefit/worsening of pain and it is an essential part of conducting this kind of research (Miller, 2008). Importantly several authors have created elegant normative work as well as empirical results on the use of deception in placebo research and pain. For example, Martin and Katz (Martin and Katz, 2010) tested the inclusion of authorized deception in the informed consent process by randomly assigning participants to an authorized deception group or a deception group without authorized deception. Interestingly, the authors found that authorized deception did not influence the size of placebo-induced placebo analgesia, recruitment, and retention of participants. Martin and Katz found that informing participants about the nature of the placebo manipulation does not cause distress and lack of trust in research (Martin and Katz, 2010).

4 * Will confederates be used?

○ Yes ● **No**

5 * Detail the elements of deception that are incorporated into the informed consent process and document:

Participants are not told in the consent - Experimental phase– that during the testing phase, all the painful stimulations are delivered at the same, medium level. However, in the consent form they are informed that this research involves some deceptive elements as follow:

Consent form (page 4): Use of Deception - At some point during the study, we will provide you with misleading information. After the study is completed we will give you a written explanation on how the information was not true and why. We will also answer any questions that you have about the procedure and the use of any misleading information.

Importantly, participants will be also informed during the debriefing process and offered to withdraw the data from the study if they feel uncomfortable with continuing their study participation. We have developed (Miller and Kaptchuk, 2008) and tested at the National Institutes of Health (Colloca et al., 2015) the so-called 'authorized deception approach' in which participants are informed about the use of deception in the consent form and are fully debriefed at the end of the study (Miller et al., 2008).

6 * Is the research likely to produce psychological discomfort or negative feelings in the participants?

◯ Yes ● **No**

6.1 If Yes, describe the arrangements made to provide professional counseling or support resources to any participants requiring such assistance following their participation in the study:

7 * Will the participants be required to decieve others?

◯ Yes ● **No**

8 * Will the participants be debriefed?

● **Yes** ◯ No

8.1 If Yes, describe the debriefing process:

Each participant will receive a written debriefing form (see attachment) reporting what was not described truthfully at the beginning of her/his participation. The investigator will: 1. provide a rationale for deception, 2. answer any questions about the study and 3. offer participants the opportunity to withdraw their data.

Upload a copy of the debriefing script:

Name	Created	Modified Date
Debriefing_vaso_v1_upload.docx(0.01)	8/31/2017 4:17 PM	8/31/2017 4:17 PM

8.2 If No, justify why the deception will not be disclosed/explained to the participants at the conclusion of the study:

9 * Describe the additional training and qualifications of the research staff who are involved in the deception process and the debriefing:

The PI published several empirical and normative works (Brody et al., 2012; Miller and Colloca, 2011, 2009) in this area and has trained NIH and UMD students and collaborators to debrief participants appropriately.

ID: VIEW4E0BC39027000
Name: v2_Deception

HP-00076723

View: v2_Sample Collection/Analysis

Sample Collection/Analysis

You indicated on the "Type of Research" page that your study involves a sample (specimen) collection and/or analysis.

1 * What type of samples will be involved in this study? (Check all that apply)

- [x] **Prospective (will be collected)**
- [ ] Existing (previously collected at the time of initial IRB submission)

2 * Will genetic analysis/testing be done on any of the samples?

● **Yes** ○ No

3 * Will this study involve banking of samples (storing for future research use)?

● **Yes** ○ No

4 * What is the purpose of the sample collection and/or analysis?

Saliva samples will be stored for future genetic analyses. Saliva samples for DNA extraction will be collected and stored at -20°C at the School of Nursing, floor 7, Dr. Colloca lab. All stored samples will be coded so that when sent for measurements the identity of each participant remains confidential.
Urine samples will only be collected for the drug and pregnancy tests and will be destroyed afterwards.

5 * Is there the possibility that cell lines will be developed with any of the samples?

○ Yes ● **No**

6 * Will the samples be released to anyone not listed as an investigator on the protocol?

● **Yes** ○ No

6.1 If Yes, give name(s) and affiliation(s):

Dr. David Goldman, Laboratory of Neurogenetics, National Institute on Alcohol Abuse and Alcoholism (NIAAA), Rockville, Maryland for DNA extraction and Drs Nicholas Ambulos and Braxton D. Mitchell, University of Maryland School of Medicine for data analyses who have an active collaboration with the PI.

7 * Will the sample material be sold or given to any third parties?

◯ Yes ● **No**

7.1 If Yes, give name(s) and address(es):

ID: VIEW4E0E1A4B80000
Name: v2_Sample Collection/Analysis

HP-00076723

View: v2_Prospective Samples

Prospective Samples

You indicated that the study involves collection of prospective samples (specimens).

1 * What type of sample will be collected? (Check all that apply)

- [ ] Blood
- [ ] Bone Marrow Aspirate/Biopsy
- [ ] Cerebrospinal Fluid
- [x] **Saliva**
- [ ] Skin
- [ ] Sputum
- [ ] Stool
- [ ] Tissue
- [ ] Tumor
- [x] **Urine**
- [ ] Other

1.1 If Other, specify:

2 For blood draws, specify the amount drawn, in teaspoons, at each visit and across the course of the subject's entire participation time:

3 * What type of samples will be collected? (Check all that apply)

- [x] **Samples obtained specifically for research purposes-obtained via a separate collection procedure done solely for the purposes of the study**
- [ ] Samples obtained specifically for research purposes-additional taken during a clinical procedure
- [ ] Leftover samples that were obtained for clinical purposes (no additional research procedures required)
- [ ] Commercial (for profit) samples

☐ Other

3.1 If Other, specify:

4 * How are these samples labeled? For example, do they contain name, initials, dates, Social Security number, medical record number, or other unique code?

All stored saliva samples will be anonymized and coded with letters and numbers (e.g. SON001) including the subject identification number.
Urine samples and drug testing kits will be destroyed after yielding the results.

5 * Will sample(s) be made available to the research subject (or his/her medical doctor) for other testing?

○ Yes ● **No**

6 * If a participant withdraws from the study, will that participant have the option to get the remaining portion of their sample(s) back?

○ Yes ● **No**

7 * If the participant withdraws, explain how their sample(s) will be handled (For example, will sample(s) be destroyed, anonymized, etc.):

If participant withdraws, all samples will be destroyed. However, any information gained from the sample that has been collected up until that point will be retained. Any participant can ask to have their sample destroyed at any time. This procedure will be clearly outlined in the informed consent process.

8 * Will the samples be destroyed after the study is over?

○ Yes ● **No**

8.1 If No, describe how the samples will be stored, where they will be stored, and for how long.

Urine samples and drug testing kits will be destroyed after yielding the results.
Saliva samples will be stored for future genetic analyses. Saliva samples for DNA extraction will be collected and stored at -20°C at the School of Nursing, floor 7, Dr. Colloca lab. All stored samples will be coded so that when sent for measurements the identity of each participant remains confidential.
There is no limit to the length of time we will store participant samples and information. We may continue using it or research unless we stop all research. However, participants can ask to have their samples destroyed at any time and no further research will be conducted on their sample.

ID: VIEW4E0E257D60C00
Name: v2_Prospective Samples

HP-00076723

View: v2_Genetics Research

Genetics Research

You indicated that genetic analysis/testing is being done on the samples.

1 * How would you classify your genetic study? (choose all that apply)

- [ ] Gene Transfer
- [ ] Pedigree Study (to discover the pattern of inheritance of a disease and to catalog the range of symptoms)
- [ ] Positional cloning (to localize and identify specific genes)
- [ ] DNA diagnostic study (to develop techniques for determining the presence of specific DNA mutations or polymorphisms)
- [x] **Other**

1.1 If Other, specify:
genetic association study (e.g. GWAS)

2 * Discuss the potential for psychological, social, and/or physical harm that could result from participation in this research. In your discussion, consider the following aspects: risks to privacy, confidentiality, insurablity, employability, immigration status, paternity status, educational opportunities, or social stigma.
Risks associated with DNA analysis:
All genetic information will be kept confidential to the greatest extent possible. The genetic testing performed in this study is done for research purposes only. Participants will be informed that the DNA testing will not provide any information about their health or ancestry and that it is our policy not to provide the results of such genetic testing.

3 * Will subjects receive any information resulting from the genetic analysis?

- ○ Yes
- ● **No**

3.1 If Yes, describe the information that subjects will receive:
Please note: genetic analysis results should only be shared if the testing will be performed in a CLIA certified lab.

4 * Will participants be offered any type of genetic or educational counseling?

- ○ Yes
- ● **No**

4.1 If Yes, who will provide the education or counseling?

4.2 Under what conditions will education or counseling be provided?

5 * Is there the possibility that a family's pedigree will be presented or published?

◯ Yes ● **No**

5.1 If Yes, describe how you will protect family members' confidentiality:

ID: VIEW4E0E7C50FBC00
Name: v2_Genetics Research

HP-00076723

View: v2_Sample Banking

Sample Banking

You indicated that the study involves banking of samples (storing for future research use).

1 * Where will the sample(s) be banked? (If this study involves the VA, please state the name of the registry/repository and the CICERO protocol number is was approved under.)
Saliva samples for DNA extraction will be collected and banked at -20°C at the School of Nursing, University of Maryland, floor 7, Dr. Colloca lab. All stored samples will be coded so that when sent for measurements the identity of each participant remains confidential.

2 * Does the banking institution have an approved policy for the distribution of samples?
○ Yes ● **No**

3 How long will the sample(s) be kept?
There is no limit on the length of time we will store the sample and information. We may continue using it for research unless the participant decides to stop taking part or we stop all research. However, the participant can ask to have his/her sample destroyed at any time and no further research will be conducted on that sample.

4 * Will sample(s) be made available to the research subject (or his/her medical doctor) for other testing?
○ Yes ● **No**

5 * If a participant withdraws from the study, will that participant have the option to get the remaining portion of their sample(s) back?
○ Yes ● **No**

6 * If the participant withdraws, explain how their sample(s) will be handled (For example, will sample(s) be destroyed, anonymized, etc.):
If a participant withdraws, their sample will be destroyed.

7 * If the participant withdraws, explain how the data obtained from their sample(s) will be handled (e.g., will it be deleted?) ***(Please note that data for FDA regulated research cannot be deleted):***
If a participant withdraws, their sample will be destroyed. However, any information from that sample that has been collected up until that point will be retained.

ID: VIEW4E0E7E82B5800
Name: v2_Sample Banking

HP-00076723

View: v2_Data Collection / Record Review

Data Collection/Record Review

You indicated on the "Type of Research" page that your study involves data collection or record review (i.e., chart review, not self-report).

1 * What type of data will be collected/analyzed in this study? (Check all that apply)

- ☐ Retrospective/Secondary Analysis (data has already been collected at the time of initial IRB submission)
- ☑ **Prospective (data is not yet in existence and/or collected)**

2 * Will this study involve adding data to a registry or database for future use?

○ Yes ● **No**

3 * Will the data be released to anyone not listed as an investigator on the protocol?

○ Yes ● **No**

3.1 If Yes, give name(s) & affiliation(s):

ID: VIEW4E0E25A8CA400
Name: v2_Data Collection / Record Review

HP-00076723

View: v2_Prospective Data

Prospective Data

You indicated that the study involves the collection of prospective data.

1 * Where is the data being collected from? (Check all that apply)

- [ ] Medical records
- [ ] Medical images
- [ ] Commercial (for profit) entity
- [ ] Publicly available records
- [ ] Schools
- [x] **Other**

1.1 If Other, please specify:
current experiment

2 * What data fields will you have access to/collect for the study? For example, name, initials, date of birth, Social Security number, income, demographic information, family units, housing, etc.
We added a CRF with the collected information during the study. We will collect information about the name and Social Security Number for payment purposes. We will also collect basic demographic data for data analysis.

You can also upload a copy of the data fields/variables to be collected for the study:

Name	Created	Modified Date
CRF_Vasov1.5 AMD4(0.02)	6/18/2019 12:32 PM	9/20/2019 3:36 PM
CRF_Vaso_EEG(0.01)	10/22/2018 3:49 PM	10/22/2018 3:49 PM
CRF_Vaso_v1.1_upload.doc(0.01)	8/31/2017 4:26 PM	8/31/2017 4:26 PM

ID: VIEW4E0E25B643800
Name: v2_Prospective Data

HP-00076723

View: v2_Clinical Trial Registration

Clinical Trial Registration

You indicated on the "Type of Research" page that your study is a clinical trial.

1 * Does the UM Clinical Trials Registry policy require registration of this trial?

● **Yes** ○ No

2 * Has this trial been registered?

● **Yes** ○ No

ID: VIEW4E093BF078C00
Name: v2_Clinical Trial Registration

HP-00076723

View: v2_Clinical Trial Registration Information

Clinical Trial Registration Information

You indicated that this clinical trial has been registered.

1 * Was this trial registered at www.clinicaltrials.gov?

● **Yes** ○ No

2 If no, was this trial registered on a site other than clinicaltrials.gov?

○ Yes ○ No

2.1 If Yes, specify the name of the other site:

2.2 Provide justification for registering this trial on this site:

3 * Registration Number

NCT03446456

ID: VIEW4E093BF1D0800
Name: v2_Clinical Trial Registration Information

HP-00076723

View: v2_Participant Selection

Participant Selection

1 * How many local potential participants (or specimens/charts) do you anticipate will be screened for this study? ***Screening includes determining potential participants' initial eligibility for and/or interest in a study.***

600

2 * How many participants (or specimens, or charts) will be enrolled/used for this study? ***A local prospective participant is considered enrolled in the study when a UM-approved Informed Consent Document (not including separate screening consent forms) is signed.***

Local - the number being enrolled at this site:

244

Worldwide - the number being enrolled total at all sites (including local enrollment):

244

3 * Gender:

- [x] **Male**
- [x] **Female**

4 * Age(s):

- [ ] 0 to 27 days (newborn infants)
- [ ] 28 days to 12 months (Infant)
- [ ] 13 months to 23 months (Toddler)
- [ ] 2 to 5 years (Preschool)
- [ ] 6 to 11 years (Child)
- [ ] 12 to 17 (Adolescents)
- [x] **18 to 88 years (Adult)**
- [ ] 89 years and older

5 * Race/Ethnicity:

- [x] **All Races Included**
- [ ] American Indian or Alaskan Native
- [ ] Asian/Other Asian
- [ ] Asian/Vietnamese
- [ ] Black or African American
- [ ] Hispanic or Latino
- [ ] Mixed Race or Ethnicity
- [ ] Native Hawaiian or Pacific Islander
- [ ] White or Caucasian

6

* Language(s):

- [x] **English**
- [ ] Chinese
- [ ] French
- [ ] Italian
- [ ] Japanese
- [ ] Korean
- [ ] Local Dialect
- [ ] Spanish
- [ ] Vietnamese
- [ ] Other

6.1 Specify Other:

7

* Are you excluding a specific population, sub-group, or class?

◯ Yes ● **No**

7.1

If Yes, indicate your justification for excluding a specific population, sub-group, class, etc.:

ID: VIEW4E0E519C1D000
Name: v2_Participant Selection

HP-00076723

View: v2_Vulnerable Populations

Vulnerable Populations

1 * Will you be targeting ANY of the following Vulnerable Populations for enrollment? (Select all that apply)

- [x] **Employees or Lab Personnel**
- [ ] Children (Minors)
- [ ] Cognitively Impaired/ Impaired Decision Making Capacity
- [ ] Pregnant Women/Fetuses
- [ ] Wards of the State
- [x] **Students**
- [ ] Prisoners
- [ ] Nonviable Neonates or Neonates of Uncertain Viability
- [ ] Economically/Educationally Disadvantaged
- [ ] None of the above

Only select populations which you will be targeting for enrollment. Do not include populations that may be enrolled incidentally. Enrollment of a vulnerable population is considered to be "targeted" if the study team will be aware that a subject is from a vulnerable group as a result of interaction with the subject or collection of specific information about the subject, and the research team does not wish to exclude them. "Incidental" enrollment is limited to situations where a study team is unaware that a subject is from a vulnerable group.

ID: VIEW4E0E519917800
Name: v2_Vulnerable Populations

HP-00076723

View: v2_Vulnerable Populations - Employees or Lab Personnel

Vulnerable Populations - Employees or Lab Personnel

You indicated that employees or lab personnel are included in this study.

1 * Describe how you will ensure particiption in this research will not affect employment and prevent undue influence:

We will include UMB employees in the recruitment. Current personnel of the PI or the Department of Pain and Translational Symptom Science will not be recruited. The participation will be voluntary without any obligation or requirement associated with the performance of regular job-related activities. Employment status will not be affected by electing to participate or by choosing not to participate. Drug test results will not be maintained and results will never be part of the permanent medical records of the individuals.

ID: VIEW4E0E5192BA800
Name: v2_Vulnerable Populations - Employees or Lab Personnel

HP-00076723

View: v2_Vulnerable Populations - Students

Vulnerable Populations - Students

You indicated that students are included in this study.

1 * Describe the types of students that are included in this study:

Undergraduate and graduate students will be recruited. Students are encouraged to seek their mentor's approval. Drug test results will not be maintained and results will never be part of the permanent medical records of the individuals. Academic status will not be affected by electing to participate or by choosing not to participate.

2 * Describe how you will prevent undue influence.

Care should be taken to eliminate or reduce the risk that undue influence by faculty or coercion that affects student participation in research. Students may feel compelled to participate, believing that failure to do so will negatively affect their grades and the attitude of the investigator and other students toward them. For this reason, the PI investigator will not include her students as subjects in the investigator's research. Although students often provide a ready source of potential participants, they are not always an appropriate or representative study sample, as compared to other subject pools. Attention should be given to whether they are being solicited because they are a convenient and accessible sample, rather than as a representative sample for the research inquiry. Therefore, we will also recruit from the general local population and the local Universities.

ID: VIEW4E0E519F32000
Name: v2_Vulnerable Populations - Students

HP-00076723 View: v2_Eligibility

Eligibility

1 * Do you have an existing Eligibility checklist(s) for this study?

● **Yes** ○ No

1.1 If Yes, upload here. If you need a template, you can download it by clicking **HERE**. The checklists you upload will also be available under the Documents tab of this application.

Name	Created	Modified Date
Eligibility_fMRI_clean(0.01)	10/26/2018 11:05 AM	10/26/2018 11:05 AM
Eligibility_fMRI_trackmode changes(0.02)	10/22/2018 4:29 PM	10/26/2018 11:01 AM
Eligibility Checklist_EEG_Vaso(0.05)	10/22/2018 3:51 PM	10/26/2018 10:59 AM
Eligibility Checklist_vaso.doc(0.07)	8/31/2017 4:30 PM	2/21/2018 2:25 PM
MRI Eligibility Checklist(0.01)	8/31/2017 4:31 PM	8/31/2017 4:31 PM

1.2 If No, create an eligibility checklist below:

List inclusion criteria (List each Inclusion Criteria individually, using the ADD button):

Number	Criteria
There are no items to display	

List exclusion criteria (List each Exclusion Criteria individually, using the ADD button):

Number	Criteria
There are no items to display	

After entering the inclusion and exclusion criteria above, click the Save link. CICERO will automatically generate a printable Eligibility Checklist for you to use in your research. To review the checklist, click on the resulting link below. This checklist is also available under the Documents tab of this application.

Eligibility Checklist for HP-00076723_2 v10-26-2018-1540566329323(0.01)

ID: VIEW4E0E5185F9000
Name: v2_Eligibility

HP-00076723 View: v2_Recruitment

Recruitment

1 * Describe plans for recruitment, including the identification of potential participants (or acquisition of charts/records/samples) and initial interactions with them: (If this study involves the VA please list all sites at which recruitment will take place.):

Participants will become aware of the study through a variety of methods:
1. paper and electronic flyers (see attached flyers) posted at university and college campuses (e.g. University of Maryland, Baltimore (UMB), University of Maryland, Baltimore County (UMBC), University of Maryland, College Park (UMCP), Johns Hopkins, University of Baltimore (UB), Community College of Baltimore County, Notre Dame, Loyola, MICA, Morgan State, Catonsville Community College, Towson University, and Coppin State) and surrounding areas, as well as student list servers across the campus (e.g. Elm, Dental Digest).
2. Advertising in newspapers (e.g. The Baltimore Sun);
3. Postings in Craigslist, participant recruitment websites such as Just Another Lab Rat, and similar online recruitment resources.
4. Reaching out to local Blogs and Archives;
5. Posting flyers at local businesses, including at restaurants and stores that have public bulletins or grant permission to us to post about our study;
6. Advertising on public transportation, including the circulator, University of Maryland shuttle, and Baltimore public transportation (busses and trains etc.);
7. Advertising on the UMB CACPR.
8. Participants may also be contacted by word of mouth and by asking participants if they are aware of anyone else who would be interested in participating in the study.
9. Advertising on social media such as Twitter, Instagram and Facebook. A CollocaLab page will be created;
10. Recruit participants for the study at academic fairs, music and arts festivals, “tabling,” health fairs, etc. We will be present to provide information about the study. We request permission to contact the organizers of the event to include approved advertisements in brochures/handouts for the event and be present in case people are interested in learning more about this research initiative.

Contact information (office email and phone number) for the Research Coordinator will be included on these advertisement and those interested in participating will be asked to use this information to contact the research staff if interested in participating. The potential participant and Research Coordinator will set up a time for a telephone screening (~15 minutes) in which potential participants will be told more about the study, what is expected from them, and it will be determined if they meet exclusionary criteria (see attached Phone script). If the individual is interested in participating and does not meet exclusionary criteria, they will be identified as a potential participant and a time for them to participate for one session will be scheduled. The potential participant will have ample opportunity to ask any questions before and after scheduling an appointment. The potential participants scheduled to participate will be emailed/ mailed directions to UMSON and their appointment date and time will be written. No charts/records/samples will be collected for this project.

2 * Describe measures that will be implemented to avoid participant coercion or undue influence (if not applicable to the study, enter "N/A"):

Participants will not be paid for the initial screening over the telephone (takes only 15 minutes), so no potential participant will be coerced to participant because of financial gain. Participants will be paid to participate in the study at the UMSON, however their payment will be a minimal amount that is standard to give at the SON for a one time study session in order to avoid coercion. Voluntary participation will be emphasized during recruitment and consent procedures.

3 * Who will recruit participants (or acquire charts/records/samples) for this study? (Check all that apply)

- [x] **PI**
- [x] **Study Staff**
- [ ] Third Party

3.1 If you are using a third party, specify Third Party Recruiters:

4 Upload any recruitment tools such as screening/telephone scripts and introductory letters (do not upload advertisements here):

Name	Created	Modified Date
PhoneScreening_VasoEEG v1.5 AMD3(0.01)	6/18/2019 12:41 PM	6/18/2019 12:41 PM
Phone_Screening_Vaso_EEG(0.01)	10/22/2018 3:52 PM	10/22/2018 3:52 PM
Phone_Screening_Script_vaso_v1.3_upload.docx(0.01)	8/31/2017 4:32 PM	8/31/2017 4:32 PM

ID: VIEW4E0BCAA0A6C00
Name: v2_Recruitment

HP-00076723

View: v2_Advertising

Advertising

1 * Will you be using advertisements to recruit potential participants?

● **Yes** ○ No

ID: VIEW4E0BCCF811000
Name: v2_Advertising

HP-00076723 View: v2_Advertising Detail

Advertising Detail

You indicated that you will be using advertisements to recruit potential participants.

1.1 * Select the mode(s) of advertising (check all that apply):

- [ ] Radio
- [x] **Internet**
- [ ] Print
- [ ] Television
- [x] **Other**

1.1.1 If Other, specify:
Posted flyers

1.2 * Provide exact text of all proposed advertisement(s):
Healthy Participants Needed
Research Study: Vasopressin and Pain in the Brain
The study investigates how vasopressin and pain is processed in the brain. Two visits are required (2-3 and 3-4 hours).
The second visit will involve magnetic resonance imaging (MRI) to investigate brain processes.
You may qualify if:
You are 18-55 years of age
You are fluent in written and spoken English
You are in good health
Compensation for both sessions and parking vouchers are provided
Contact:
Email: NRSCollocaLab@umaryland.edu
Telephone: 410-706-5975

Healthy Participants Needed
Research Study: Vasopressin and Pain in the Brain
The study investigates how vasopressin and pain are processed in the brain. One visit is required (Approx. 4 hours).
will involve Electro-encephalography (EEG) to investigate brain processes.
You may qualify if:
You are 18-55 years of age
You are fluent in written and spoken English
You are in good health
Compensation for both sessions and parking vouchers are provided
Contact:
Email: NRSCollocaLab@umaryland.edu

Telephone: 410-706-5975

1.3 * Upload advertisement(s) here:

Name	Created	Modified Date
Flyerfull_Vaso_EEG(0.01)	10/22/2018 3:54 PM	10/22/2018 3:54 PM
Flyerssmall_Vaso_EEG(0.01)	10/22/2018 3:52 PM	10/22/2018 3:52 PM
small flyers(0.01)	8/31/2017 4:34 PM	8/31/2017 4:34 PM
flyer full page(0.01)	8/31/2017 4:34 PM	8/31/2017 4:34 PM

ID: VIEW4E0BCE82B8C00
Name: v2_Advertising Detail

HP-00076723

View: v2_Research Related Risks

Research Related Risks

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.

1 * Individually list each research-related risk, using a separate line for each. Next to each risk, delineate the likelihood/seriousness of the risk, and the provisions for minimizing the risk:

Risks associated with the thermal stimulation:
The thermode is placed on the patient's skin to induce experimental pain by warming the area of the skin. Participants respond to the temperature stimuli by pushing a button. Sensory and pain threshold will be recorded. During pain threshold calibration, participants can stop the stimulation by pressing a button. This procedure has been extensively applied to test pain perception and has been used by other researchers working in the field of pain (Eippert et al., 2009; Wager et al., 2004).
Adverse Reaction such as skin irritation (in addition to pain sensation) beneath the thermode has been commonly observed at verycan be observed at very high temperatures with the use of a thermodestimulator, which was based on similar technology as the Pathway ATS device. We will not use temperature in such a range. We have already studied more than 70 350 participants here at the SON as well as more than 100 at NIH and we observed skin redness in <5% of the cases. The redness goes away spontaneously in less than one hour and without any consequences. The probe will be moved between runs to minimize redness. There are several safety mechanisms (hardware and software) in the Pathway System in place to avoid burning the skin of a participant. We have studied at UMB more than 450 participants and did not have any case of burning. The thermode is used in many pain research groups around the world and no burns have been reported with the pathway system. The equipment is FDA approved and the letter from the Medoc Company has been uploaded under testing materials.

Precautions: We will use the thermode under the suggested operational precautions. The computer that is used to operate the PATHWAY system must never be connected to network while it is used for running tests.
Risk of thermal stimulator malfunction: The Pathway thermal stimulation equipment will be maintained exactly as specified by the manufacturer, and will be operated and monitored by trained personnel. Participants will be instructed to pull the stimulator off their arm in the unlikely event that the pain becomes too intense to tolerate. The manufacturer (Medoc, Inc.) has recently added enhanced hardware safety mechanisms to the equipment (see below). These procedures are expected to be highly effective in ensuring minimal risk to participants.

Temperature Safety Mechanisms: The company has implemented several safety mechanisms in the system to safeguard against extreme temperatures.
These safety mechanisms include:
1. a software program that stops the heating when the temperature reaches limit;
2. a software program that halts the heating or cooling in the thermode;
3. a hardware mechanism that overrides the software if the temperature reaches 50°C.

Risk associated with AVP:
AVP is a hormone naturally produced in the brain. It is usually given in a disease called diabetes insipidus in which the hormone is not produced by the body. In our study we use an intranasal spray of arginine AVP. Participants may experience some side effects which last only a short time. Possible side effects are increased heart rate, fatigue, and weakness. Side effects of AVP when given orally include headache, tremor, nausea, nasal congestion, a runny nose, flushing, stomach cramps, palpitations, increased blood pressure, nosebleeds, sore throat, cough and upper respiratory infections. When vasopressin is given intranasally the systemic adverse events are minimized. However, intranasal AVP may increase fear and agitation. The effects of AVP are usually mild and last only a short time. Finally, there is a very small chance for allergic reaction.
Participants will be excluded if they have a history of angioedema, high blood pressure (above 140 mmHg) or symptomatic low blood pressure or a history of fainting.
During the experimental session, participants will be told to inform a staff member if they note the occurrence of some of the listed side effects or any kind of discomfort during the participation in this research. Participants will be monitored for 3 hours after the application of vasopressin to make sure that assistance is present in case of unexpected side effects. They will also be provided a phone number to call in case they experience discomfort after they leave CTRIM.
During the second visit when the AVP is administered, the PI (medical doctor by training) and a medical doctor from UMB will be available for medical advice. There will also always be a dedicated certified nurse or a medical doctor available who is part of our protocol within 5-10 minutes of the CTRIM center. In case of an urgent medical emergency, 911 will be called for immediate medical assistance. In case of serious adverse events (SAEs), the PI will also contact the pharmacy to know the drug allocation and report an SAE.

Risks associated with data confidentiality:

There is a minimal risk for a breach of confidentially of data. However, participant identifying numbers (PID#) will be used instead of personally identifiable information on all paper and electronic documents.
All documents will be stored in a locked cabinet in the PI's office. Electronic data will be password protected and accessible to designated research personnel. This risk is unlikely to occur because adequate mentorship and training is provided.

Risk associated with breach of privacy:
There is a minimal risk for breach of privacy. However, to minimize this, participants will be accommodated in a separate room to be screened and to let them the time to read the consent form and complete the questionnaires. This solution let participants the possibility to ask any explanation to the experimenter and decide to participate or not in the study research without breaching their privacy.

Risks associated with psychological questionnaires:
There is a possibility that a participant could become emotional distressed or fatigued while completing questionnaires and other parts of the study. Participants will be told that they are not required to answer any questions that make them feel emotionally distressed. If a participant reports distress, the PI will be notified and a psychological, psychiatric, or appropriate referral will be made if needed. If a psychiatric emergency arises because of a verbalization of suicidal ideations or thoughts, research personal will call 911 to ensure that the participant will safely arrive at a hospital for medical evaluation. In order to minimize fatigue, participants will be offered breaks throughout the study procedure and participants can discontinue their participation at any time and are not required to provide a reason. All potential risks will be clearly delineated and verbalized to the participant during the informed consent form procedure. We used this set of questionnaires in more than 200 healthy participants and never observed distress and / or uncomfortable reactions.

Risks associated with DNA analysis:
All genetic information will be kept confidential to the greatest extent possible. The genetic testing performed in this study is done for research purposes only. Participants will be informed that the DNA testing will not provide any information about their health or ancestry and that it is our policy not to provide the results of such genetic testing.

Risks Associated with Saliva Collection:
There are no known risks associated with the collection of saliva other than the participant may experience some discomfort from being asked to salivate.

Risks associated with MRI:
MRI uses powerful magnetic fields and weak electromagnetic radiation (radiowaves) which have not been associated with side effects in patients studied under conditions used in clinical imaging. The feeling of being isolated or confined by the scanner may cause some patients to request that the study be stopped, and it is to be expected that some patients will be unwilling to participate or will need to stop the study participation. We will minimize these problems by explaining the procedure and by maintaining voice contact with the subject in each experimental phase. Participants will be given a squeeze ball that activates an alarm in case of emergency or to notify staff if they are feeling any discomfort in the scanner or if they are unable to complete the study (see MRI Guide).

Moreover, there are risks for injury from the MRI magnet. 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 become harmful for study participants being scanned. Welders and metal workers are also at risk for injury because of possible small metal fragments in the eye of which study participants may be unaware. To minimize these risks, we will screen study participants for Phase II using the MRI screening form (see attachment under Eligibility section). Moreover, trained personnel will double-check these conditions before having any scan, and if participants have any, they will not receive the MRI scan. In addition, all magnetic objects (for example, watches, coins, jewelry, and credit cards) will be removed before entering the MRI scan room. Also, it is not known if MRI is completely safe for a developing fetus. Therefore, all women of childbearing potential will have a pregnancy test performed no more than 24 hours before each MRI scan. The scan will not be done if the pregnancy test is positive.

Risks Associated with EEG:
From wearing the EEG cap, participants may experience slight sensations as the scalp is lightly rubbed at the recording sites. Also, a small number of people may be allergic to the conducting gel and/or adhesive used to attach the other sensors on the skin, but this is rare. Participants may experience irritation in the area where we place the sensor electrodes. Lastly, participants may experience a temporary redness of the skin around the areas where sensor electrodes are placed and, this typically goes away within an hour or so.

Risks associated with deception:
In general deception may cause:
1. Infringement of the autonomy of research subjects
2. Distress and lack of trust in research

3. Negative emotional reactions

In our case, risk 1 is sensitively minimized when prospective subjects are given an “authorized deception” disclosure that alerts them to the use of deception in the research during the informed consent process. We inform research participants about the use of deception, the fact they have the opportunity to decline to participate, and that they will learn the specific nature of deception at the end of their study participation. As to risk 2 and 3, revealing the truth about the study during the debriefing process may potentially result in participant’s distress who can be upset at learning how they were deceived. However, based on literature on deception in placebo research and our experience, no lack of trust in research, no negative reactions or lasting negative consequences from learning the details regarding the use of deception have been observed.
These risks are unlikely to be observed. In our experience, participants showed interests in being informed about the final results of the research but did not complain about the nature of the deception and the need for using it to investigate the role of expectancies.

Unknown Risks:
There may be unknown risks or discomforts involved with participating in this study that are not yet known. Research study staff will update participants in a timely manner if any information related to this study surfaces that could impact a participant’s health, welfare, and decision to remain in the study.

ID: VIEW4E1B52509F000
Name: v2_Research Related Risks

HP-00076723

View: v2_Potential Benefits and Alternatives

Potential Benefits and Alternatives

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Describe the potential direct benefit(s) to participants:
Participants will not directly benefit from participating in this study.

2 * Describe the importance of the knowledge expected to result from the study:
This research will provide important knowledge about how AVP modulates observational learning and pain, which is critical for improving the social context of treatments. This research might inform future approaches on how AVP and the social treatment context can benefit patients.

3 * Describe how the potential risks to participants are reasonable in relationship to the potential benefits:
The long term benefits of this research are to improve the therapeutic context for patients, thereby increasing therapy efficiency. The risks to the participants in this study are low, therefore there is a net advantage in performing this research.

4 * Describe the alternatives to participation in this study. If there are no alternatives, state that participation is voluntary and the alternative is not to participate. For intervention studies, describe appropriate alternative clinical procedures or courses of treatment available to subjects.
The participation is voluntary and the alternative is not to participate.

ID: VIEW4E1B5251B0400
Name: v2_Potential Benefits and Alternatives

HP-00076723

View: v2_Withdrawal of Participants

Withdrawal of Participants

If the questions below are not applicable to the research (i.e., chart review), enter "N/A".

1 * Describe anticipated circumstances under which subjects will be withdrawn from the research without their agreement:

There may be circumstances under which the participant may need to withdraw from the research without agreeing to it. Such cases include:
a. Participants who do not follow instructions given by team members.
b. Participants who are not able to perform the tasks described in the protocol.
c. Participants who repeatedly miss appointments.

2 * Describe procedures for orderly termination:

Orderly termination of the study will occur as the end of the investigation is reached and data analysis is complete.

3 * Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection:

If partial withdrawal from procedures is desired by the participant, the PI will make a decision about whether the data can still be used or whether to censor the data from further analysis.

ID: VIEW4E1B52531F800
Name: v2_Withdrawal of Participants

HP-00076723

View: v2_Privacy of Participants

Privacy of Participants

If the study does not involve interaction with participants, answer "N/A" to the questions below.

1 * Describe how you will ensure the privacy of potential participants throughout the study ***(privacy refers to persons and their interest in controlling access to themselves):***

To ensure participant privacy, participants will be able to choose a time that is suitable to discuss the study over the telephone. While the participants are in the UMSON clinical suites, study personnel will make sure others on the floor do not associate with participants of the research study. When any participant completes forms or any part of the study, this will be done in a separate exam room in the UMSON and UMSOM suites.

2 * Describe the location where potential participants will receive research information and detail the specific actions the study team will take to ensure adequate privacy areas:

Participants will first receive information about the study only over the telephone. After the participant is successfully screened and deemed eligible to participate, they will be provided with further information in a private room in the clinical suites on the 7th in the SON. These clinical suites (which include a general waiting area that is separated from the three secured exam rooms) were created for the conduction of human research. All doors in this suite are locked and only accessible to designated research personnel. No information will be provided about this study to the participant outside of a locked clinical suite room. Participants will be required to sign a release of information form in order to authorize release of information. No information will be included in publications that identify the individual subjects.

3 * Describe potential environmental stressors that may be associated with the research:

There are no known potential environmental stressors besides the ones associated with completing the questionnaires and tasks required for participation. The clinical suites and exam rooms are quiet and were created for human research purposes and to control for potential stressors, such as hallways. The research personnel will limit or eliminate any environmental stressors that could affect the participants.

4 * Will this study have a site based in the European Union?

○ Yes ● **No**

5 * Will the study have planned recruitment or data collection from participants while they are located in the European Union?

○ Yes ● **No**

Access link below for information about the EU General Data Protection Regulations to assist in answering these questions.
https://www.umaryland.edu/oac/general-data-protection-regulation/

ID: VIEW4E1B525B87C00
Name: v2_Privacy of Participants

HP-00076723

View: v2_Confidentiality of Data

Confidentiality of Data

1 * Will stored research data contain identifiers or be able to be linked to and identify individual participants (either directly or through a code/research ID)?

- (●) **Yes**
- ( ) No, the data will be stored de-identified/anonymous (stripped of all identifiers, no way to identify individual participants)

2 * Where will research data be kept (address electronic and paper data as applicable)? (If this is a VA study please list specific sites that data will be kept.)

Paper data collected by research team members will be secured in the PI's Office in a locked file cabinet and in a locked cabinet located in the clinical studies suite at the School of Nursing, Floor 7, Room 729A and 730. The research charts will be maintained in locked file cabinets.

3 * How will such data be secured?

All electronic data will be kept on a secured UMSON computer that requires a log in username and password. The identifiable electronic data will be saved in files that are password protected and only designated staff will have access to this password and know where the files are saved. All paper data will be kept in a locked cabinet in a locked room in the PI's office in the UMSON. Only designated research personnel will have a key to this locked cabinet and room. The only personally identifiable information kept is contact information needed for follow-up purposes and it will be kept strictly confidential. Only non-identifiable information will be used for data analysis and compilation. Data entered into RedCap will only be accessible by research staff and will not contain personal identifiers, such as names or contact information. Backups for conducted and stored data will occur weekly on a password protected external hard drive that will be kept in a locked cabinet in the PI's office.

4 * Who will have access to research data?

Luana Colloca (PI) and delegated study staff, as well as, internal or external monitors for purposes of ensuring quality and compliance. All access to data will be terminated when a staff member is no longer a member of the research team via password or permission changes.

5 * Will study data or test results be recorded in the participant's medical records?

( ) Yes (●) **No**

6 * Will any data be destroyed? ***(Please note that data for FDA regulated research and VA research cannot be deleted)***

( ) Yes (●) **No**

6.1 If Yes, what data (e.g., all data, some recordings, interview notes), when and how?

7 Do you plan to obtain a Certificate of Confidentiality?

○ Yes ● **No**

7.1 If Yes, upload your Certificate of Confidentiality. If you have not yet obtained the Certificate, please note that once it is obtained, you will need to submit an amendment to attach the document, make any needed changes to the submission and make needed changes to the Informed Consent Document.

Name	Created	Modified Date

There are no items to display

8 * Discuss any other potential confidentiality issues related to this study:

Drug test results will not be maintained and results will never be part of the permanent medical records of the individuals. There is always a chance for a breach of data confidentiality, although the small likelihood of this occurring will be further reduced by ensuring that all paper data collected by research team members will be secured in a locked cabinet in locked room or password protected on a UMSON computer. Moreover, all documentation will only contain codes and no personally identifiable information when possible.

ID: VIEW4E1B5265E0400
Name: v2_Confidentiality of Data

HP-00076723

View: v2_Monitoring Plan Selection

Monitoring Plan Selection

1 * Type of data safety monitoring plan for the study:

- ○ Will use/defer to the external sponsor's Data Safety Monitoring Plan
- ○ Data Safety Monitoring by a Committee
- ● **Data Safety Monitoring by an Individual**
- ○ There is no data safety monitoring plan in place

ID: VIEW4E1B00E30D400
Name: v2_Monitoring Plan Selection

HP-00076723

View: v2_Monitoring Plan - Individual

Monitoring Plan - Individual

You indicated that the monitoring will be done by an Individual.

1 * Identify the individual who will be performing the safety monitoring:
Cynthia Renn

2 * Describe this individual's role in relation to the protocol:
Dr. Renn has experience with human research and she has been serving as an individual monitoring Dr. Colloca 's active protocols.

3 * What data will be reviewed?

- [x] **Adverse Events**
- [x] **Enrollment Numbers**
- [ ] Patient Charts/Clinical Summaries
- [ ] Laboratory Tests
- [ ] Medical Compliance
- [ ] Procedure Reports
- [ ] Raw Data
- [ ] Outcomes (Primary, Secondary)
- [x] **Preliminary Analyses**
- [ ] Other

3.1 If Other, specify:

4 * What will be the frequency of the review?

- (●) **Annually**
- ( ) Bi-Annually

- ○ Other

4.1 If Other, specify:

5 * Safety monitoring results will be reported to:

- ☑ **IRB**
- ☐ GCRC
- ☐ Sponsor
- ☐ Other

5.1 If Other, specify:

ID: VIEW4E1B026A2A400
Name: v2_Monitoring Plan - Individual

HP-00076723

View: v2_Research Related Costs

Research-Related Costs

1 * Is the study's financial supporter (e.g., commercial sponsor, federal or state grant or contract, private foundation, physician-sponsor) covering any research-related costs?

- ○ No
- ● **Yes**

1.1 If Yes, check all that apply:

- ☑ **Research-Related Services (personnel costs, tests, supplies, exams, x-rays, or consultations required in the study)**
- ☑ **Investigational or Study Device**
- ☑ **Investigational or Study Drug**
- ☐ Investigational Procedure(s)

1.2 If No, who is responsible for payment?

2 * Who is responsible for the uncovered research-related costs?

- ☐ Participant
- ☐ Sponsor
- ☐ UM
- ☐ Other
- ☑ **There will be no uncovered research-related costs**

2.1 If Other, specify:

3 If the participant is responsible for any research-related costs, identify and estimate the dollar amount:

ID: VIEW4E1B5D9641800
Name: v2_Research Related Costs

HP-00076723 View: v2_Compensation for Research-Related Injury

Compensation for Research-Related Injury

1 * Is this study under a master agreement that includes a provision requiring the sponsor to provide compensation to participants for research-related injury?

○ Yes ● **No**

1.1 If Yes, please provide the date and title of the agreement and upload the portion of the contract language relevant to compensation for research-related injury:

Name	Created	Modified Date

There are no items to display

1.2 If No (the study is not under a master agreement), is there proposed contract language concerning payment to participants for treatment in the event of a research-related injury?

○ Yes ● **No**

1.2.1 If Yes, indicate the status of the contract review/approval with the ORD and upload the proposed language relevant to compensation for research-related injury:

1.2.2

Name	Created	Modified Date

There are no items to display

ID: VIEW4E1B629EEC000
Name: v2_Compensation for Research-Related Injury

HP-00076723

View: v2_Payment to Participants

Payment/Reimbursement to Participants

1 * Will participants receive payment (money, gift certificates, coupons, etc.) or reimbursement for their participation in this research?

● **Yes** ○ No

ID: VIEW4E1C52A5D7800
Name: v2_Payment to Participants

HP-00076723 View: v2_Payment Detail

Payment/Reimbursement Detail

You indicated that participants will receive payment (money, gift certificates, coupons, etc.) or reimbursement for their participation in this research.

1 * Payment/reimbursement to participants will be for: (check all that apply)

- [ ] Travel
- [x] **Parking**
- [ ] Meals
- [ ] Lodging
- [x] **Time and effort**
- [ ] Other

1.1 If Other, specify:

2 * What is the total dollar value of the payments/reimbursements over the duration of the study? ***Total payment(s) for participation in research of $600 or more in a calendar year is required to be reported on an IRS Form 1099.***

$170

3 * Describe the timing and distribution plan for the payment/reimbursement (schedule, means, etc.)?

Participants will be compensated for time and research-related inconveniences based on NIH standards for time devoted to research projects.
Participants will receive $25 for the first session and will receive additional $125 for participating in the second session (fMRI part) of this study project. This protocol does not include reimbursement for subsistence but voucher of $10 covering for 4 parking hours is offered for both study visits. Participants will receive $150 for the EEG experiment and parking voucher. Participants will still be paid even if they choose to withdraw their data after they are debriefed but they will not be paid if they do not meet inclusion criteria or if they meet exclusionary criteria prior to signing the informed consent form. Participant will not be paid if they test positive on the drug or the pregnancy (women only) test. The worksheet log necessary to complete for participant payment will be submitted regularly to Financial Services, therefore all participants can expect to be paid within approximately 4-6 weeks of them signing their informed consent form and participating in the study. For those participants who do not have a social security number, a gift card of the same amount will be provided to the participant. Also, the gift card can be given to participants based on their expressed preference. Participants invited to come back for any missing or additional collection of data will be compensated $25.
The campus policies and procedures will be followed to maintain the appropriate records and to set up and reconciled payment logs as appropriate.

4 * Method(s) of payment/reimbursement to be Used:

- [x] **Cash**

- [x] **Check**
- [ ] Money Order
- [x] **Gift Certificate/Gift Card**
- [x] **Other**

4.1 If Other, specify:
Parking vouchers - $10 ($10 for each of the 2 visits if they attend both)
EEG - Parking vouchers - $16 (5 hours)

ID: VIEW4E1C54A6ACC00
Name: v2_Payment Detail

HP-00076723

View: v2_HIPAA

HIPAA (Health Insurance Portability and Accountability Act)

1 * Are you affiliated with, or will you be accessing data from a HIPAA-covered entity? A covered entity might be a hospital, a physician practice, or any other provider who transmits health information in electronic form.

• At UMB, this includes UMB schools designated as covered entities (School of Medicine and School of Dentistry) and entities under the University of Maryland Medical System (UMMS). The Baltimore VA Medical Center is also a covered entity.

• If you are a researcher from any school that is not a covered entity but is accessing electronic medical records from a covered entity (such as UMMC), HIPAA would be applicable. Please see a list of covered entities included under UMMS here: *executed-ace-designation-042018.pdf*

◯ Yes ◯ No

ID: VIEW4E1B0A2114400
Name: v2_HIPAA

HP-00076723

View: v2_Informed Consent Process

Informed Consent Process

If the study does not involve interaction with participants or a waiver of consent is being requested , answer "N/A" to the questions below.

1 * Indicate the type(s) of consent that will be involved in this study: (check all that apply)

- [ ] Not applicable (study may qualify as exempt)
- [ ] Request to Waive Consent/Parental Permission (Consent is not being obtained)
- [ ] Request to Alter Consent (Some Elements of Consent Waived)
- [ ] Request to Waive Documentation of Consent (Verbal/Oral Consent)
- [x] **Written Consent Form**
- [ ] Electronic Consent

2 * Describe the Informed Consent process in detail:

Before participation in any stage of the research study, eligible participants will be required to read and sign an informed consent form, and then correctly answer questions presented by trained research personnel about critical study details. Participants will be asked what is expected of them by participating, if they fulfill any of the exclusion criteria (see Eligibility criteria), if they are fully aware that participation is voluntary and if they have any questions about the study and procedure. Participants will be able to read the consent form in a quiet and separate room with no distractions and will be provided with a copy of their signed forms and the PIs contact information to take with them.

3 * Confirm that the consent process will explain the following:

- The activities involve research.
- The procedures to be performed.
- That participation is voluntary.
- The name and contact information for the investigator.

● **Yes** ○ No

4 * Describe who will obtain Informed Consent:

Luana Colloca (PI) and delegated study staff. All research personnel will be adequately trained to administer the informed consent form, and to answer and ask questions to test the participant's knowledge.

5 * If obtaining consent from a legally authorized representative (LAR), describe how you will confirm that the individual is the LAR and can provide legally effective informed consent. *(Answer "N/A" if not obtaining consent from LARs)*

N/A

6 * Describe the setting for consent:

The consent procedure will occur in a quiet and separate room with no distractions located in the clinical suites. Participants can take as much time as they would like to read over the form and to ask questions before agreeing to participate in the study.

7 * Describe the provisions for assessing participant understanding:

After a participant agrees to participate, they will be asked verbally the following questions to test their knowledge about the study:
1) What is expected of you when participating in this study?
3) Are you fully aware that participation is entirely voluntary?
4) Do you have any questions about the study and procedure?

8 * Describe the consideration for ongoing consent:

Consent will be obtained for the entire experimental session, including the behavioral and fMRI or EEG part.

ID: VIEW4E1C661D0AC00
Name: v2_Informed Consent Process

HP-00076723

View: v2_Consent Forms - Draft

Consent and HIPAA Authorization Forms - Draft

1 Upload all of your Consent Forms for approval. Use only Microsoft Word.

Name	Created	Modified Date
Updated Consent Form_vaso.doc - track mode changes(0.09)	8/31/2017 4:54 PM	10/22/2018 4:45 PM
Updated fMRI Consent - Clean version(0.01)	10/22/2018 4:46 PM	10/22/2018 4:46 PM
Updated Consent form _Vaso_EEG_NEW(0.02)	10/22/2018 4:01 PM	10/22/2018 4:39 PM

IMPORTANT NOTE: the above list of consent forms (if any) are DRAFT versions. Under no circumstances should copies of these be distributed to patients/study subjects. If/when this research submission is approved by the IRB, approved consent forms will be available for download and use from the "Documents" tab of the Submission's workspace (click Exit and then look for the Documents tab - approved submissions only)

1A Archived Consent Forms:

Name	Created	Modified Date
There are no items to display		

2 Upload any HIPAA authorization forms here:

HIPPA_v1.1_upload.doc(0.02)	8/31/2017 4:54 PM	12/18/2017 6:05 PM

Please refer to HRPO's website for specific instructions for preparing informed consent documents and to access current templates: http://hrpo.umaryland.edu/researchers/consents.html

ID: VIEW4E1C7712D3000
Name: v2_Consent Forms - Draft

HP-00076723

View: v2_Organization Review Requirements (other than IRB)

Organization Review Requirements (other than IRB)

Answer the following questions to determine additional organizational review requirements:

1 **Department/Division Review** - All research submissions are required to undergo department/division/institutional review prior to IRB review. The following entity is listed as the required department/division/institutional review:

SON Pain & Trans Symptom Sci

If this information is incorrect, please notify the HRPO office.

2 **RSC Review Criteria** - select 'Yes' if the answer is 'Yes' for any of the following questions. Review by the Radiation Safety Committee may be required.

* 2.1 Does the research involve the use of ionizing radiation? ○ Yes ● **No**

2.2 Does the research involve the sampling of radioactive human materials for subsequent use or analysis in a laboratory?

3 **IBC Review Criteria** - select 'Yes' if the answer is 'Yes' for any of the following questions. Review by the Institutional Biosafety Committee may be required.

* 3.1 Does the research involve human gene transfer? ○ Yes ● **No**
-OR-
Does the research specifically apply to human studies in which induction or enhancement of an immune response to a vector-encoded microbial immunogen is the major goal, and such an immune response has been demonstrated in model systems, and the persistence of the vector-encoded immunogen is not expected? This type of research is often referred to as recombinant vaccine trials.

3.2 Does the research involve the exposure of human subjects to pathogenic microorganisms, or the exposure of research staff to human subjects or samples known or reasonably expected to carry infectious disease(s)?

3.3 Does the research involve the sampling of materials from persons with no known infectious disease and where the only risk to study staff is occupational exposure to bloodborne pathogens as defined by the OSHA Bloodborne Pathogen Standard?

4 **Cancer Center Criteria** - Answer the following to determine if review by the Cancer Center (Hematology-Oncology) may

be required.

* Does the protocol involve in any way studies related to the prevention, treatment, diagnosis, or imaging of neoplastic diseases? ○ Yes ● **No**

5

General Clinical Research Center Review Criteria - the GCRC offers free and/or cost shared resources for patient-oriented research. Click Here for more information.

Answer the following to determine if review by the GCRC may be required.

* Will the General Clinical Research Center (GCRC) facility or resources be used to conduct this activity? ○ Yes ● **No**

6

VA Review Criteria - Answer the following questions to determine if review by the VAMHCS R&D Committee may be required.

* 6.1 - Will the research be conducted by VA Investigators including PIs, Co-PIs, and Site Investigators on VA time (serving on compensated, WOC, or IPA appointments)? ○ Yes ● **No**

* 6.2 - Will the research utilize VA resources (e.g., equipment, funds, medical records, databases, tissues, etc.)? ○ Yes ● **No**

* 6.3 - Will the research be conducted on VA property, including space leased to and used by VA? ○ Yes ● **No**

PLEASE NOTE that the research may be funded by VA, by other sponsors, or may be unfunded.

ID: VIEW4E1AF91AB2400
Name: v2_Organization Review Requirements (other than IRB)

HP-00076723

View: v2_Summary of Required Reviews (other than IRB)

Summary of Required Reviews (other than IRB)

1 **Additional Committee Reviews** - Based on your responses to the previous questions, you have identified the following additional reviews. To complete or view these additional committees' forms, click on the links below or exit this application and click on the appropriate button on left side of this submission's webpage.

Name of Related Submission

This protocol has no related submissions (RSC, GCRC, IBC, etc)

2 **Required Department and Specialty Reviews** - Based on the PI's organization (department, division, etc.) affiliation and answers to previous questions (use of Cancer Center, etc.), the organizations listed below are required to review this application. These reviews are conducted online and no additional forms or steps by the study team are required.

Name of Organization	Review Status
SON Pain & Trans Symptom Sci	Complete

ID: VIEW4E1C8D9AE4000
Name: v2_Summary of Required Reviews (other than IRB)

HP-00076723

View: v2_Additional Documents

Additional Documents

1

Upload all additional documents here:

Name	Created	Modified Date
Participants Instruction BEFORE AVP (B)(0.01)	9/20/2019 3:38 PM	9/20/2019 3:38 PM
Participants Instruction BEFORE AVP (A)(0.01)	9/20/2019 3:38 PM	9/20/2019 3:38 PM
Participant Instruction Before EEG (B)(0.01)	10/22/2018 4:02 PM	10/22/2018 4:02 PM
Participant Instruction Before EEG (A)(0.01)	10/22/2018 4:02 PM	10/22/2018 4:02 PM
ClinicalTrials.Gov registration(0.01)	1/8/2018 3:50 PM	1/8/2018 3:50 PM
GCP_Murthi(0.01)	1/8/2018 3:50 PM	1/8/2018 3:50 PM
CITI_Murthi(0.01)	1/8/2018 3:49 PM	1/8/2018 3:49 PM
GCP Certificate Lola.pdf(0.01)	11/10/2017 5:18 PM	11/10/2017 5:18 PM
GCP Certificate Patel.pdf(0.01)	11/10/2017 5:18 PM	11/10/2017 5:18 PM
Participant Instruction before MRI (B)(0.01)	8/31/2017 4:56 PM	8/31/2017 4:56 PM
Participant Instruction before MRI (A)(0.01)	8/31/2017 4:56 PM	8/31/2017 4:56 PM
Figures and Tables(0.01)	8/31/2017 4:56 PM	8/31/2017 4:56 PM

ID: VIEW4E0962513A000
Name: v2_Additional Documents

HP-00076723

View: v2_Final Page of Application

Final Page of Application

You have reached the final page of this application. It is recommended that you click on the "Hide/Show Errors" link on the upper or lower breadcrumb row of this page. The "Hide/Show Errors" will do a search of your application, and highlight areas that are required or need to be completed prior to submitting.

By submitting this application, you are electronically routing the protocol for departmental scientific review and all other necessary reviews. According to information you have provided, this application will be routed to the following Departments for review prior to being forwarded to the IRB for review. These reviews are conducted online and no additional forms or steps by the study team are required.

Name of Organization	**Review Status**
SON Pain & Trans Symptom Sci	Complete

Required Safety Committee Reviews - In addition to the IRB, the following committees must review this submission. Each additional committee has a separate online form that the study team will be required to fill out. All committee applications (IRB plus those listed here) must be completed properly before the 'package' of applications can be submitted. The team may complete these additional forms in any order or at any time prior to submission of the IRB Application. To complete or view these additional committees' forms, click on the links below or exit this application and click on the appropriate button on left side of this submission's Workspace.

Name of Related Submission

This protocol has no related submissions (RSC, GCRC, IBC, etc)

You may check the progress of your application at any time by returning to the Workspace of this submission. A detailed history, including notes, dates, and times of events, is provided to you for this purpose.

If a reviewer returns the application to you, you must address their concerns and resubmit the protocol for review to all designated departments. After all departments have reviewed the application, it will automatically be sent to the IRB for review. Changes made to the submission after its approval must be submitted as modifications.

Investigator Attestation
By submitting this application, I, the Principal Investigator (PI), certify that the information provided in this application is complete and correct. Research will be conducted according to the submission as described, only by the approved principal investigator and study team members.

In addition, I agree to the responsibilities of a PI, including:

- Obtaining informed consent (if applicable) from all subjects as outlined in the submission.
- Reporting new information to the IRB per the requirements of the Investigator Manual.
- If Required, obtaining renewal of the protocol prior to the expiration of the approval period or halt all study activities upon study expiration.
- Accepting ultimate responsibility for the protection of the rights and welfare of human subjects, conduct of the study and the ethical performance of the project.
- Ensuring performance of all research activities by qualified personnel according to the IRB approved submission.
- Ensuring that research personnel have or will receive appropriate training.
- Ensuring no changes will be made in the research until approved by the IRB (except when necessary to eliminate apparent immediate hazards to subjects).

Click the "Finish" button and then click "Submit Application" in the submission Workspace.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Sarah Murthi

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Sarah Murthi, MD is a medical doctor and assistant professor at UMMC. She will primarily help with medical advice and orders for the vasopressin.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Chika Okusogu

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Chika Okusogu is another UMSON nursing student and will assist with research endeavors at UMB as well as learn first-hand about the research process. He will assist with data collection and data entry.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Rachel Cundiff

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Rachel is a PhD candidate in the Graduate Program In Life Sciences (GPILS) Program in Neuroscience with expertise in brain imaging. She will assist with various PI-delegated aspects of this protocol, including but not limited to fMRI imaging preprocessing, data collection and entry, and manuscript preparation.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Titilola Akintola

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Titilola Akintola is a PhD student in the lab. She will primarily help during the data collection process.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Kristina Park

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Kristina Park is currently a student at UMSON, Master of Science in Nursing: Clinical Nurse Leader, and will assist with data entry and analyses.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Sharon Thomas

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Sharon Thomas, NP, is a PhD student in the lab. She is a nurse practitioner with considerable clinical experience who will help during the data collection process and can consent participants.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Christina Tricou

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Christina Tricou holds a BA in biophysics awarded by Scripps College. Her primary research experience has been rooted in coding. She has written and modified code to set up experiments and record data as well as to analyze data collected by others. Her duties will include recruitment, assisting with study procedures, data entry, and contacting participants for additional information.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Yang Wang

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
● **Yes** ○ No

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Yang Wang PhD, will be added. She has expertise in EEG/fMRI data analysis and will be completing post-doctoral studies with our lab. She will assist with all aspects of this protocol and can consent participants.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Elizabeth Olson

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
◯ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
◯ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
◯ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Elizabeth Olson, BA, is an MD student at the University of Maryland School of Medicine. She obtained her BA in Neuroscience and French from Wellesley College where she conducted research on language, learning and memory. She is interested in sex/gender influences on pain perception and nociception. She has completed all HRPO-required trainings. Among other PI-delegated duties like recruitment, data collection and entry, and data analysis, she can consent participants.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Margaret Yin

2 Research Role:
Technician or Assistant

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Margaret Yin is a research assistant who will help with various administrative tasks (i.e. filing), phone screening, and data entry (among other PI-delegated tasks). She will work directly under the supervision of the research coordinator. She has completed all required HRPO trainings.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Alexis Saunders

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Alexis Saunders is an MPowering the State scholar for Summer 2019, and she will assist with delegated aspects of the protocol, from phone screening and conducting study procedures to data entry and analysis. She has completed all required HRPO trainings.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Se Eun Lee

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Se Eun Lee, ADN, BSN graduated from Harford Community College with ADN and from UMB with a BSN. She is experienced in healthcare and is currently working at UMMC in the interventional radiology department. She is certified with BLS and ACLS and will be helping with recruitment, data collection, and data entry.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Rachel Massalee

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
● **Yes** ○ No

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Rachel Massalee obtained a B.S. in Molecular Biology, Biochemistry and Bioinformatics from Towson, University and is currently completing a Master's of Physiology and Biophysics from Georgetown University. As part of her master's practicum, she will work as a reseach assistant for our lab and help with various PI-delegated tasks including phone screening, study procedures, data entry and analysis, manuscript preparation, and administrative duties. She has completed all HRPO-required trainings.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Kathryn Smith

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Kathryn Smith graduated from Vanderbilt University in 2018 with a Bachelor of Science degree in Psychology and Child Development. As an undergraduate, she studied peer victimization and adolescent depression. She is currently working towards earning a Master of Science degree in the Clinical Nurse Leadership program at University of Maryland Baltimore School of Nursing. She will assist with recruitment, data collection and entry, REDCap, study procedures, sample storage, and manuscript preparation, among other PI-delegated tasks. She has completed all HRPO-required trainings.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Charlene Tugwete

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Charlene is a work study student pursuing a Doctor of Pharmacy from UMSOP. She will assist with various PI-delegated aspects of this protocol, including but not limited to data collection, data entry, and manuscript preparation.

HP-00076723

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Nandini Raghuraman

2 Research Role:
Technician or Assistant

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
○ Yes ● **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
○ Yes ● **No**

5 * Does this study team member have a potential conflict of interest, financial or otherwise, related to this research?
○ Yes ● **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Nandini Raghuraman is a master's student working in the lab, who will assist in data collection and entry, participant recruitment, and redcap.