

# PROTOCOL NARRATIVE FOR EXPEDITED OR FULL COMMITTEE RESEARCH

University of California, Irvine  
Institutional Review Board  
Version: May 2011

**IMPORTANT: CAREFULLY READ THE INSTRUCTIONS FOR EACH SECTION BEFORE COMPLETING THE PROTOCOL NARRATIVE.**

**WHEN CUTTING AND PASTING FROM ANOTHER APPLICATION OR PROTOCOL, PLEASE ENSURE THAT THE INFORMATION IS COMPLETE, SUPPLEMENTED WHERE NECESSARY, PASTED IN A LOGICAL ORDER, AND IS RELEVANT TO THE SPECIFIC SECTION.**

**NEED HELP? CONTACT THE [HRP STAFF](#) FOR ASSISTANCE.**

HS#: 2012-8760  
For IRB Office Use Only

**Lead Researcher Name:** Larry Cahill, PhD

**Study Title:** fMRI investigation of sex hormone influences on emotion and memory

## **NON-TECHNICAL SUMMARY**

Provide a non-technical summary of the proposed research project that can be understood by IRB members with varied research backgrounds, including non-scientists and community members. The summary should include a brief statement of the **purpose of the research** and **related theory/data supporting** the intent of the study as well as a brief description of the **procedure(s) involving human subjects**. *This summary should not exceed ½ page.*

Functional MRI will be used to investigate how sex hormone variation in healthy, younger women influences brain function both at rest, and in response to emotional stimuli, and to memory for those stimuli. In particular, the brain responses to naturally cycling women will be compared to those of women currently taking hormonal contraception. This will be the first study examining potential influences of hormonal contraception on brain function.

## **SECTION 1: PURPOSE AND BACKGROUND OF THE RESEARCH**

1. Describe the **purpose of the research** project and state the overall objectives, specific aims, hypotheses (or research question) and scientific or scholarly rationale for performing the study.
2. Provide the **relevant background information** on the aims/hypotheses (or research question) to be tested and the procedures/products/techniques under investigation.
3. Include a description of the **predictor and outcome variables**, as appropriate.
4. Include a critical evaluation of **existing knowledge**, and specifically identify the information

Approved by IRB on: 07/20/12

HS# 2012-8760

Void After: 04/19/13

IRB USE ONLY - DO NOT ALTER THIS FOOTER



gaps that the project intends to address.

5. Describe **previous research** with animals and/or humans that provides a basis for the proposed research. **Include references/citations**, as applicable.

***This section should not exceed 4 pages.***

**1, 2, 5.** The purpose of the research project is to investigate the influence of different sex hormone states on functional brain activity. We will use two techniques to achieve this: first, we will measure functional connectivity at rest, and second, participants will complete a subsequent memory experiment. In the former, brain activity at rest is correlated between regions, allowing us to infer functional connectivity between regions where activity is highly correlated. In the latter, brain activity is measured while participants undergo an encoding task, and the amount of activity at the time of encoding is correlated with the stimuli that participants later remember. Both experimental paradigms are well-validated and have been used in our laboratory and many others.

In order to investigate the role of hormones, women in different hormonal states will complete these two experiments, and their brain activity will be compared to one another. We will recruit women in two different stages of the menstrual cycle: the early follicular stage, during which ovarian sex hormones are relatively low, and the mid-luteal stage, during which the hormones estrogen and progesterone are significantly higher. We will also recruit an equal number of women using hormonal contraception (HC), which uses powerful synthetic analogs of ovarian hormones to decrease their endogenous levels. While these endogenous levels remain consistently low in women using HC, they also experience two distinct hormonal states. The majority of HC varieties are designed to have a 28-day cycle, in which 4 to 7 days are placebo pills. Thus, most HC users take approximately 1 week of placebo pills (no hormones) and approximately 3 weeks of active pills (synthetic hormones).

We hypothesize that in our subsequent memory experiment, we will see a shift in the lateralization of the subsequent memory effect. The subsequent memory effect has been well established and replicated, and previously, sex differences in laterality have been observed. In men, activity in the right amygdala predicts subsequent memory, whereas in women, activity in the left amygdala predicts subsequent memory (Cahill et al., 2004; Canli et al., 2002). We propose that these laterality differences are at least in part attributable to the activity of sex hormones, which differ dramatically between men and women, and which have been shown to alter arousal circuitry reactivity.

Investigations into the effects of hormones on arousal circuitry have shown that activity in the amygdala and associated structures was attenuated during the high-estrogen late follicular phase (Goldstein et al., 2005), and potentiated during the high-progesterone mid-luteal phase (Andreano and Cahill, 2010). Further, synthetic progesterone administration significantly increased amygdala reactivity (van Wingen et al., 2007). These findings suggest that arousal circuitry activity critical to emotional memory is sensitive to hormonal changes, hence our hypothesis that subsequent memory networks dependent on arousal circuitry may change in different hormonal environments.

As previously discussed, the hormonal influences we plan to investigate include those in both naturally cycling women as well as women using hormonal contraception. Approximately 100 million women worldwide use oral hormonal contraception (HC), which directly affects sex hormones (Trussell, 2007). Thus, characterizing HC's effects on emotional memory are of tremendous interest to both the scientific and lay communities. The hypothesis that HC affects arousal circuitry activity has never been explicitly tested, despite evidence that HC alters stress reactivity by reducing levels of evoked cortisol in response to CPS. Further, as behavioral evidence that HC influences memory accumulates (Griksiene and Ruksenas, 2010; Mordecai et al., 2008; Nielsen et al. 2011) it becomes increasingly important to understand whether HC: (1)

prevents any changes in arousal seen across the menstrual cycle in the presence of endogenous sex hormones, since these are reduced to approximately early follicular levels in HC women; (2) mimics the actions of endogenous sex hormones such that arousal circuitry shows no differences between HC and NC women, (3) exaggerates the actions of endogenous sex hormones, producing relative increases and decreases in arousal reactivity that correspond to those seen across the menstrual cycle, or (4) induces a shift in laterality such that the right, instead of left, amygdala predicts subsequent memory.

3. Our predictor variable is hormone status. This can be divided initially by synthetic vs. endogenous hormone use (HC vs. NC), and further subdivided into low and high hormone groups within each of those. In the HC women, those on the placebo week are low hormone and those on an active week are high hormone; in the NC women, those in the early follicular phase are low hormone and those in the mid-luteal phase are high hormone. This permits us to dose-dependently examine synthetic and endogenous hormones without any experimenter manipulation.

Our outcome variable is the blood-oxygen-level-dependent hemodynamic response, both at rest and during the different elements of the encoding task.

4. The existing knowledge base regarding hormone influences on emotional memory show that: (1) Ovarian sex hormones have important effects on memory (Ertman et al., 2011; Griksiene and Ruksenas, 2010; Mordecai et al., 2008; Nielsen et al. 2011); (2) Ovarian sex hormones have important effects on brain structure (Hagemann et al., 2011; Pletzer et al., 2010); and (3) Ovarian sex hormones have important effects on functional activity in brain regions associated with emotional arousal and memory (Andreano and Cahill, 2010; Goldstein et al., 2005; van Wingen et al., 2007). However, no study to date has considered the effects that hormonal contraception may have on functional connectivity, nor have the effects of menstrual cycle related hormone changes on functional activity been considered. Additionally, in light of the behavioral changes reviewed above, we are proposing the first ever fMRI analysis of HC's effects on memory, and the first fMRI investigation of menstrual cycle effects on subsequent memory.

## **SECTION 2: ROLES AND EXPERTISE OF THE STUDY TEAM**

***List all study team members below.***

1. Identify each **member's position** (e.g., Associate Professor, graduate or undergraduate student) and **department**, and describe his or her **qualifications, level of training and expertise**. Include information about relevant licenses/medical privileges, as applicable.
2. Describe each team member's **specific role and responsibility** on the study.
3. **Faculty Sponsors** - list as Co-Researchers and describe their role on the project; include oversight responsibilities for the research study.
4. Explain who will have **access to subject identifiable data**.
5. Indicate who will be **involved in recruitment, informed consent process, research procedures/interventions, and analysis of data**.

### **Lead Researcher:**

Larry Cahill, Ph.D is a leading investigator of brain and emotional memory, with extensive prior experience in conducting MRI studies of emotional memory and hormone changes. He will oversee all

aspects of the proposed research.

**Co-Researcher(s):**

Nicole Ertman is a 4<sup>th</sup> year graduate student in the Cahill laboratory. She will be primarily responsible for the day-to-day conduct of the study, including all recruitment and obtaining informed consent.

Belinda Pletzer is a post-doctoral fellow in the Cahill lab with extensive MRI experience. She will work with Nicole in the scanning conduct and analysis. Both researchers will be responsible for research procedures and analysis of data.

**Research Personnel:**

Azaadeh Goharзад is a student assistant who will work with Nicole Ertman in the conduct of the study.

Only the personnel listed here (Professor Cahill, Ms. Ertman, Dr. Pletzer, and Ms. Goharзад) will have access to identifiable subject data.

**SECTION 3: RESEARCH METHODOLOGY/STUDY PROCEDURES**

**A. Study Design and Procedures**

1. Provide a **detailed chronological description of all study activities** (e.g., pilot testing, screening, intervention/interaction/data collection, and follow-up) and **procedures**. Include an explanation of the study design (e.g., randomization, placebo-controlled, cross-sectional, longitudinal, etc.)
  - a. Indicate how much **time will be required of the subjects**, per visit and in total for the study.
  - b. Indicate the **setting where each procedure will take place**/be administered (e.g. via telephone, clinic setting, classroom, via email). **Note: If any of the procedures will take place at off-campus locations (e.g., educational institutions, businesses, organizations, etc) Letters of Permission are required.**
  - c. If a procedure will be completed more than once (e.g., multiple visits, pre and post survey), indicate **how many times** and the **time span** between administrations.
2. **For studies that involve routine (standard of care) medical procedures:** Make clear whether procedures are being done for clinical reasons or for study purposes, including whether the procedures are being done more often because of the study. Use the following guidelines to determine the extent to which standard procedures and their associated risks need to be described in protocol:
  - a. If the standard procedure is not explicitly required by the study protocol, the protocol need not describe that procedure or its risks.
  - b. If the standard procedure is a main focus of the study (e.g., one or more arms of a randomized study is standard) or is explicitly required by the study protocol, the protocol must include a full description of the procedure and its risks.]
3. It is **strongly recommended** that you include a table of visits, tests and procedures. Tables are easier to understand and may help to shorten long repeated paragraphs throughout the narrative.
4. If study procedures include collecting **photographs, or audio/video recording**, specify whether any subject identifiable information will be collected and describe which identifiers

will be collected, if any.

5. Describe how the **subject's privacy will be protected** during the research procedures.  
*Note: This is not the same as confidentiality (see the [Privacy and Confidentiality web page](#)).*
6. Be sure to submit **data collection instruments** for review with your e-IRB Application (e.g., measures, questionnaires, interview questions, observational tool, etc.).

**1a, 1b, 1c.** This investigation involves a quasi-experimental (non-randomized) design in which participants will be assigned to groups based on (1) whether or not they currently take hormonal contraception, and (2) their menstrual cycle phase at the time of the experiment. Of the naturally cycling women, we will include one group in the early follicular phase and one in the mid-luteal. Of the hormonal contraception users, we will include one group of women using placebo pills at the time of the experiment, and one group of women using active pills. The placebo pills are a normal part of oral contraceptive use and not a modification made for the purposes of this experiment.

The maximum number of subjects to be consented will be 25 per group, aiming for a final "n" of 20/group, and assuming loss of about 5 subjects/group for reasons such as head motion in the MRI scanner. Study activity will begin with recruitment of UCI students using flyers in addition to recruitment from the Social Sciences subject pool. Upon contacting us, participants will be screened by phone. In addition to basic demographic information, we will ask participants about their contraceptive status (hormonal, non-hormonal, or no contraceptive use) and menstrual cycle phase. We will also screen participants to ensure they meet all safety requirements for entering the 3T MRI.

Those who meet criteria will be scheduled for two separate experiment appointments. The first will take place at the UCI Research Imaging Center's 3T scanner. Upon arriving participants will again undergo metal screening both verbally and visually to ensure their safety in the scanner. Throughout the experiment, we will periodically collect 2mL saliva samples (maximum 6) through direct expectoration, a non-invasive procedure that poses no foreseeable risks to participants. In the scanner, participants will be scanned at rest for later functional connectivity analysis, and then will view a slideshow of mixed emotional and neutral images taken from the International Affective Picture System (IAPS), used extensively in our previous research and that of others on emotion and memory. Subjects will identify and rate their emotional reaction to each slide.

Participants will return for the second and final testing session on a subsequent day (2-7 days later) to our laboratory. We will administer incidental recall and recognition memory tests for the slides viewed while in the MRI scanner. Some brief, standardized psychological tests (such as the BEM sex-role inventory) may be administered as well for use as co-variates in the analyses.

After completing both sessions, we may re-contact some participants with follow-up questions between 1 and 4 weeks later in order to insure we have accurate menstrual cycle information, which is crucial to the analyses.

Naturally-cycling women may be asked to verify the stage of their menstrual cycle with a simple, take home luteinizing hormone (LH) urine analysis kit. Participants using LH strips will be given seven strips to take home and use one per day until a positive reading is found, and they will receive detailed instructions as per the kit about their care and use during the first experimental session. Participants will urinate on the strip, and colored bands will appear, which they will note and report to us. In some instances it may be necessary to begin the LH testing before the first experimental session, in which case a separate meeting time would be established with the participant to receive strips and instructions after consent. All participants will be instructed to discard any unused strips.

All participants will be fully debriefed as to the purposes of the study at the end of their participation.

Total participation should take no more than 3 hours:

Screening interview: 5 to 15 minutes

Scanning session: 45 to 90 minutes

Retrieval session: 60 minutes

Follow up interview: 5 minutes

LH strip testing: 1 to 4 minutes

2. No medical procedures are involved with this experiment.

3.

Screening interview	Brief phone interview
Experimental Session 1	Consent Metal rescreening Questionnaires/inventories Saliva sample 1 Resting state functional scan Presentation of IAPS slides Saliva sample 2
Experimental Session 2	Saliva sample 3 Free recall incidental memory test Recognition incidental memory test Saliva sample 4 Questionnaires/inventories
Follow-up interview	Brief phone interview

4. No photographs or audio/video recordings will be collected.

5. Participants' privacy will be protected at all times. All participants will be assigned a subject number, and that number will be used on all of their data sheets. The code for the numbers will be kept in a separate, locked location.

6. The standardized data collection instruments we use include visual stimuli from the International Affective Picture System (IAPS), as well as well-validated, non-invasive, standardized cognitive and mood inventories such as the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI).

**Special note regarding incidental findings:** It is possible, although unlikely, that during the course of the MRI scanning, an apparent abnormality in the brain may be observed by the researchers despite lack of medical training. Should this occur, anonymized scans will be sent to a qualified neuroradiologist for review. If the neuroradiologist concludes that the scans likely indicate illness or disease, the participant will be informed of this by the research team and advised to bring it to the attention of a qualified medical practitioner.

## B. Statistical Analysis Plan

1. **Variables of Interest** - Clearly identify the primary outcome(s) and key factor(s) of interest.

2. **Statistical goal** - State the statistical goal(s) of the study (e.g., Comparison of group means, estimation of the proportion of success, estimation of variability for future study design, etc.).
3. **Statistical approach** - Describe the statistical approach(es) to be used to address the study's statistical goal(s) (e.g., T-test to compare means, confidence interval estimate(s), etc.). **Note: Required for ICTS SRC review.**
4. **Secondary analyses** - Clearly state any secondary analyses to be performed including secondary outcomes and comparison groups along with the statistical methods that will be used to perform the secondary analyses. **Note: Required for ICTS SRC review.**

***If a statistical analysis plan is not appropriate for your study design, please describe a non-statistical plan for assessing your study results.***

1. Our primary goal is to investigate the contribution of sex hormones to functional brain activity. This design allows us to investigate sex hormones in two different ways: (1) by comparing the effects of endogenous hormone activity on functional brain activity in women who are in different stages of the menstrual cycle, and (2) by comparing the functional brain activity in these naturally cycling women to that of women whose endogenous hormones have been suppressed by synthetic hormones. Our primary investigation will be using a subsequent memory design previously used by our laboratory. In this, functional activity in different brain regions can be correlated with the degree to which stimuli are later retained. As a secondary goal, we will also be investigating any differences in functional connectivity at rest. We will compare resting state functional connectivity in our two naturally cycling groups as well as compare activity in these groups to that of the hormonal contraception group.
2. Our statistical goal is to compare the hemodynamic response as measured by functional MRI in women with different hormonal profiles. We will compare both the blood-oxygen-level-dependent (BOLD) response to emotional and neutral stimuli as well as a correlative analysis of BOLD activity at rest, which permits us to infer resting state functional connectivity.
3. Statistical analyses will be performed in SPM8 running on MATLAB 2009b. Initial data acquisition yields raw data in PAR/REC format that will be converted to .hdr and .img files via a reconstruction script in MATLAB. Data will be realigned, reoriented, normalized to a template brain, and smoothed. First-level analysis will contrast activity in brain regions associated with subsequently remembered versus subsequently forgotten images for each individual participant via t-test. Once this subsequent memory activation map has been generated, group-level analysis will compare brain regions associated with subsequent memory in the different groups: follicular vs. luteal, active pill vs. placebo, and naturally cycling vs. hormonal contraception users, again by t-test and with appropriate multiple comparison corrections.
4. Secondary analyses will include confirmation of group hormonal differences in saliva using commercially available hormonal assay kits. We will use optical ELISA to measure sex hormone levels and may elect to use an kinetic, enzymatic assay to measure salivary alpha-amylase levels.

## **SECTION 4: SUBJECTS (PERSONS/CHARTS/RECORDS/SPECIMENS)**

### **A. Number of Subjects (Charts/Records/Biospecimens)**

<ol style="list-style-type: none"> <li>1. Indicate the <b>maximum number of subjects to be recruited/consented</b> on this UCI protocol. This is the number of potential subjects you may need to recruit to obtain your target sample size. This number should include projected <b>screen failures and early withdrawals</b>. <i>Note: The IRB considers individuals who sign the consent form to be "enrolled" in the research.</i></li> <li>2. For <b>Mail/Internet surveys</b> include the number of people directly solicited.</li> <li>3. If the study involves use of <b>existing charts, records, biospecimens</b>, specify the maximum number that will be reviewed/tested to compile the data or the sample population necessary to address the research question.</li> </ol>
<ol style="list-style-type: none"> <li>1. We anticipate recruiting no more than 40 participants per group for a total of 120 participants.</li> <li>2. n/a</li> <li>3. We will collect no more than six saliva samples per subject.</li> </ol>
<ol style="list-style-type: none"> <li>4. Of the maximum number of subjects listed above, indicate the <b>target sample size</b> for the study. This is the number of subjects expected to complete the study or the number necessary to address the research question.</li> <li>5. <i>For social/behavioral research</i>, the maximum sample size is often similar to the target sample size. If the <b>maximum sample size</b> is significantly greater (i.e., <math>\geq 1.5x</math>) than the <b>target sample size</b> provide a justification.</li> <li>6. For studies where multiple groups of subjects will be evaluated, <b>provide a breakdown per group</b> (e.g. controls vs. experimental subjects; children vs. adults; by age group).</li> </ol>
<ol style="list-style-type: none"> <li>4. Target sample size is 20 per group.</li> <li>5. n/a</li> <li>6. We will recruit 20 early follicular women, 20 mid-luteal women, 20 placebo week hormonal contraception users, and 20 active week hormonal contraception users for a total of 80 participants.</li> </ol>
<ol style="list-style-type: none"> <li>7. For <b>multi-center research</b>, indicate the overall sample size for the entire study (across all sites).</li> </ol>
<p><input checked="" type="checkbox"/> Not applicable - This study is <u>not</u> a multi-center research study.</p>
<ol style="list-style-type: none"> <li>8. Explain <b>how the overall target sample size was determined</b> (e.g., power analysis; precision estimation).</li> <li>9. Demonstrate that the <b>target sample size will be sufficient</b> to achieve the study goal and should coincide with the statistical approach <b>described in Section 3B</b>.</li> <li>10. <b>Sources and information</b> of assumed group effects and variability should be supplied (e.g., pilot data; data from related literature).</li> </ol>
<p><b>8, 9.</b> Target sample size was determined on the basis of our previous research and that of others indicating the approximate sample size needed to obtain the key subsequent memory effect on which the study is built.</p> <p>Further, Hayasaka et al. (2007) used random field theory validated with Monte-Carlo simulations to show that a sample size of approximately 20 is sufficient for this kind of BOLD investigation.</p>

**10.**

N = 17	Andreano JM and Cahill L. (2010). Menstrual cycle modulation of medial temporal activity evoked by negative emotion. <i>NeuroImage</i> , 53(4): 1286-1293.
N = 12	Goldstein JM, Jerram M, Abbs B, Whitfield-Gabrieli S, and Makros N. (2010). Sex differences in stress response circuitry activation dependent on female hormonal cycle. <i>Journal of Neuroscience</i> , 30(2): 431-438.
N = 12	Goldstein JM, Jerram M, Poldrack R, Ahern T, Kennedy DN, Seidman LJ, Makris N. (2005). Hormonal cycle modulates arousal circuitry in women using functional magnetic resonance imaging. <i>Journal of Neuroscience</i> , 25(40): 9309-16. N = 12.
Recommends N = 20	Hayasaka S, Peiffer AM, Hugenschmidt CE, Laurienti PJ. (2007). Power and sample size calculation for neuroimaging studies by non-central random field theory. <i>Neuroimage</i> , 37(3): 721-730.
N = 18	Van Wingen GA, van Broekhoven F, Verkes RJ, Petersson KM, Bäckström T, Buitelaar JK, and Fernández G. (2008). Progesterone selectively increases amygdala reactivity in women. <i>Molecular Psychiatry</i> , 13: 325-333.

**B. Inclusion and Exclusion Criteria**

<ol style="list-style-type: none"> <li>1. Describe the <b>characteristics and provide justification</b> for inclusion of the proposed subject population. At a minimum include information about the age and gender of the study population.</li> <li>2. Describe <b>different subject groups</b> (e.g., students and teachers; control group and treatment group(s), children and adults) separately.</li> </ol>
<ol style="list-style-type: none"> <li>1. We will be including pre-menopausal women aged 18 or older. This population is experiencing hormonal changes that allow us to investigate the contributions of hormones without experimental manipulation.</li> <li>2. Half of the participants will be using hormonal contraception and half will not.</li> </ol>
<ol style="list-style-type: none"> <li>3. Provide the <b>inclusion and/or exclusion criteria</b> for the proposed subject population, as applicable.</li> </ol>
<p><input checked="" type="checkbox"/> Not applicable – This is not a clinical investigation and/or the characteristics of the population sufficiently describe the proposed subject population.</p>
<ol style="list-style-type: none"> <li>4. If <b>exclusion</b> is based on age, gender, pregnancy/childbearing potential, social/ethnic group, or language spoken (e.g., Non-English Speakers), <b>provide a scientific rationale</b>.</li> </ol>
<p>Because men do not have menstrual cycles or take hormonal contraception, we cannot include them in this investigation. Women who are no longer experiencing menstrual cycles due to their age or who have irregularities in their menstrual cycle will not be able to participate. We will be unable to include participants who do not speak English as we will be unable to communicate with them.</p>

## **SECTION 5: RECRUITMENT METHODS AND PROCESS**

### **A. Recruitment Methods**

Please check **all** applicable recruitment methods that apply to the study. Place an “X” in the bracket [ ] next to the recruitment method.

- [ ] This study involves no direct contact with subjects (i.e., use of existing records, charts, specimens)
- **Skip to Section 6.**

- [ x ] UCI IRB approved advertisements, flyers, notices, and/or media will be used to recruit subjects. **Submit advertisements for IRB approval.**
- Passive Recruitment - Potential subjects initiate contact with the study team.
  - **Complete Question 5B - Explain where recruitment materials will be posted.**

- [ ] The study team will recruit potential subjects who are unknown to them (e.g., convenience sampling, use of social networks, direct approach in public situations, random digit dialing, etc.)
- Active Recruitment – Researchers contact potential subjects.
  - **Complete Question 5B.**

- [ ] The UCIMC Clinical Trials web page will be used. **[Submit the UCIMC Standard Research Recruitment Advertisement for IRB approval.](#)**
- Passive Recruitment - Potential subjects initiate contact with the study team.
  - **Skip to Section 6.**

- [ ] The study will be listed on [Clinicaltrials.gov](http://Clinicaltrials.gov). **Note: This is required for all clinical trials.**
- Passive Recruitment - Potential subjects initiate contact with the study team.
  - **Skip to Section 6.**

- [ x ] The UCI Social Sciences human subject pool will be used. **[Submit the Social Science Human Subject Pool Recruitment Advertisement for IRB approval.](#)**
- Passive Recruitment - Potential subjects initiate contact with the study team.
  - **Skip to Section 6.**

- [ ] Study team members will contact potential subjects who have provided permission to be contacted for participation in future research studies.
- Active Recruitment – Researchers contact potential subjects.
  - **Complete Question 5B – Explain when and how these individuals granted permission for future contact; provide the IRB protocol numbers, if applicable.**

- [ ] Study team members will approach their own patients, students, employees for participation in the study.

- Active Recruitment – Researchers contact potential subjects.
- **Complete Question 5B.**

- [ ] Study team members will send UCI IRB approved recruitment materials (e.g., recruitment flyer, introductory letter) to colleagues asking for referral of eligible participants.\*
- Passive Recruitment – Potential subjects initiate contact with the study team or
  - Active Recruitment – Colleagues get permission from interested individuals to release contact information to researchers. Researchers contact potential subjects.
  - **For Active Recruitment, complete Question 5B.**

*\*Note: Additional requirements for using this recruitment method are included in the Protocol Narrative instructions.*

- [ ] Study team members will provide their colleagues with a UCI IRB approved introductory letter. The letter will be signed by the treating physician and sent to his/her patients to inform them about how to contact study team members.
- Passive Recruitment - Potential subjects initiate contact with the study team.
  - The IRB approved letter must be sent by the treating physician.
  - The study team does not have access to patient names and addresses for mailing.
  - **Skip to Section 6.**

- [ ] UCI study team members will screen UCIMC medical records to determine subject eligibility and approach patients directly about study participation.\*
- Active Recruitment – Researchers contact potential subjects.
  - **Complete Appendix T to request a partial waiver of HIPAA Authorization.**
  - **Complete Question 5B.**

*\* Note Additional requirements for using this recruitment method are included in the Protocol Narrative instructions.*

- [ ] Other Methods: <indicate the recruitment method(s) here>
- **Complete Question 5B, as applicable.**

## B. Recruitment Process

1. Based on the methods checked above, describe and provide **details of the recruitment process** (i.e. when, where, by whom and how potential subjects will be approached, e.g. screening medical charts, findings subjects during routine patient visits, etc.).
2. If you will recruit by mail, e-mail, or phone, explain how potential subjects' **contact information will be obtained**.
3. If active recruitment methods will be used (i.e., researchers will make direct contact with subjects for the purpose of recruitment), explain how the individual's **privacy will be protected**. *Note: This is not the same as confidentiality (see the [Privacy and Confidentiality web page](#)).*

Participants will be passively recruited through flyers and word of mouth. The flyers will be placed

around campus and in public spaces around the community with permission from business owners, such as coffee shops and grocery stores. An electronic version of the flyer will be used to advertise on Craigslist, a classified advertisement website.

## **SECTION 6: INFORMED CONSENT PROCESS**

1. Specify **how consent will be obtained** and describe the specific **steps for obtaining informed consent**.
2. Include information about **when and where** consent will take place and the **length of time** subjects will be given to decide whether they wish to participate.
3. If study team members will approach their own patients, students, or employees for participation in the study, explain what precautions will be taken to **minimize potential undue influence or coercion**, and **how compromised objectivity will be avoided**.
4. If children are involved in this study, please describe the **parental permission** process and the **child assent** process.
5. Be sure to **submit the consent/assent document(s)** with your e-IRB Application (i.e. Study Information Sheet, Recruitment script, Consent Form, etc.).
6. If this study involves the creation, use, or disclosure of Protected Health Information (PHI), specify the process for **obtaining HIPAA Authorization**. Be sure to submit the HIPAA Research Authorization form with your e-IRB Application.

### **Check all that apply:**

- Written (signed) informed consent will be obtained from subjects.** Signed informed consent, parental permission, and/or child assent will be obtained from subjects, as applicable. ***Describe the informed consent process.***
- Requesting a waiver of written (signed) informed consent** (i.e., signed consent will not be obtained). Informed consent, parental permission and/or child assent will be obtained from subjects, as applicable. **Explain how informed consent will be obtained. *Complete Appendix P.***
- Requesting a waiver of informed consent** (i.e., consent will not be obtained). ***Complete Appendix O. Skip to Section 7.***

**1, 2.** Written informed consent will be obtained when participants arrive at the Research Imaging Center for their first appointment.

**3, 4, 6.** n/a

7. **Non-English Speaking Participants:** In order to consent subjects who are unable to read and speak English, the English version of the consent form must be translated into appropriate languages once IRB approval is granted.

### **Check all that apply:**

- Not applicable - Only individuals who can read and speak English are eligible for this

study.

- ] The English version of the consent form will be translated into appropriate languages for non-English speaking subjects once IRB approval is granted. An interpreter will be involved in the consenting process. **Note: The IRB must officially stamp the translated consent forms.**
- ] Requesting a short form consent process. **Complete Appendix Q.**  
The short form process will be used for the following languages:
  - ] All non-English languages
  - ] All non-English languages except Spanish
  - ] Other languages (specify): <Type here>

## **SECTION 7: RISK ASSESSMENT AND POSSIBLE BENEFITS**

**Note: Review of the instructions for this section is strongly recommended.**

### **A. Risk Assessment**

Place an "X" in the bracket [ ] next to the level of review (based upon the investigator's risk assessment).

- ] This study involves greater than minimal risk to subjects and requires **Full Committee review.**
- ] This study involves no more than minimal risk and qualifies as **Expedited research.**  
**Provide justification below for the level of review and for the applicable Expedited Category(ies) that you have chosen:**

This study involves procedures of very little or no risk. The primary consideration is that we are asking participants to view images that by necessity are emotionally arousing. The consent form indicates that they may view unpleasant arousing material, and stipulates that they can stop at any time. The most graphic materials of the collection that we use have been sent to the IRB office and approved on at least 2 occasions in the past decade. The material is no more arousing than that seen by the subjects on many occasions in movies and television. Any subject who wishes to withdraw due to their concern about seeing the emotional material will be clearly told that they can do so and still receive full compensation. Having run over 2000 people using these materials, we have never had a single subject express concern about the materials to the IRB.

The only other potential concern involves the use of the MRI. When proper safety guidelines are followed, the MRI poses no physical risk whatsoever. Claustrophobia is a potential concern, thus participants with a history of it are asked not to participate. Participants are also made aware that they can terminate the scan at any time. Only trained personnel are permitted to enter the 3T trailer and strict safety precautions are followed at all times.

This study qualifies as expedited under Categories 3, 4, and 7:

(3.) Prospective collection of biological specimens for research purposes by noninvasive means.

(4.) Collection of specimens through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays and microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

(7.) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

## B. Risks and Discomforts

1. Describe the **risks/potential discomforts** (e.g., physical, psychological, social, economic) associated with **each** intervention or research procedure.
2. Describe the expected frequency (i.e., **probability**) of a given side effect or harm and its severity (e.g., mild, moderate, severe).
3. If subjects are **restricted from receiving standard therapies** during the study, describe the risks of those restrictions.
4. If collecting identifiable private information, address the risk of a **potential breach of confidentiality**.

1. It may be uncomfortable for participants to view the emotionally arousing images in our slideshow. It may be uncomfortable for participants to lie still in the scanner for the duration of the experiment. They may experience some anxiety associated with it.
2. Some emotional discomfort in viewing the images is relatively likely, however its severity is extremely mild. Any physical or emotional discomfort in lying in the scanner is very unlikely, and its severity is also considered to be mild.

5. Discuss what steps have been taken and/or will be taken to **prevent and minimize** any risks/ potential discomforts to subjects (address physical risks as well as other risks such as the potential for a breach of confidentiality). Examples include: designing the study to make use of procedures involving less risk when appropriate; minimizing study procedures by taking advantage of clinical procedures conducted on the subjects; mitigating risks by planning special monitoring or conducting supportive interventions for the study.

The potential risks of the experiment are minimal. Only trained personnel will be permitted in the 3T trailer. Participants will undergo two verbal metal screens, a visual inspection, and be taken through a metal detector before entering the scanner.

## C. Potential Benefits

1. Discuss the potential benefits that may accrue **directly to subjects**. **Note: Compensation is not a benefit. Do not include it in this section.**

] There is no direct benefit anticipated for the subjects.

**OR**

We believe there is a clear direct benefit to the subjects, at least to the ones that care. They learn something interesting about our knowledge of the brain, and about the scientific process. In our experience this is a good learning experience for them.

2. Describe the **potential societal/scientific benefit(s)** that may be expected from this study.

These experiments should help us better understand neural mechanisms of emotional memory, and thus be better positioned to treat the many disorders related to emotional memory, like PTSD.

#### **D. Risk/Benefit Assessment**

Explain why the study risks are reasonable in relation to the **potential benefits** to subjects and society.

The risks are very low, and the benefits to scientific knowledge are very high.

### **SECTION 8: ALTERNATIVES TO PARTICIPATION**

1. Describe the **standard or usual care** activities at UCI (or study site) that are available to prospective subjects who do not enroll in this study, as applicable.
2. Describe other **appropriate alternative procedures** to study participation that are available to prospective subjects.
3. If no alternatives exist, indicate that the only alternative is non-participation

] No alternatives exist. The only alternative to subjects is not to participate in the study.

**OR**

<Type here>

### **SECTION 9: ADVERSE EVENT REPORTING/MANAGEMENT AND COMPENSATION FOR INJURY**

#### **A. Adverse Events and Unanticipated Problems**

1. Indicate that you are familiar with **UCI's Adverse Events/Unanticipated Problems** reporting policy and procedures. See <http://www.research.uci.edu/ora/hrpp/adverseexperiences.htm> for details.

] **Although this study involves no interaction/intervention with research subjects** (i.e., involves the use of records, charts, biospecimens) an unanticipated problem may still occur (e.g., a breach in confidentiality), the researchers are aware of UCI's Unanticipated Problems involving Risk to Participants or Others reporting policy and procedures and will comply with this policy.

] **This study involves interaction/intervention with research subjects.** The researchers are aware of UCI's Unanticipated Problems involving Risk to Participants or Others reporting policy and procedures and will comply with this policy.

2. **If this study involves interaction/intervention with research subjects**, explain how the research team will **manage adverse events and unanticipated problems** that may occur during the study or after completion of the study (i.e., provide a plan).

] Not applicable - This study involves **no interaction/intervention** with research subjects (i.e., involves the use of records, charts, and/or biospecimens).

OR

<Type here>

## B. Compensation for Injury

For **Full Committee protocols**, explain how costs of treatment for research related injury will be covered.

] Not applicable - This study involves no more than minimum risk and qualifies as **Expedited research**.

] Researchers are familiar with and will follow UC policy regarding treatment and compensation for injury. If subjects are injured as a result of being in the study, UCI will provide necessary medical treatment. The costs of the treatment may be covered by the University of California, the study sponsor, or billed to subject or the subject's insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury.

] Other: <Type here>

## **SECTION 10: PARTICIPANT COSTS**

1. If subjects or their insurers will be charged for study procedures, **identify and describe those costs**.
2. Explain why it is **appropriate to charge those cost** to the subjects or their insurers. Provide supporting documentation as applicable (e.g., FDA Device letter supporting charges).

Not applicable - This study involves no interaction/intervention with research subjects (i.e., involves the use of records, charts, biospecimens).

There are no costs to subjects/insurers.

OR

<Type here>

## **SECTION 11: PARTICIPANT COMPENSATION AND REIMBURSEMENT**

1. If subjects will be compensated for their participation, explain **the method/terms of payment** (e.g., money; check; extra credit; gift certificate).
2. Describe the **schedule and amounts of compensation** (e.g., at end of study; after each session/visit) including the total amount subjects can receive for completing the study.
3. Specify whether subjects will be **reimbursed for out-of pocket expenses**. If so, describe any requirements for reimbursement (e.g., receipt).

**Note:** *Compensation should be offered on a prorated basis when the research involves multiple sessions.*

Not applicable - This study involves no interaction/intervention with research subjects (i.e., involves the use of records, charts, biospecimens).

No compensation will be provided to subjects.

No reimbursement will be provided to subjects.

OR

Participants will receive \$60 for participating, prorated for attending only the first session to \$40.

## **SECTION 12: CONFIDENTIALITY OF RESEARCH DATA**

1. Indicate all identifiers that may be included in the research records for the study. Check all that apply:

**Note:** *If this information is being derived from a medical record; added to a medical record; created or collected as part of health care, or used to make health care decisions it qualifies as PHI under HIPAA. The subject's HIPAA Research Authorization is required or a waiver of HIPAA Authorization must be requested (Appendix T).*

- No subject identifiers are obtained (i.e., researchers will not collect information that can link the subjects to their data)

**OR**

- |   |  |  |
|---|--|--|
| <input checked="" type="checkbox"/> Names         | <input type="checkbox"/> Social Security Numbers     | <input type="checkbox"/> Device identifiers/Serial numbers |
| <input type="checkbox"/> Dates*                   | <input type="checkbox"/> Medical record numbers      | <input type="checkbox"/> Web URLs                          |
| <input type="checkbox"/> Postal address           | <input type="checkbox"/> Health plan numbers         | <input type="checkbox"/> IP address numbers                |
| <input checked="" type="checkbox"/> Phone numbers | <input type="checkbox"/> Account numbers             | <input type="checkbox"/> Biometric identifiers             |
| <input type="checkbox"/> Fax numbers              | <input type="checkbox"/> License/Certificate numbers | <input type="checkbox"/> Facial Photos/Images              |
| <input checked="" type="checkbox"/> Email address | <input type="checkbox"/> Vehicle id numbers          | <input type="checkbox"/> Any other unique identifier       |

- Other (Specify all): [<Type here>](#)

\* birth date, treatment/hospitalization dates

2. Explain how data will be **recorded**.

**Check all that apply:**

- Paper documents/records  
 Electronic records/database  
 Audio recording  
 Video recording  
 Photographs  
 Biological specimens  
 Other(s) (specify): [<Type here>](#)

3. Indicate **how data will be stored, secured** including paper records, electronic files, audio/video tapes, biospecimens, etc.

**Note:** *If the research data includes subject identifiable private information and/or Protected Health Information, the storage devices or the electronic research files must be encrypted.*

**Electronic Data (check all that apply):**

- Coded data; code key is kept separate from data in secure location.  
 Data includes subject identifiable information. **Note:** *Encryption software is required.* (Provide rationale for maintaining subject identifiable info): [<Type here>](#)  
 Data will be stored on secure network server.  
 Data will be stored on stand alone desktop computer (not connected to network/internet)  
 Other (specify here): [<Type here>](#)

**Hardcopy Data, Recordings and Biospecimens (check all that apply):**

- Coded data; code key is kept separate from data in secure location.  
 Data includes subject identifiable information (Provide rationale for maintaining subject identifiable info): [<Type here>](#)  
 Data will be stored in locked file cabinet or locked room at UCI/UCIMC.  
 Data will be stored locked lab/refrigerator/freezer at UCI/UCIMC.  
 Other (specify here): [<Type here>](#)

**Data on Portable Devices:**

4. Describe the **portable device(s) to be used** (e.g. laptop, PDA, iPod, portable hard drive including flash drives).
5. Specify whether **subject identifiable data** will be stored on the device. If so, **justify why** it is necessary to store subject identifiers on the device.

***Note:** Only the “minimum data necessary” should be stored on portable devices as these devices are particularly susceptible to loss or theft. If there is a necessity to use portable devices for initial collection of identifiable private information, the portable storage devices or the research files **MUST BE ENCRYPTED**, and subject identifiers transferred to a secure system as soon as possible.*

Not applicable – No study data will be maintained on portable devices.

**OR**

Data will be stored on password protected laptops in many cases. No subject identifiable data will be stored in this way.

**Data Access:**

6. Specify who, besides the entities listed below, will have **access to subject identifiable private data and records**.
7. If there is a **code key**, specify who on the research team will hold the key, and who will have access to the key.
8. If publications and/or presentations will include **subject identifiable information**, specify where the data will be **published and/or presented** and address how the study team will obtain permission from subjects.

***Note:** Authorized UCI personnel such as the research team and the IRB, the study sponsor (if applicable), and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to study records to protect subject safety and welfare. Any study data that identifies the subjects should not be voluntarily released or disclosed without the subjects’ separate consent, except as specifically required by law. Publications and/or presentations that result from this study should not include subject identifiable information; unless the subject’s separate consent has been obtained.*

Not applicable – No subject identifiers will be collected.

Not applicable – Only the entities listed above will have access to subject identifiable private data and records.

No one besides study personnel will have access to the data.

**Data Retention:**

9. Explain **how long subject identifiable research data** will be **retained**. The data may include a code with a separate code key or the data may include subject identifiers.

**Notes:**

- *If more than one of the options below is applicable [e.g., the study involves children], records should be kept for the longer period.*
- *Research documentation involving Protected Health Information (PHI) should be retained for*

*six years (e.g., IRB documentation, consent/assent forms – **NOT** the actual PHI). Investigators must destroy PHI at the earliest opportunity, consistent with the conduct of this study, unless there is an appropriate justification for retaining the identifiers or as required by law.*

- Not applicable. No subject identifiable research data will be retained.
- Destroy once data collection is completed
- Destroy at the earliest opportunity, consistent with the conduct of this research. Specify timeframe: [<Type here>](#)
- Destroy after publication/presentation
- Maintain for approximately [<Type here>](#) years. (e.g., 3 months, etc.)
- Maintain in a repository indefinitely. Other researchers may have access to the data for future research. Any data shared with other researchers, will not include name or other personal identifying information. Note: **Appendix M is required.**
- Research records will be retained for seven years after all children enrolled in the study reach the age of majority [age 18 in California] as this study includes children .
- Research records will be retained 25 years after study closure as this study involves in vitro fertilization studies or research involving pregnant women.
- As this is a FDA regulated study, research records will be retained for two years after an approved marketing application. If approval is not received, the research records will be kept for 2 years after the investigation is discontinued and the FDA is notified.
- Other: [<Type here>](#)

**Data Destruction:**

- 10. If audio or video recordings will be taken, specify the **timeframe for the transcription and/or destruction of the audio and video recordings.**
- 11. If photographs will be collected, specify the **timeframe destruction of photographs.**

- Not applicable – No audio/video recordings or photographs will be collected.
- Audio or video recordings transcribed; specify time frame: [<Type here>](#)
- Audio or video recordings destroyed; specify time frame: [<Type here>](#)
- Audio or video recordings maintained indefinitely
- Photographs destroyed; specify time frame: [<Type here>](#)
- Photographs maintained indefinitely

**Certificate of Confidentiality:**

- 12. Specify whether a Certificate of Confidentiality (COC) has been or will be requested from the NIH. If yes, explain in what situations personally identifiable information protected by a COC will be disclosed by the UCI study team.

**Note:** *If the COC has been secured a copy of the COC Approval Letter should accompany the IRB application or be provided to the IRB upon receipt.*

Not applicable – No COC has been requested for this study.

**OR**

<Type here>