VA | U.S. Department of Veterans Affairs

National Center for PTSD
POSTTRAUMATIC STRESS DISORDER

CHOIR
Center for Healthcare Organization and Implementation Research

Neurosteroids and PTSD during Select Menstrual Cycle Phases

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Visiting Student, Lady Margaret Hall

Veteran Affairs Intern

Dr. Suzanne Pineles

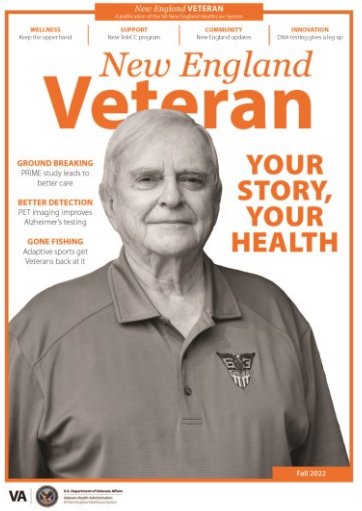
About me

- Senior at Wellesley College
  - MIT, Cross-registered student
  - BA in Neuroscience, pre-medicine
  - Boston, MA and Charleston, SC in the US
  - Interested in pursuing M.D. or M.D./PhD programs
    - Women's Health
    - Veteran Affairs Program in Boston

My Research Training

Medical University of South Carolina:
Optogenetics Neuroscience Lab
Stem Cell Lab, Type 1 Diabetes

Boston Children's Brigham and Women's Hospital
Harvard Medical School:
Cardiology and Diabetes, Pollin Summer Scholar

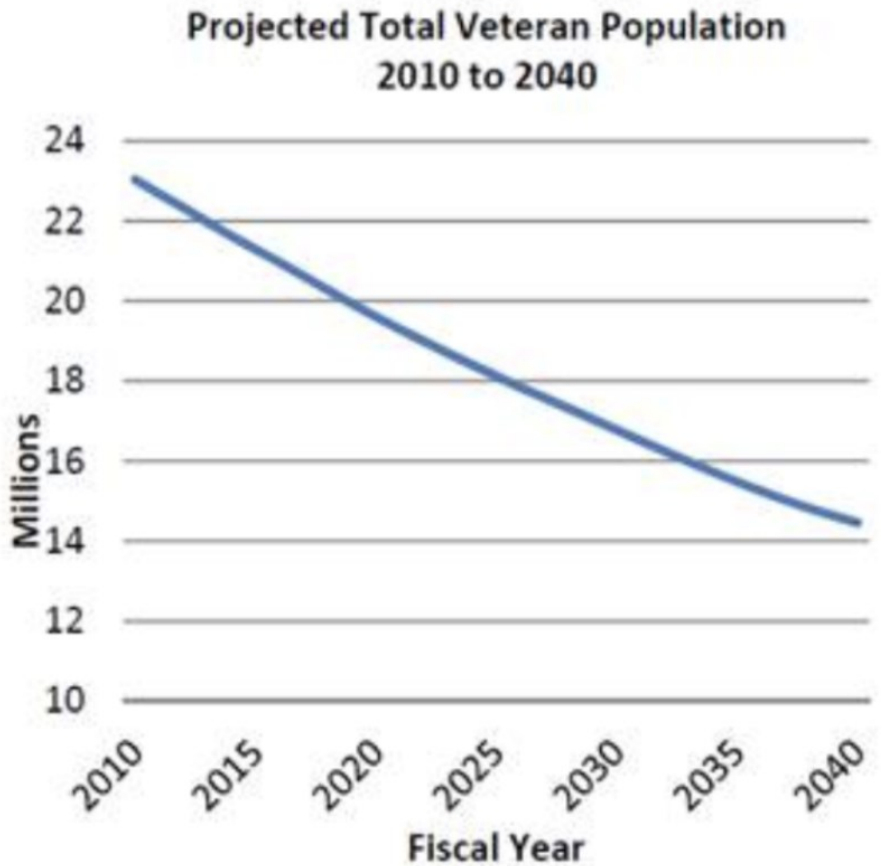


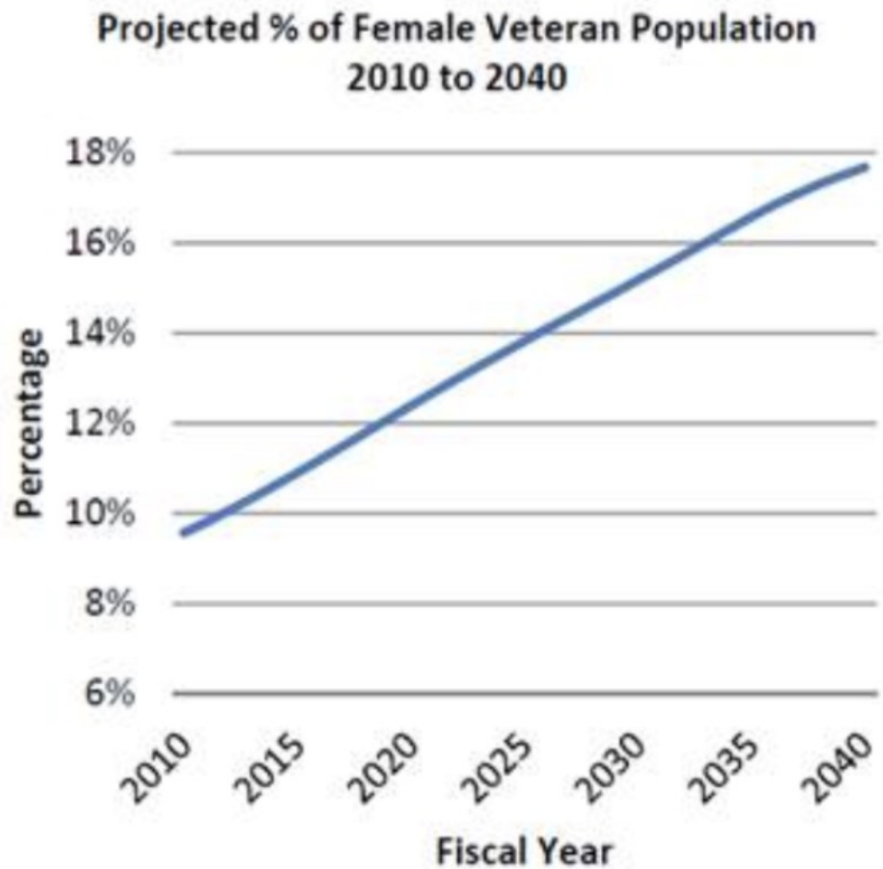
Wellesley Mayo Microbiome Study:
Vaginal and Gut Microbiome Neuroscience Lab, Co-lead and Head of Logistics

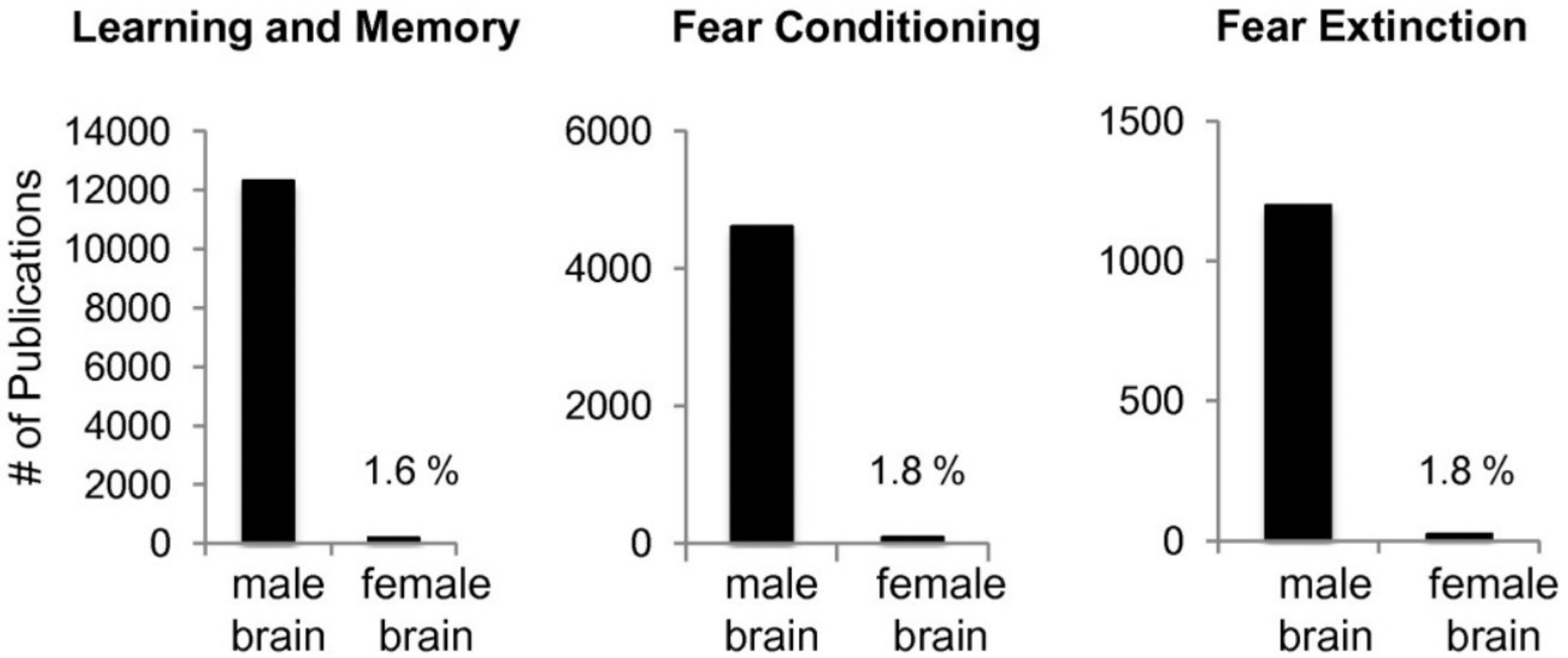
MIT: BIPOC Maternal Health Disparities Group

Chemical Engineering

MUSLIMS FOR HUMANITY
ICNARelief
SHIFA CLINIC, SC

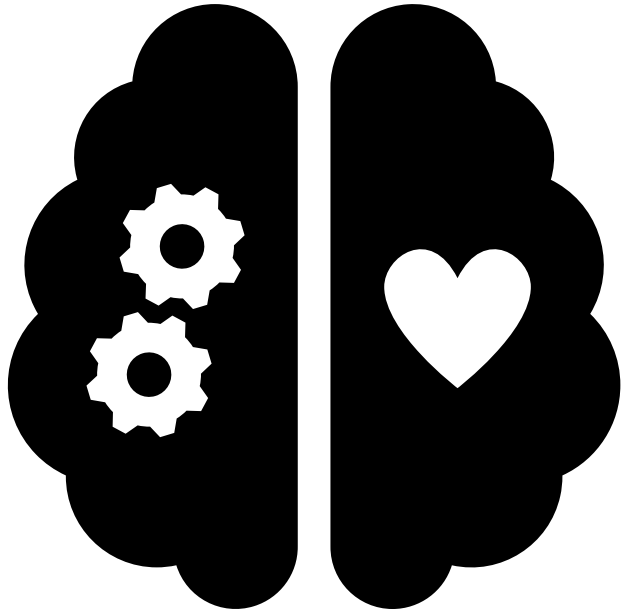

Projected Total Veteran Population
2010 to 2040
24
22
20
18
16
14
12
10
Millions
2010
2015
2020
2025
2030
2035
2040
Fiscal Year


Projected % of Female Veteran Population
2010 to 2040
18%
16%
14%
12%
10%
8%
6%
Percentage
2010
2015
2020
2025
2030
2035
2040
Fiscal Year


Learning and Memory
# of Publications
14000
12000
10000
8000
6000
4000
2000
0
1.6 %
male brain
female brain
Fear Conditioning
6000
4000
2000
0
1.8 %
male brain
female brain
Fear Extinction
1500
1000
500
0
1.8 %
male brain
female brain

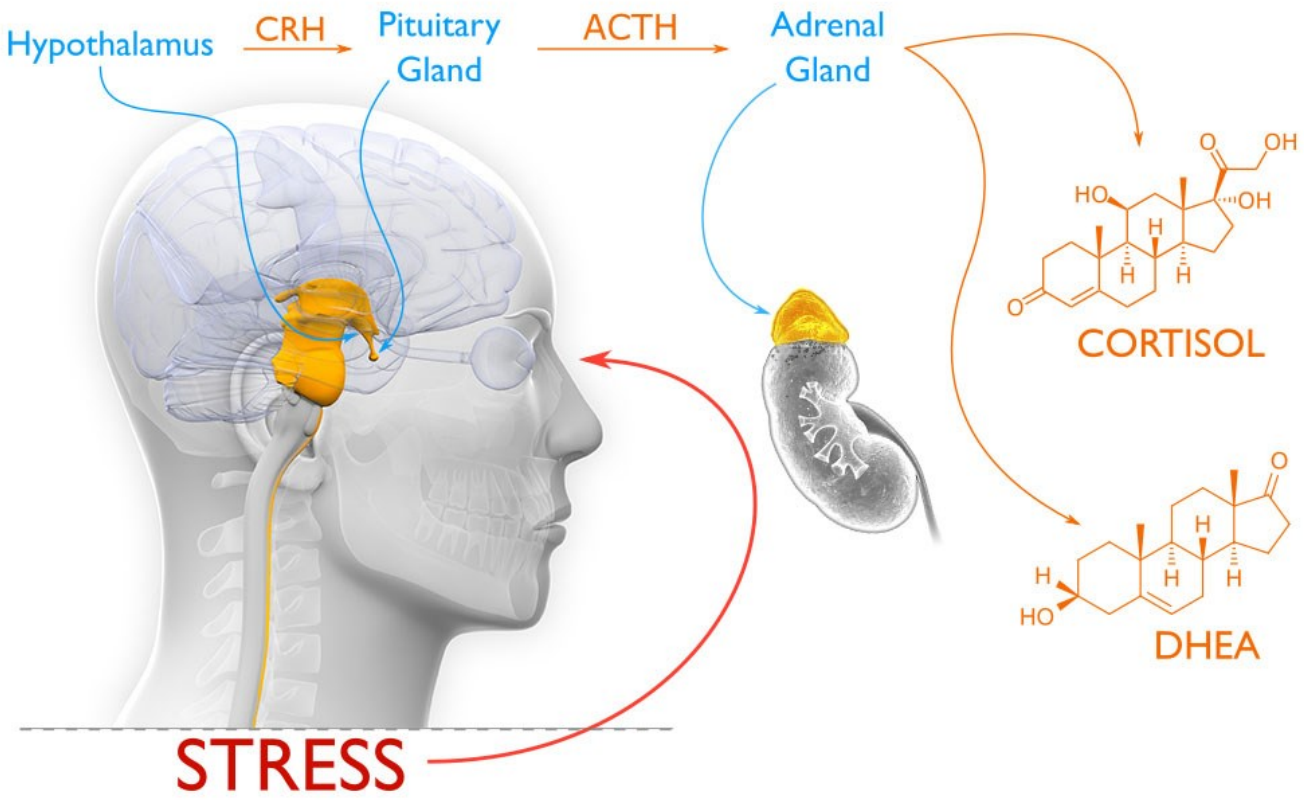
My Role

- Composed and organized methods for this study
- Complete a literature review and search for the background

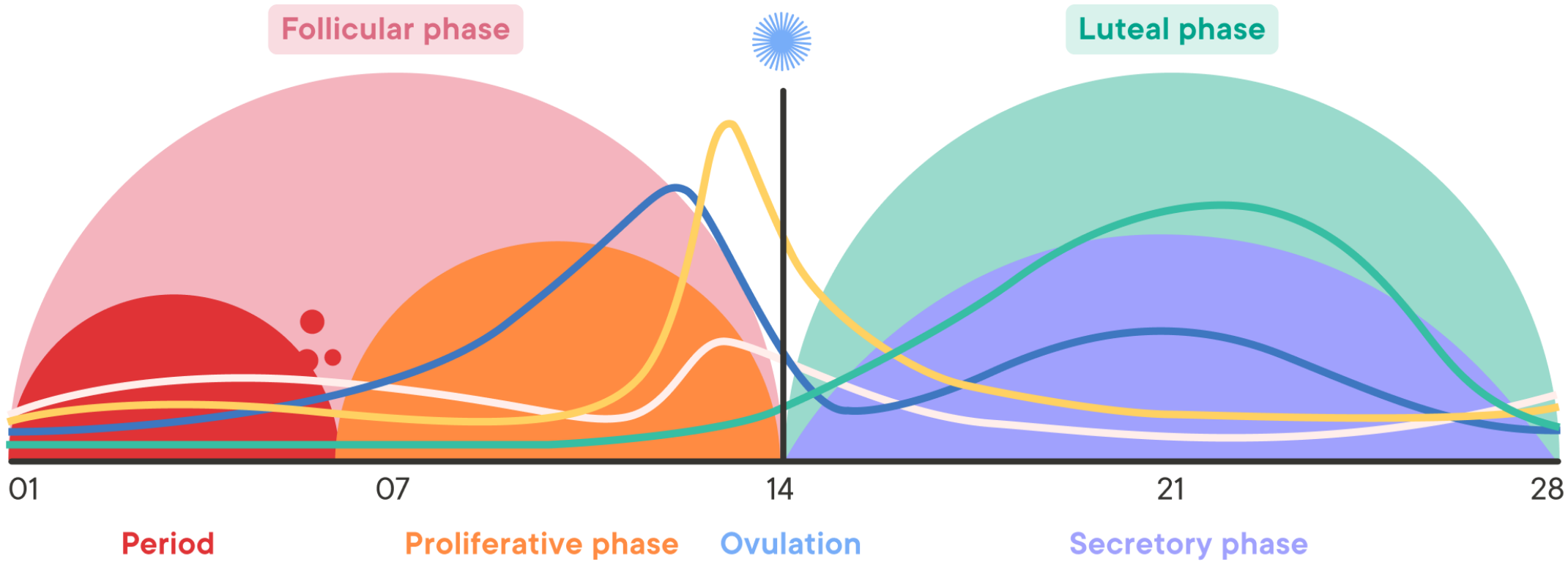


Background

- Association between abnormal levels of neurosteroids and PTSD symptom severity
- Neurosteroids cortisol and dehydroepiandrosterone (DHEA)
  - Neurosteroid function and dysfunction



Complete Menstrual Cycle



Specific aims and hypothesis

The overarching aim of this study is to investigate the impact of PTSD and menstrual cycle phase on cortisol and DHEA.

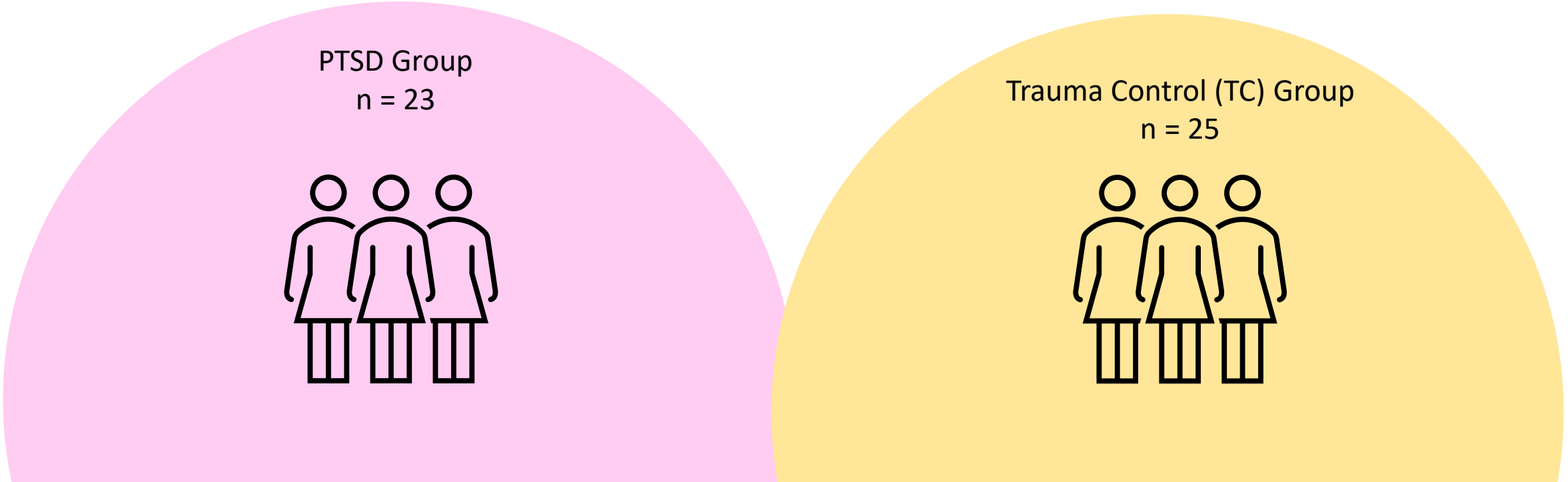
We hypothesize that greater PTSD symptom severity will be associated with:

- lower cortisol
- Higher DHEA:cortisol ratio

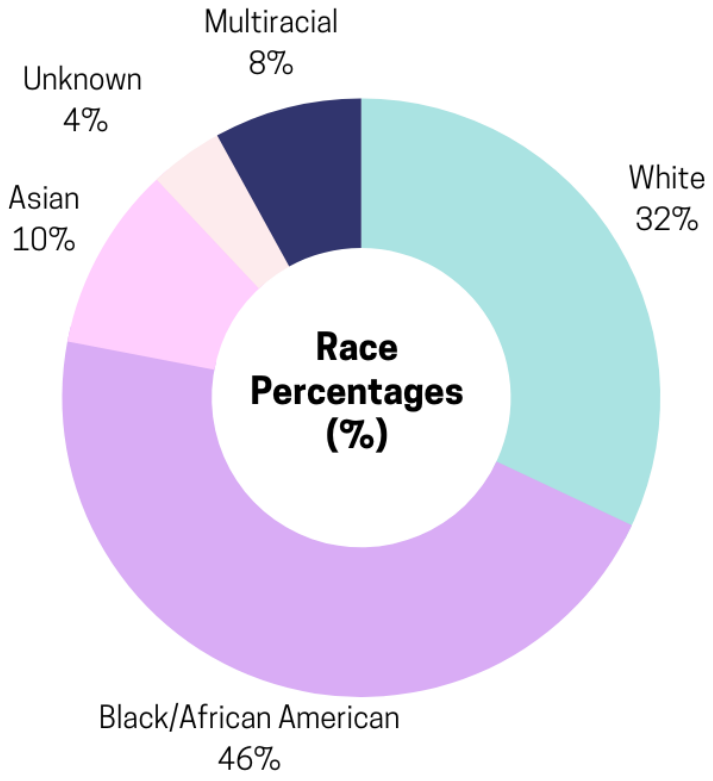
These associations were looked at separately during the mLP and ePF to test if these associations differed across the menstrual cycle.

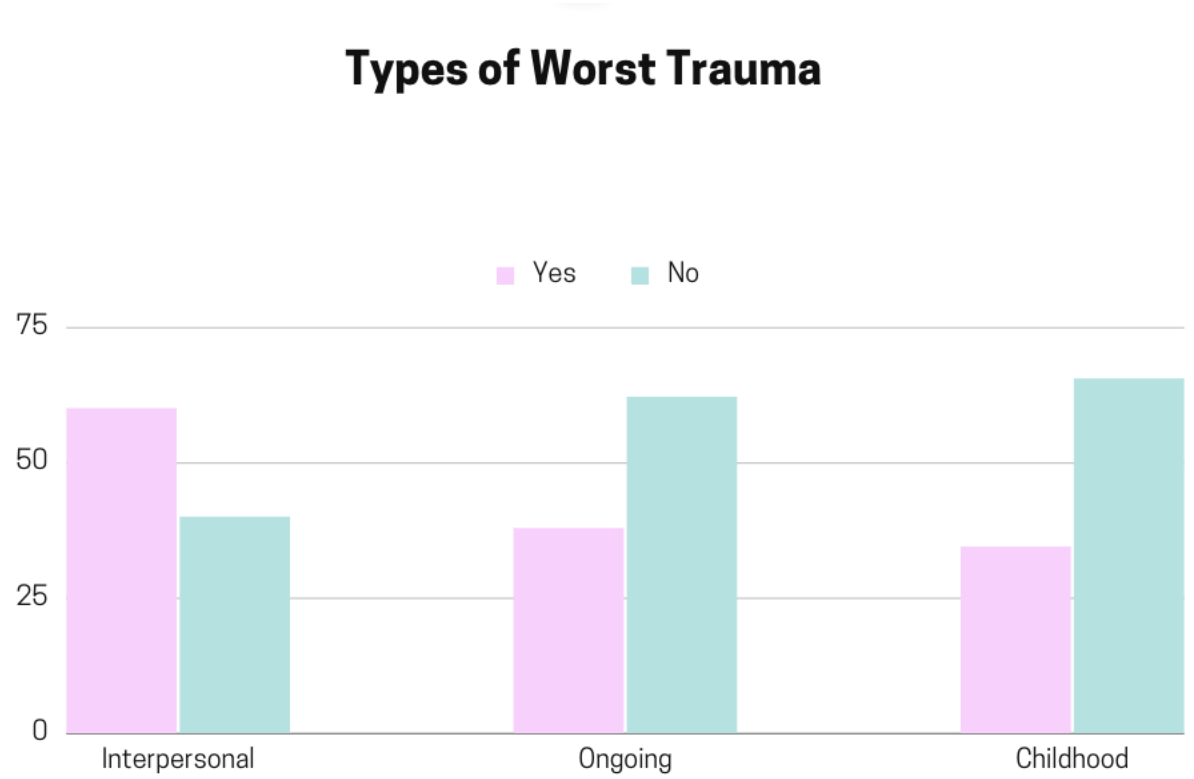
Methods

- Participants
  - 18-55 years old and experienced at least one form of trauma
  - Total participants (n=48)



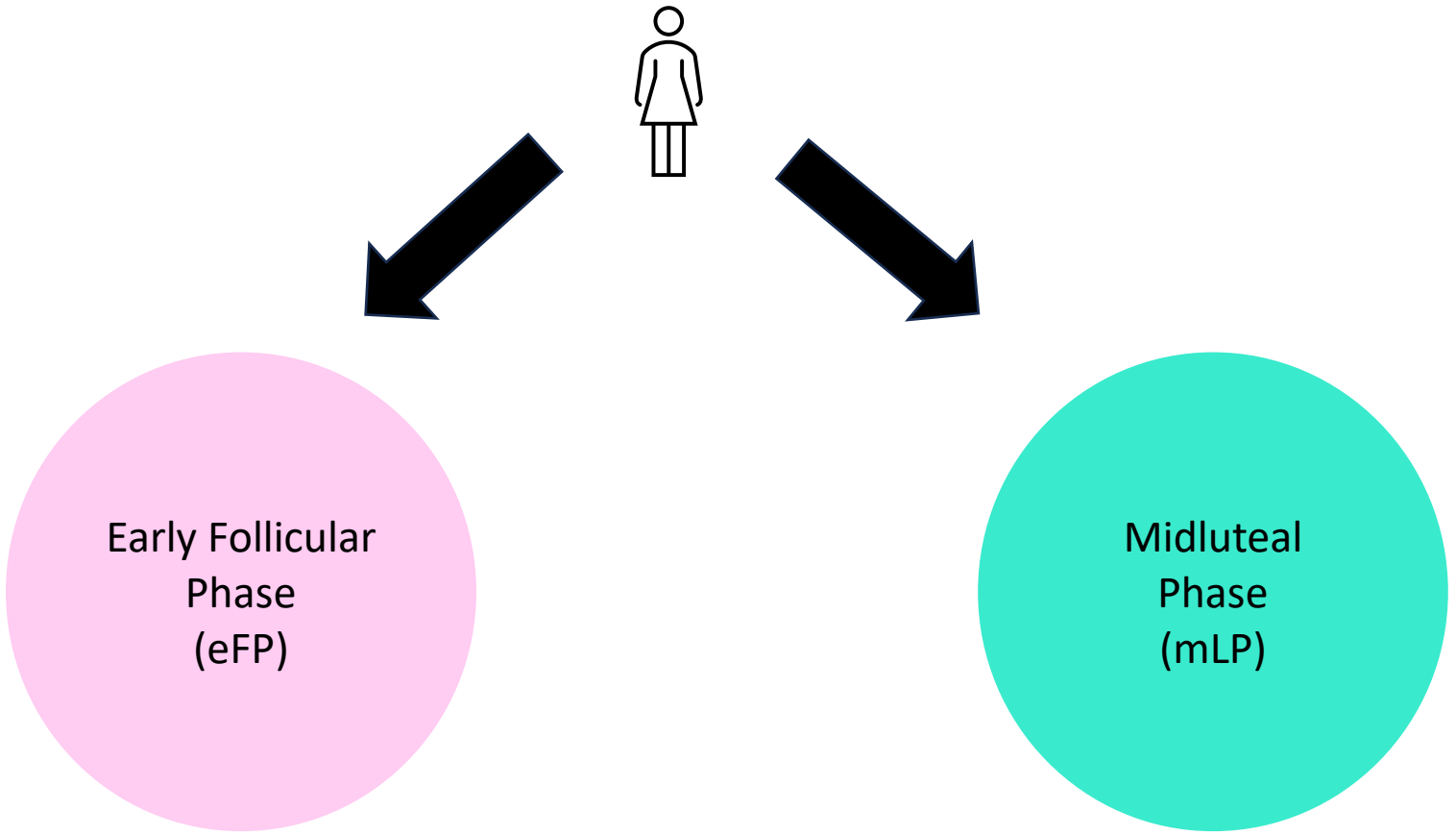
Participant Characterization





4% of participants were Hispanic
Median age was 28.8 years old

Study Procedures



- Abstinence from:

Alcohol
1 week

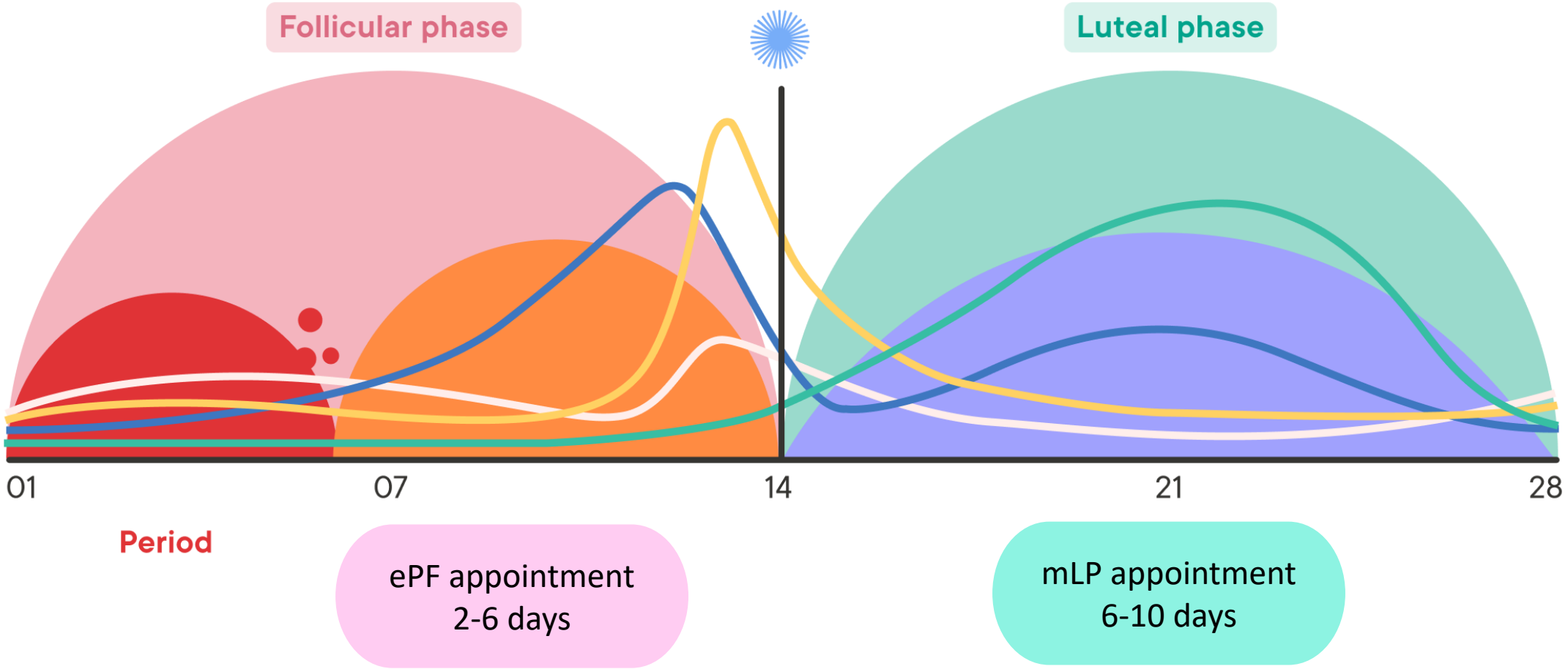
Illicit Substances
2 weeks

Caffeine
4 hours

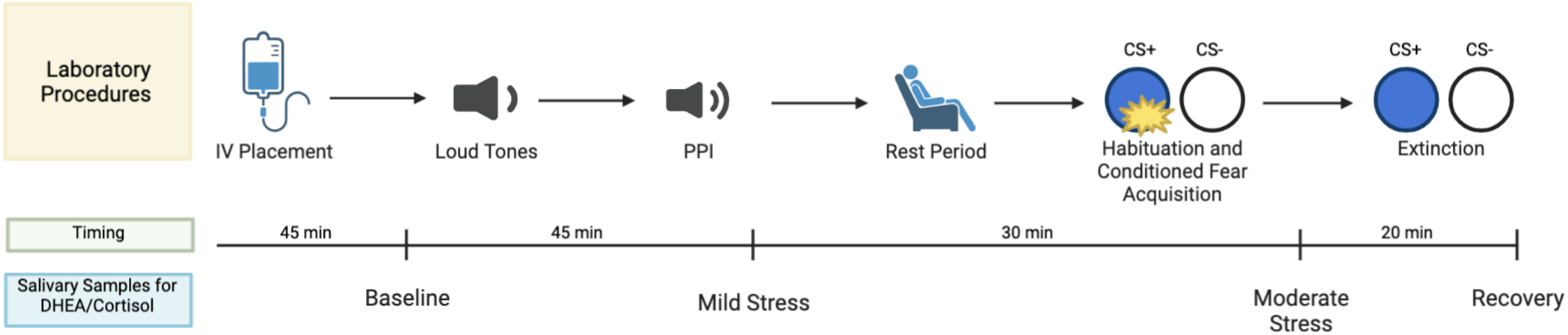
Eating
2-3 hours

Nicotine
1 hour

Menstrual cycle confirmation

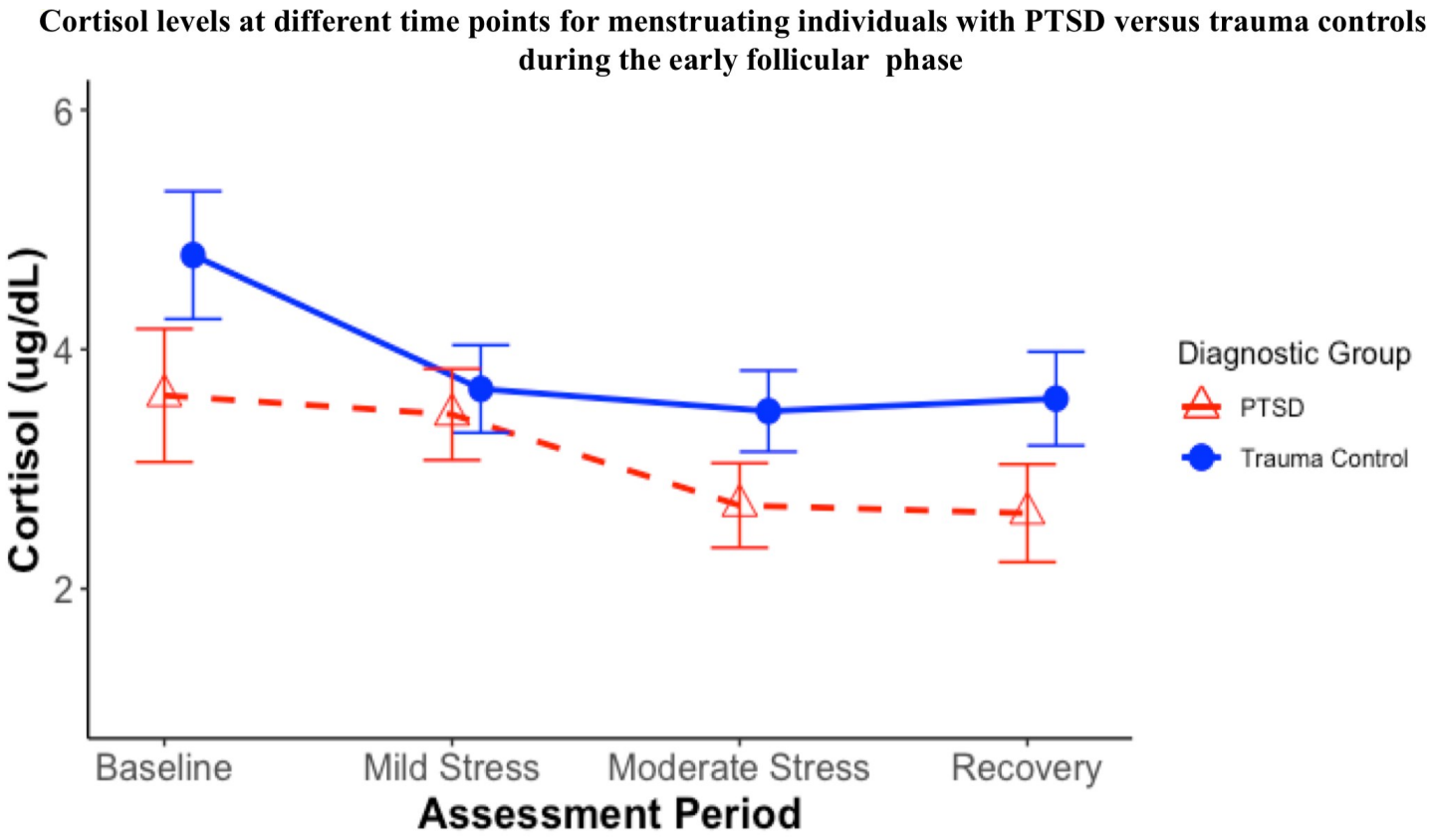


At-home urine luteinizing hormone (LH) surge test for mLP.
Confirmation of phases were measured with resting plasma progesterone and 17B-estradiol levels at each session.


Laboratory Procedures
IV Placement
Loud Tones
PPI
Rest Period
CS+
CS-
Habituation and Conditioned Fear Acquisition
CS+
CS-
Extinction
Timing
45 min
45 min
30 min
20 min
Salivary Samples for DHEA/Cortisol
Baseline
Mild Stress
Moderate Stress
Recovery

Results

- Cortisol levels significantly lower in the PTSD group than the TC group during eFP (p=0.001) but not during mLP.
- Cortisol levels greatest at baseline and decreased from post-mild stressor to recovery during eFP (p=0.028) but not mLP (0.542)
- DHEA levels or DHEA/cortisol ratio did not differ

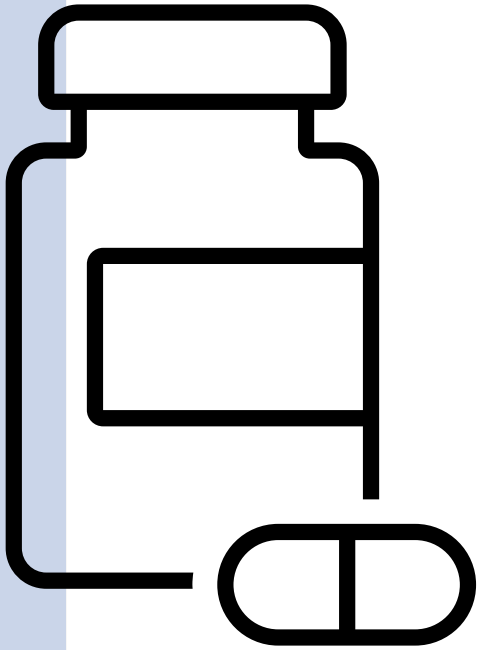


Discussion

- Mixed findings related to cortisol and PTSD in the literature. These studies have not considered menstrual cycle phase differences
  - It is possible that menstrual cycle phase differences may contribute to the mixed findings in the literature
- Use results as a potential contribution to future research and personalizing of PTSD treatment based on sex differences.
- It is important to consider menstrual cycle phase in mechanistic studies for PTSD.

Limitations

- Does not include peri or post-menopausal women or women on hormonal birth control.



Future Directions

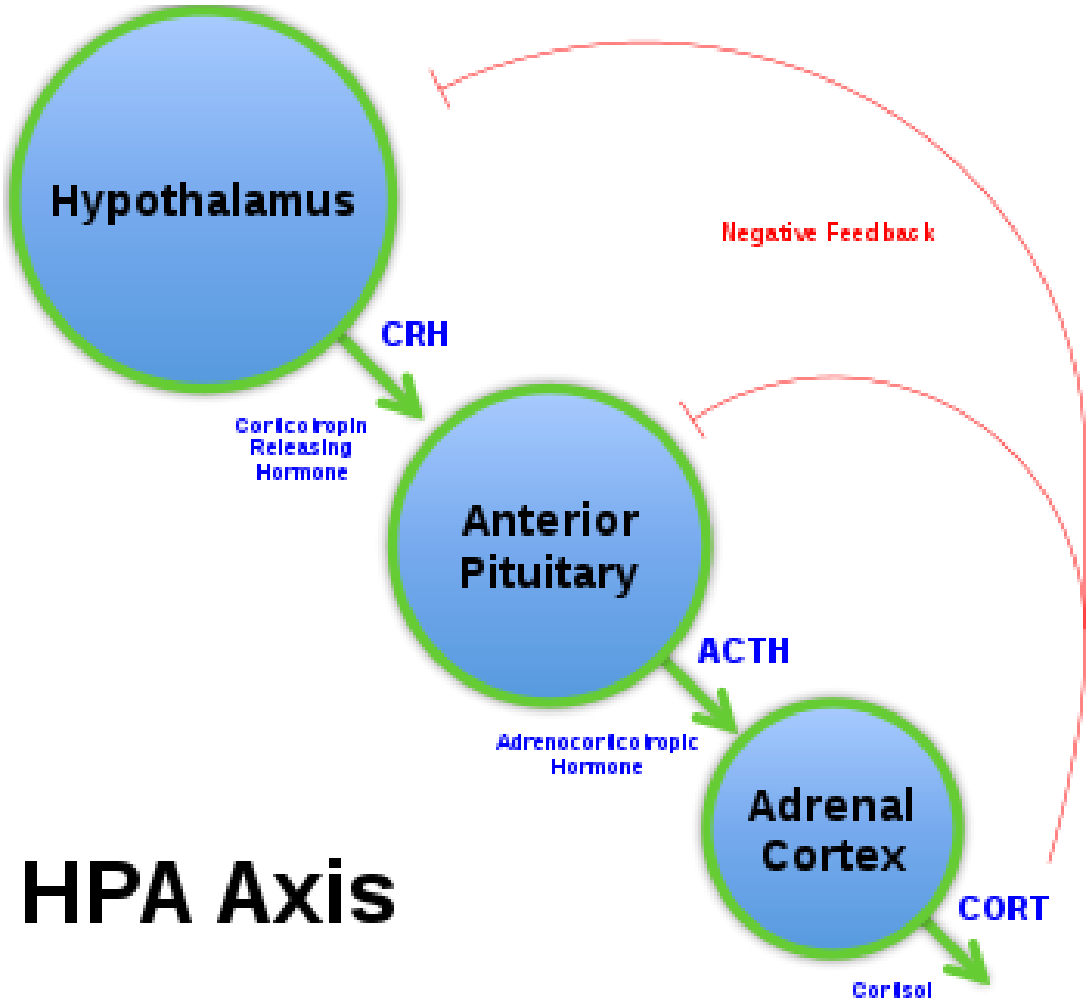
- Main goal: Pharmacological interventions and understanding biological factors to ameliorate PTSD treatment

- Continuing with working on this project with the National Center for PTSD
- After completion of paper, submission to publication.
- Perhaps presentation at veteran and scientific conferences.

Acknowledgements

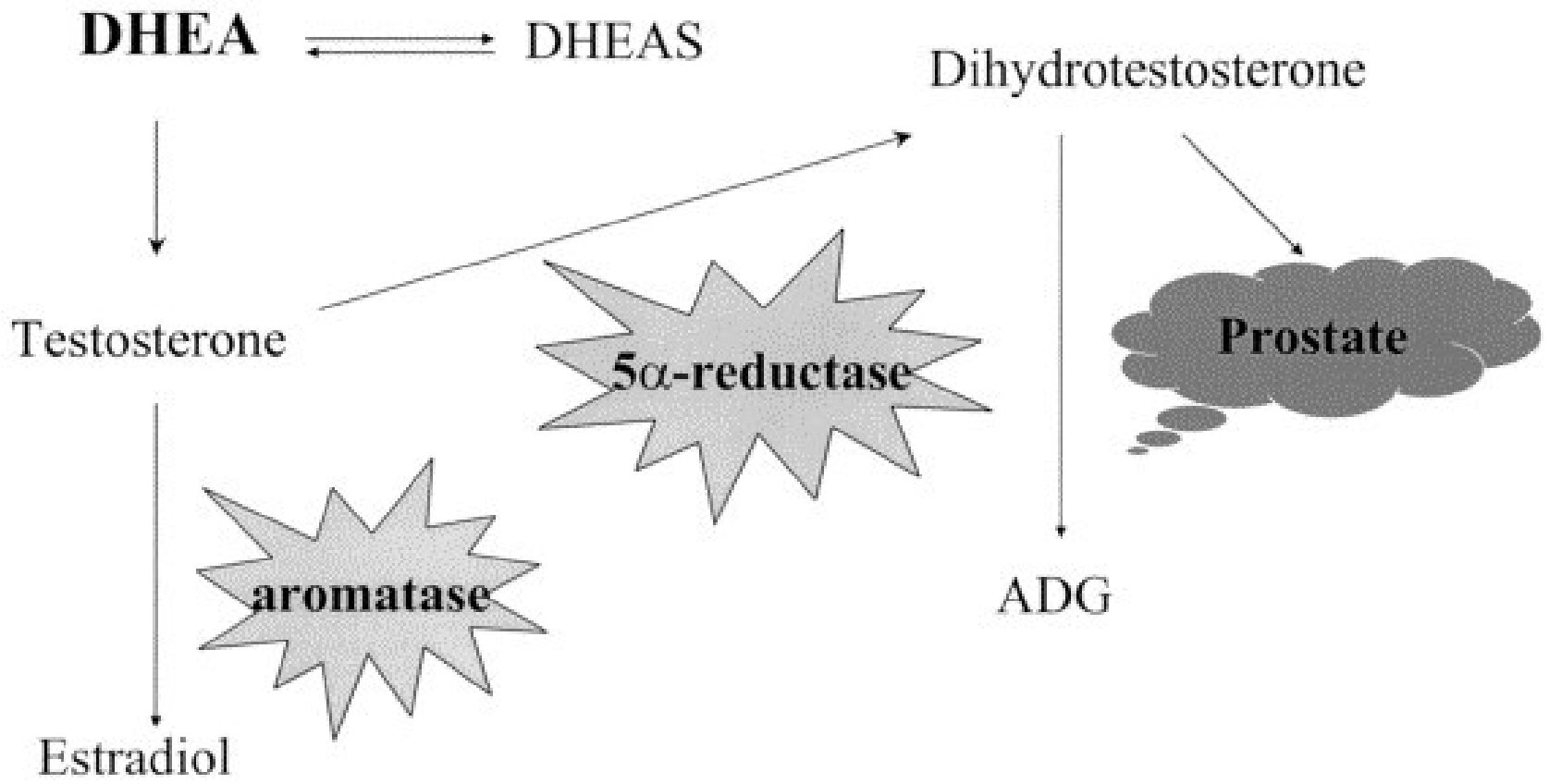
- Dr. Suzanne Pineles, Mentor
- Jackie Pendergast and Justin Goodridge, Program Coordinator
- National Center for PTSD
- Women's Health Science Division Team
- CHOIR Interns
- Pineles Research Team
- CHOIR Summer Program

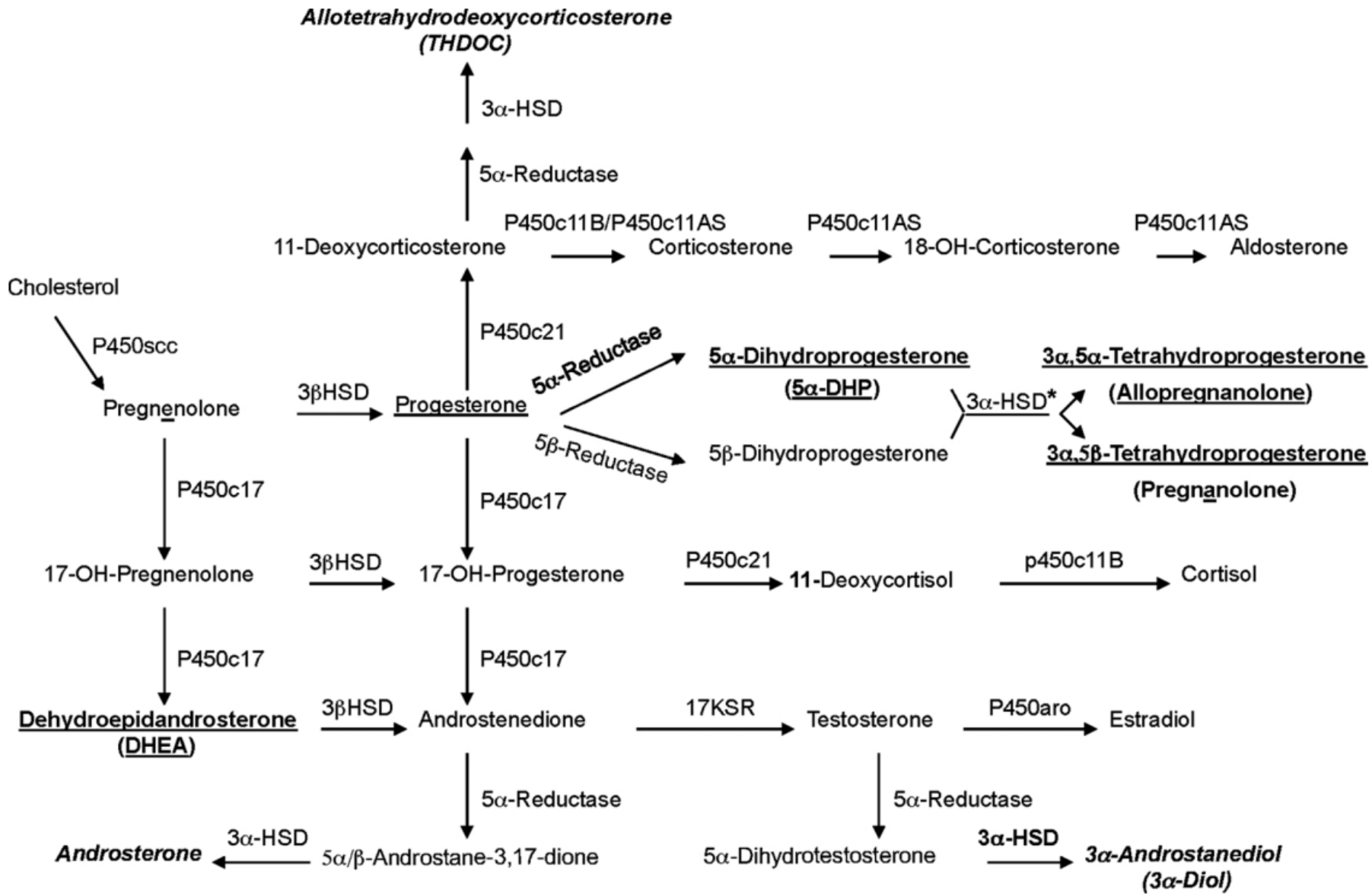
Thank you!


Hypothalamus
Negative Feedback
CRH
Corticotropin Releasing Hormone
Anterior Pituitary
ACTH
Adrenocorticotropic Hormone
Adrenal Cortex
CORT
Cortisol

HPA Axis

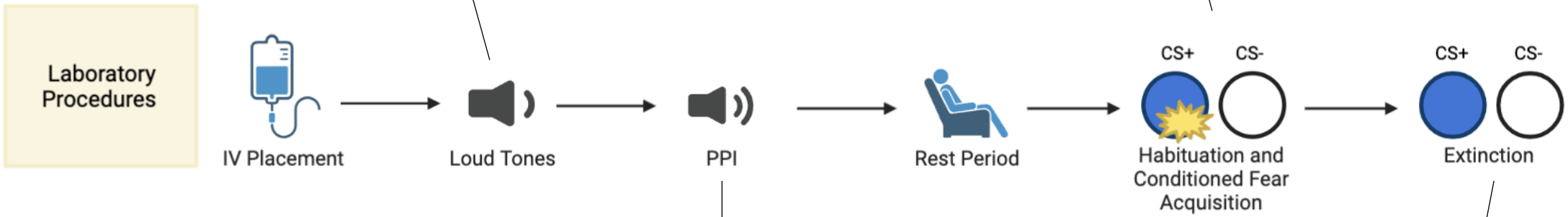
Metabolism of DHEA




Allotetrahydrodeoxycorticosterone
(THDOC)
3α-HSD
5α-Reductase
11-Deoxycorticosterone
P450c11B/P450c11AS
Corticosterone
P450c11AS
18-OH-Corticosterone
P450c11AS
Aldosterone
Cholesterol
P450scc
Pregnenolone
3βHSD
Progesterone
P450c21
5α-Reductase
5α-Dihydroprogesterone
(5α-DHP)
3α,5α-Tetrahydroprogesterone
(Allopregnanolone)
3α-HSD*
5β-Reductase
5β-Dihydroprogesterone
3α,5β-Tetrahydroprogesterone
(Pregnanolone)
P450c17
P450c17
17-OH-Pregnenolone
3βHSD
17-OH-Progesterone
P450c21
11-Deoxycortisol
p450c11B
Cortisol
P450c17
P450c17
Dehydroepidandrosterone
(DHEA)
3βHSD
Androstenedione
17KSR
Testosterone
P450aro
Estradiol
5α-Reductase
5α-Reductase
3α-HSD
Androsterone
5α/β-Androstane-3,17-dione
5α-Dihydrotestosterone
3α-HSD
3α-Androstanediol
(3α-Diol)

- Habituation:
  - Habituate to new stimulus
- Conditioned fear acquisition:
  - Learn about the relationship between two different stimuli
  - Understand to not fear white circle stimuli

- Physiological reactivity
- Habituation to several loud tones
- Testing how reactivity to non-trauma related stressors for arousal measurement



- Sensory gating

- Learn that neither circle means shock
- Recall of associations

Participant Characterization

- Median age (28.8 years old)
- Comorbid depression
- Smokers (N=10)