Title: Examining the Role of Pain in the Link Between Early Childhood Adversity and Psychopathology

NCT Number: NCT06445712

Document Date: 12/17/2025

Pain Project

PI: Susan Perlman
IRB ID #: 202312107

Project Details

1. Demographics

1.1 Project Title:
Examining the Role of Pain in the Link Between Early Childhood Adversity and Psychopathology

1.2 Short Title (required):
Pain Project

1.3 Project is primarily:
Biomedical

1.3.a Does this study require review under ICH-GCP?
No

1.4 Type of Study:
Other Interventional

1.4.a Is your research study one 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 (NIH clinical trial definition).
Yes

1.5 Select how you plan to obtain consent:
- Sign a consent document or a consent letter
- Letter or information sheet with no signature

2. Source(s) of Support

2.1 Source(s) of Support

Type/Source	Grant Title	Name of PI on Grant
Federal Agency NIH, NCATS	Washington University Institute of Clinical and Translational Sciences	William Powderly

Attachment Name	Category	Version	Date Attached
informed consent 2025 mod.rtf	Funding Source Status of Other	2	02/03/25
Funding Memo.pdf	Funding Source Status of Other	1	12/14/23

3. Research Team

3.1 Principal Investigator

Name	E-mail	Title	School
Susan Perlman	perlmansusan@wustl.edu	Prof of Psychiatry (Child)	School of Medicine

3.2 Team Members

Research Team Members

Role	Name	Role Desc	Student	Email	Title	School	Department	Contact	Consent Process Involvement	Epic Contact Person
PI	Susan Perlman, PHD		No	perlmansusan@wustl.edu	Prof of Psychiatry (Child)	School of Medicine	Psychiatry	Yes	Yes	Yes
	Giulia Bottomley, BA, Psychology			bgiulia@wustl.edu	Neuroimaging Research Technician II	School of Medicine	Psychiatry	No	Yes	No
	Kendyll Klingensmith, BA			kendyll@wustl.edu	Neuroimaging Research Technician II	School of Medicine	Psychiatry	No	Yes	No
	Bedilia Mata-Centeno, BA			bedilia@wustl.edu	Neuroimaging Research Technician II	School of Medicine	Psychiatry	No	Yes	No
	Linda Ortega, BA			linda.o@wustl.edu	Clinical Research Coordinator I	School of Medicine	Psychiatry	No	Yes	No
	Khalil Thompson, PHD		No	khalilt@wustl.edu	Postdoc Research Associate	School of Medicine	Psychiatry	No	No	No
	Yiwen Zhang, PHD			zyiwen@wustl.edu	Postdoc Research Associate	School of Medicine	Psychiatry	No	No	No

Team Member Financial Interest

Name	Financial Interests
Susan Perlman, PHD	none
Giulia Bottomley, BA, Psychology	none
Kendyll Klingensmith, BA	none
Bedilia Mata-Centeno, BA	none
Linda Ortega, BA	none
Khalil Thompson, PHD	none
Yiwen Zhang, PHD	none

4. Other Institutional Reviews/Requirements

4.1 Do any of the objectives of this study involve:

- the diagnosis of cancer,
- the prevention of cancer,
- screening for cancer,
- the treatment of cancer,
- the treatment of pre-cancerous conditions,
- the treatment of conditions that increase a person's risk of developing cancer,
- the support of patients with cancer or their caregivers, or
- the evaluation of healthcare processes involving any of the above?

No

4.2 Are more than 30% of the patients involved in this study likely to have an active cancer diagnosis?
No

4.3 Will any subject be asked to undergo a radiation therapy procedure (including external beam therapy, brachytherapy, or radiopharmaceutical therapy)?
No

4.4 Does your study involve the administration of non therapeutic radiopharmaceuticals (radioactive drugs) for research purposes?
No

4.5 Will any participant be asked to undergo any of the following:

- a standard radiology procedure involving ionizing radiation (includes X-rays, fluoroscopy, DEXA, CT)
  OR
- a standard nuclear medicine examination with FDA-approved radioactive drugs (including bone scans, radionuclide ventriculogram (RVG or MUGA), myocardial perfusion imaging, FDG-PET)
- **DO NOT include a nuclear medicine examination performed with the investigational radioactive drug(s) listed above in Question 4.4.**
- DO NOT include MRI or ultrasound

No

4.6 Will the study involve any of the following activity **PROSPECTIVELY** at WUSM or any BJC hospitals, even if subjects or their insurance will not be billed for the item or service, and regardless of the study funding source (including studies with departmental or no funding)?

- Procedures, tests, examinations, hospitalizations, use of Pathology, Laboratory, Cardiology, or Radiology services, use of clinic facilities or clinical equipment, or any patient care services, including services conducted in the Clinical Research Unit; or
- Physician services or services provided by non-physicians who are credentialed to bill (ARNPs, Physician Assistants, etc.)

No

4.7 Does this study involve administration of recombinant or synthetic nucleic acids (gene therapy or mRNA vaccines) or microorganisms?
No

4.8 Does this study involve the use of human embryonic stem cells or human induced pluripotent stem cells?
No

4.9 Does this study involve research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero?
No

4.11 Will the study require any of the following from WUSM Pathology dept, BJH or SLCH clinical labs:

- Patient specimens, tissue (fresh, fixed or frozen) or retained microbial specimens
- Pathology services, including processing tissue, not performed for routine patient care, or digital pathology images
- Cellular therapy and apheresis
- Diagnostic testing not performed for routine patient care or requiring procedure changes

No

4.12 Will a Certificate of confidentiality be used for this research?
Yes, certificate automatically issued by funding agency

4.13 Does this project need to be registered on ClinicalTrials.gov?
No

4.14 Title that should appear in Epic (and will be visible in the patient medical record):
CARE Project Extension

4.15 Select one person from the study team that should appear in Epic as the contact person for this study:
Susan Perlman

4.16 Do you want to request that an ordering tool be built for your study in Epic?
No

4.17 Would you like to submit a request for the Epic team to consider your study for the use of BPA (Best Practice Advisory) in Epic?

No

4.18 Would you like to submit a request for the Epic team to build your questionnaires in Epic for the purposes of recruitment?
No

4.19 Will any external monitors require access to this study in Epic?
No

4.21 Mark all that apply to your study:

1. Protocol

1.1 Is there a separate, written protocol that will be submitted in addition to this form? (Note: a grant application is not considered to be a protocol)
Yes

Attachment Name	Category	Version	Date Attached
CARE Extension Project IRB Protocol_updated 1.23.2025.rtf	Intervention: Separate Written Protocol	9	02/03/25

1.1.a Who initiated/provided the protocol?
WashU Investigator

1.1.b Protocol#:

1.1.c Protocol Version#:

1.1.d Protocol Date
12/13/2023

1.1.e Provide a list of the amendments for this study (this may be left blank if none). Any amendments previously listed should not be removed.

1.2 Select up to three key words below that best describe this research study:
- Psychiatry
- Psychology

1.3 Provide a short summary/abstract of the purpose and procedures of the study proposed in this IRB application.

- DO NOT include information on studies not proposed in this application.
- Use LAY terminology only. This must be easily understandable by IRB community members and nonscientists.
- DO NOT cut and paste technical abstracts from source of support applications that may not be understood by a general audience.

This study seeks to investigate the impacts of adversity in early life pain and psychopathology symptoms in middle childhood. Specifically, we will investigate children aged 5 – 9.5 years old who have experienced a parental separation, divorce, or breakup, and a matched control group. We will use a Cold Pressor Test to asses experimental pain sensitivity with and without parental support. Additionally, we will use neuroimaging methods including, an optional fNIRS protocol to characterize changes in patterns of brain activities. We will also employ the use of surveys and questionnaires, to investigate pain and psychopathology symptoms, as well as parental support. By imaging the neural circuitry supporting these different aspects in children and their caregivers, the proposed research will explore the impacts of family related stress on the developing brain.

1.8 Check all materials/methods that will be used in recruiting participants:
- Ads/Brochures/Posters/News Release/Fliers
- Email or letters
- Other Research Study - Child Affect and Resilience to Experiences Study- IRB#: 202007029 We will contact existing CARE Study participants 1 year post-completion of their final visit (V2), or those who have expressed interest in our ongoing studies for the CARE Study extension. Their contact information, including name, phone number, and email address will be obtained through the CARE Study's password-protected subject database. Only authorized research staff will be permitted to access this information and make conac
- Existing Registry/database - Laboratory Research Registry, IRB ID# 201910090
- Medical Records or Other PHI

Attachment Name	Category	Version	Date Attached
Pain project email contact_updated 2025.rtf	Recruitment: Email or letters	3	02/03/25
CAREx Recruitment Flyer.pdf	Recruitment Materials: Ads/Brochures/Posters/News Release/Fliers	3	01/29/25

1.8.a Specify the facility that holds medical records or other PHI:
- Washington University

1.8.b List the individual data elements you will access from the medical records (or other source of PHI) to identify potential participants for recruitment and, if applicable, any individual data elements that you will include on a screening log prior to consent.
We will be accessing participants' names, phone number, and email addresses, which were previously collected during other ongoing studies in the lab (CARE Study, P-CAT Study, Research Registry).

1.8.c What is the plan for individual identifiers obtained to identify participants and, if applicable, those identifiers maintained on a screening log prior to consent?
Identifiers for those who do NOT enroll will be destroyed at the earliest opportunity, consistent with the conduct of the research (for example when recruitment and enrollment are completed.)

1.8.d Does the research team agree that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the study, or for other research for which the use or disclosure of the requested information would be permitted by the HIPAA Privacy Rule?
Yes

1.10 Describe where the consent discussion will occur (check all that apply):
- Private room or area

1.11 Participants and/or their legally authorized representative will have (check all that apply to the consent process and explain process in Question 1.12 below):

- As much time as they desire to consider enrolling in the study, including:
    - An opportunity to thoroughly review the consent materials with knowledgeable members of the research team, and with family and/or friends as appropriate
    - Sufficient time to have all of their questions answered

1.12 Provide a description of the enrollment and consent process in sequential order and address EACH of the bulleted points below:

- Describe each study population separately, including any control populations or those enrolled under waivers of consent
- Describe when recruitment and consent materials are used. This includes the use of social media or other communication platforms
- Describe the use of any mobile devices, software platforms or 3rd party vendors
- If applicable, justify why participants will only have a limited amount of time to consider enrolling in the study.
- If eConsent will be used to obtain an electronic signature, describe how the eConsent will be presented to participants, how their questions will be answered and how the participant will receive a copy of the final, signed consent
- Describe the steps that will be taken by the research team to minimize the possibility of coercion or undue influence during the consent process

Participants will be recruited through the ongoing CARE Study or through our Research Registry. Participants will be contacted following 1 year of their final CARE R01 visit (V2) for an additional visit (V3), or If they have expressed interest in our labs ongoing work. Both participants from the CARE R01 stress and control group will be contacted. Initial contact will be made through both email and phone, with the approved flyer included. The flyer will be used as a supplemental graphic to aid participants in understanding key points about the extension study.
Participants will be electronically sent the link to consent info sheet (a short consent to allow us to fill out questionnaires prior to their lab session) on REDCap. The full consent form will then be emailed ahead of the laboratory session for the participant to review. The participant will have ample time to review the consent form and formulate questions before the laboratory session where the consent form will be signed in person.
Families who qualify and are interested in participation will be scheduled for their laboratory visit. Parents will be given as much time as they would like to decide whether to make an appointment for the laboratory visit, however, it will be noted that this visit must occur while their children remain within the age range or no longer than 6 months after their CARE V2 visit. At the start of the laboratory visit, participants will be guided through the consent form by the staff member administering consent procedures. Note that the family will already have had access to the consent form as our consent form will be emailed ahead of potential participation. After discussing informed consent, the staff member will note that they can decide to participate today or consider participation at a later date. The staff member will remind the family that their decision to participate (or not participate) will have no effect on the care they may be receiving through Washington University Medical Center. The staff member will ask the family if they would like to be left alone in the room to discuss participation.
In the unlikely event that a parent completes all or part of questionnaires but does not show up for their laboratory visit, the family will be contacted twice. If the family does not respond to contact or says that they are no longer interested in participation, their questionnaire responses will be destroyed. No data from any family will be exported from RedCap to laboratory databases until informed consent is signed in the laboratory. If a family chooses not to sign consent, all questionnaire data will be destroyed as described previously.
Participants are able to stop participating at any time. In the event that a participant declines to continue participating, the session will be stopped and the participant will be compensated for their time in proportion to how much of the session was completed (e.g., if 1 hour of a 3 hour session was completed, the participant would be compensated $25). There are no potential adverse consequences to ending participation before the end of the study, thus no further follow up or care is needed should the participant opt out of further research activity with the lab.
Participant data will be kept for participants who have both consented to participate in the study and have completed at least 1 component of the study. In the unlikely event that a participant withdraws before study completion, partially completed measures or measures for which consent was withdrawn will be destroyed.

1.14 Will participants be randomized?
Yes

1.15 Will any of the following be used to collect information from the participant or others?

- Screening questions or screening/eligibility questionnaires
- Surveys
- Questionnaires
- Stimuli
- Any other written assessments

Yes

Attachment Name	Category	Version	Date Attached
PHQ-9_PatientHealthQuestionnaire.pdf	Subject Data Collection Instruments	1	05/31/24
ASRI 4R.pdf	Subject Data Collection Instruments	1	05/31/24
PRQ.docx	Subject Data Collection Instruments	1	05/31/24
AssessmentOfParentAndChildAdversity (APCA).pdf	Subject Data Collection Instruments	1	02/26/24
Difficulties in Emotion Regulation Scale.pdf	Subject Data Collection Instruments	1	02/26/24
Drug Use Screening Inventory (DUSI-R).pdf	Subject Data Collection Instruments	1	02/26/24
GAD-7_GeneralizedAnxietyDisorders.pdf	Subject Data Collection Instruments	1	02/26/24
ACES_PEARLS.pdf	Subject Data Collection Instruments	1	02/26/24
Pain Sensitivity Questionnaire.pdf	Subject Data Collection Instruments	1	02/26/24
Macarthur SES_Demographics.pdf	Subject Data Collection Instruments	1	02/26/24
Temperament in Middle Childhood (TMCQ).pdf	Subject Data Collection Instruments	1	02/26/24
PROMIS_Parent_Proxy_Numeric_Rating_Scale_v1.0_-_Pain_Intensity_1a_1-8-2021.pdf	Subject Data Collection Instruments	1	02/26/24
Questionnaire of Unpredictability in Childhood (QUIC-parent).pdf	Subject Data Collection Instruments	1	02/26/24
Coping with Children's Negative Emotions (CCNES).pdf	Subject Data Collection Instruments	1	02/26/24
PROMIS_Parent_Proxy_Bank_v2.0_-_Pain_Interference_7-29-2016.pdf	Subject Data Collection Instruments	1	02/26/24
CONFLICT TACTICS SCALE.docx	Subject Data Collection Instruments	2	04/24/24

MacArthur Health and Behavior Questionnaire (HBQ).pdf	Subject Data Collection Instruments	1	02/26/24
Perceived Stress Scale (PSS).pdf	Subject Data Collection Instruments	1	02/26/24
PROMIS_Parent_Proxy_SF_v1.0_-_Pain_Behavior_8a_10-25-2019.pdf	Subject Data Collection Instruments	1	02/26/24

1.16 Does this project involve creating any audio, video, or photographs?
Yes

1.17 Does the study include any form of deception (e.g., providing participants with false information, misleading information, or withholding information about certain study procedures)?
Examples:

- Procedure includes a cover story that provides a plausible but inaccurate account of the purposes of the research.
- Participants will be provided with false information regarding the particular behaviors of interest in the research.
- Procedures include a confederate pretending to be another participant in the study.
- Participants will be told that the research includes completion of a particular task, when in fact, that task will not be administered.
- Study is designed to introduce a new procedure (or task) that participants are not initially told about.
- Participants are interacting with computer programs or artificial intelligence when told they are interacting with another person.

No

1.18 Indicate any payments or reimbursements to participants (check all that apply)
- Forte Debit Card

1.19 Does this study have a plan to have an individual or committee review combined data from all participants on a periodic basis (such as summary or aggregate safety and/or efficacy data)?
No

1.20 What have you done to minimize any risks?
- Psychological consultation and/or referrals readily available
- Emergency medical treatment is immediately available

1.25 Will any data from this project be stored for use in future research studies?
Yes - contribution for future use is mandatory for participation in the study

1.26 Does this project involve the collection or use of biological samples or genetic data?
Yes

1.26.a Will genetic/genomic research occur as part of this study?
No

1.26.d Will biologic samples or genetic data be stored for future research?
Yes - contribution for future use is mandatory for participation in the study

1.26.e Will genetic/genomic research occur as part of future research?
No

1.26.f Will participants be able to request at a later time that the biological samples or genetic data be destroyed?
Yes

1.27 Are you requesting institutional certification to contribute human data or samples to a repository or database for broad sharing (public or restricted access)?
No

2. Participants

2.1 Will there be any adult participants?
Yes

2.1.a How many adult participants do you expect to consent or enroll under a waiver for this project?
80

2.1.b What is the age of the youngest adult participant?
18.0

2.1.c What is the age of the oldest adult participant?
No age limit

2.2 Will there be any minor participants?
Yes

2.2.a How many minor participants do you expect to consent or enroll under a waiver for this project?
80

2.2.b What is the age of the youngest minor participant?
5.0

2.2.c What is the age of the oldest minor participant?
9.5

2.3 Will there be any emancipated minor participants?
No

2.4 You may indicate in the table below either a single, or multiple approaches for obtaining assent from minors in your study.

- If you will use the same method for all minors, you only need to enter one row.
- If you will use different assent methods depending on age, add multiple rows, breaking the minors into different age range(s)
- Indicate in each row the appropriate assent method(s) for each age range. Be sure to include the entire age range of your minor population.

Youngest	Oldest	Obtain Assent?	Assent Method(s)	Rationale
6.5	9.5	Yes	• Sign an assent document	Participants will be read a simple assent statement stating that they are free to stop at any time. They will sign their name if they agree.

2.5 Will any minors reach the age of majority during their participation in this study?
No

2.6 Will any of the participants enrolled be in foster care or Wards of the state?
No

2.7 Do you plan to recruit/enroll non-English speaking people?
No

2.8 Do you propose to enroll any of the following in this study as participants?

- Employee of the PI or employee of a research team member
- Individual supervised by PI or supervised by member of research team
- Individual subordinate to the PI or subordinate to any member of the research team
- Student or trainee under the direction of the PI or under the direction of a member of the research team

Yes

2.8.a Provide justification for why these participants must be included in the study.
In the original CARE study, colleagues of the PI (not directly under the supervision of the PI or subordinate to the PI) enrolled their children. Dr. Perlman does not have any direct hiring/firing or supervisory power over these colleagues. They saw a study advertisement, or heard Dr. Perlman speak about the study, and chose to enroll their child. Dr. Perlman also enrolls her own children in the research of her colleagues. In the case that a colleague participates in the current study, Dr. Perlman will not be involved in their data collection and will not access their identifiable data. Dr. Perlman will not be involved in the consenting process, allowing colleagues to make choices to participate or not participate without potential feelings of coercion.

2.9 Is this project about pregnant women?
No

2.10 Will this project involve fetuses?
No

2.11 Does this project involve the use of fetal tissue from any source?
No

2.12 Does this project recruit adult participants who may be incompetent or have limited decision-making capacity on initial enrollment into the study?
No

2.13 Does this project involve prisoners as participants?
No

3. Performance Sites

3.1 Indicate type of site(s) where research will occur (check all that apply):
- Academic Institution

3.2 Where will project procedures take place (check all that apply)?
- School of Medicine

3.3 Is this project also being conducted by other researchers at their own sites (e.g. a multi-site collaborative project)?
No

4. Drugs/Devices

4.1 Does this project involve:

	Yes	No
Drug(s) (including radioisotopes)	○	●
Use of contrast agent(s)	○	●
Other substance injected, ingested, or applied to the body	○	●
Testing a Device (Including companion devices, software, mobile health devices, assays, not FDA approved or outside approved indications, etc.)	○	●
Combination product (as determined by the FDA - must have FDA documentation identifying this as a combination product)	○	●

4.2 Does this project involve a drug washout (asking participant to stop taking any drugs the participant is currently taking)?
No

4.3 Will any participants receive a placebo in place of standard therapy?
No

5. Privacy & Confidentiality

5.1 Indicate your plans to protect the privacy interests of the participants during the conduct of the study (check all that apply):

- Only the minimum necessary private information is collected for the purposes of the study
- Any procedures or interventions conducted as part of the study will be conducted in private setting to the extent possible
- Recruitment/consent will occur in a private setting
- Participants will be able to ask questions in a private setting

5.2 Are you collecting or using the Social Security Number of any participants for any purpose?
Yes

5.2.a Provide the intended usage of SSN:

- To provide compensation to participants

5.3 Project uses paper or hard copy consents, surveys, data collection forms, research subject binders, or other hard copy materials (check all that apply):
Yes

- All materials are stored in secured environment
- Access is limited to research team members only

5.4 Project collects, stores and/or transmits electronic data on mobile devices, desktop computers, servers including cloud servers, email, or any other information in electronic form (check all that apply):
Yes

- Data in Redcap
- Password protected
- Access is limited to research team only

5.5 Project collects or uses biologic specimens (check all that apply):
Yes

- Stored in secured environment
- Access is limited to research team only
- Coded and the identifiers or key is stored separately from the data
- Transported securely/shipped with tracking mechanism

5.6 Identify any additional protections in place for data and or samples (check all that apply):

- Formal research staff training process

Statistical Analyses: All analyses will be conducted with data collected from the timepoint of our assessment of pain sensitivity. However, we will also leverage our longitudinal data of early-life adversity, psychopathology, and biological measures aggregating the data using the worse or maximum, the timepoint prior to our measurement of pain sensitivity, and the slope up to the timepoint of assessment of pain sensitivity. The relatively small sample size of this project (n=40) is expected to produce preliminary effect sizes to guide hypotheses for future NIH applications.

Aim 1: To test the relationships between pain and both early-life adversity and psychopathology symptoms.

Hypothesis 1: Early-life adversity will predict both higher pain sensitivity and psychopathology symptoms. Hypothesis 2: Pain and psychopathology symptoms will be positively associated. Analysis: We will examine early-life adversity, based primarily on the ACES and RDAS, with both pain sensitivity and psychopathology symptoms individually. We will use Pearson's correlations between each of our measures of pain (temperament, self and parent-reported pain impairment, and experimental pain sensitivity).

Aim 2: To examine the relationship between emotion dysregulation and pain.

Hypothesis 1: Biological and parent-reported emotion dysregulation will be positively associated with pain sensitivity. Analysis: We will examine the relationship of salivary cortisol and parent-reported emotion dysregulation with multi-modal assessments of pain using Pearson's correlations. We will use also use regression analyses with leading factors of pain identified from variable reduction methods as dependent variables, and each of the emotion regulation measures as independent variables and control for covariates.

Aim 3: To experimentally test the role of parental support in the relationships between early-life adversity, biological and parent-reported emotion dysregulation, pain, and psychopathology.

Hypothesis 1: Parental support, assessed through parent-report of attachment and parent-child neural and behavioral synchrony measured through fNIRS and video coding, will buffer the effects of early-life adversity on pain sensitivity and psychopathology symptoms. Analysis: We will examine three measures of parent-support 1) the difference in child report of experimental pain sensitivity (pain intensity ratings and cold pain tolerance) and cortisol from the parent hand-holding vs. alone conditions in the parent-report cold pressor task from the current project; 2) parent report of parental support primarily using the CCNES and PRQ; and 3) dyadic behavioral and brain synchrony from the CARE R01. We will employ multivariate regression models to test the effects of early-life stress and emotion dysregulation, individually, as an independent variable on both pain sensitivity and psychopathology as the dependent variables with parent-support variables as a moderator.