Trauma, Posttraumatic Stress Disorder, and Perinatal Health

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Overview

• The intersection of mental health and reproductive health
• Impact of trauma and PTSD on perinatal health, particularly among women Veterans
• Potential mechanisms
• Potential treatments
Women and Mental Health

Kessler et al., 1994; Kessler et al., 2003; NCS, 2005
• Mental health problems coincide with reproductive events across a women’s life-cycle
  • Ovarian hormones

Barth et al., 2015; Seeman, 1997
Mental Health Across the Reproductive Life-Cycle

*Women exposed to greater amounts of hormonal flux across their lifetime
*Increased vulnerability to mental health problems/symptoms during hormonal flux

Bebbington et al., 1998; Hayward & Sanborn, 2002; Howard et al., 2014; McGee et al., 1992; Nillni et al., 2009; Nillni et al., 2015; Reardon et al., 2009
Mental Health Across the Reproductive Life-Cycle: Gender Disparity in Psychopathology

Gender disparity in psychopathology begins in puberty and ends at menopause

Barth et al., 2015; Bebbington et al., 1998; Nilni et al., 2009; Hayward & Sanborn, 2002; McGee et al., 1992; Reardon et al., 2009
Mental Health Across the Reproductive Life-Cycle: Premenstrual Exacerbations

Premenstrual exacerbation of symptoms

Hendrick et al., 1996; Nillni et al., 2015
Mental Health Across the Reproductive Life-Cycle: Fertility

Depressive Symptoms

38% Decrease in Fecundability

Nillni et al., 2016
Mental Health Across the Reproductive Life-Cycle: Menstrual Cycle Characteristics

Depressive Symptoms
Perceived Stress

Irregular menstrual cycles

Nillni et al., 2018
Mental Health Across the Reproductive Life-Cycle: Perinatal Health

Psychopathology during pregnancy and the postpartum period

Howard et al., 2014
Leading Causes of Maternal Mortality in the First Year Postpartum

- Overdose
- Suicide

Goldman-Mellor & Margerison, 2019
Periods of hormonal flux are associated with the initiation and/or exacerbation of mental health symptoms for some women AND mental health symptoms impact facets of reproduction
The Impact of PTSD on Pregnancy Outcomes
Prevalence of Perinatal PTSD

- 8% perinatal PTSD
- 14% perinatal PTSD among racially diverse low-income communities
  - 85% of prenatal MDD is comorbid with full or subthreshold PTSD

Seng et al., 2009; 2011
Childbirth-Related Postpartum PTSD (PP-PTSD)

- Development of PTSD from a childbirth experience
- 4.6 - 6.3% prevalence of acute PP-PTSD

Dekel et al., 2017
Risk Factors for PP-PTSD

**Negative Perception of Childbirth**
- Negative experience during delivery
- Fear of childbirth
- Low internal locus of control during childbirth

**Maternal Mental Health**
- Previous trauma, particularly childhood sexual trauma
- PTSD or other mental health symptoms during pregnancy

**Delivery Mode and Complications**
- Emergency c-section
- Complications with pregnancy and/or baby
- Instrumental delivery

**Low Social Support**
- Staff
- Partner
- Family

Dekel et al., 2017
The Impact of Trauma on Perinatal Outcomes in the General Population

- **Trauma History**
- **Adverse Childhood Experiences (ACES)**

  - Negative obstetric outcomes (e.g., pre-term birth, miscarriage, low birth weight infants) and conditions (pre-eclampsia)
  - Postpartum mental health problems

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Lev-Weisel et al., 2009; Seng et al., 2001, 2011; Smith et al., 2016; Shapiro et al., 2013; Yonkers et al., 2014
The Impact of PTSD on Perinatal Outcomes in the General Population

PTSD

- Negative obstetric outcomes (e.g., pre-term birth, miscarriage, low birth weight infants) and conditions (pre-eclampsia)
- Postpartum mental health problems

Lev-Weisel et al., 2009; Seng et al., 2001, 2011; Smith et al., 2016; Shapiro et al., 2013; Yonkers et al., 2014
The Impact of PTSD on Preterm Birth in the General Population

Perinatal PTSD + MDD → 4-fold increased risk for preterm birth

- This risk is significant even when controlling for age, race/ethnicity, education, cigarette use, substance use, heavy alcohol use, other psychiatric disorders, psychotropic medication use, and history of preterm births

Yonkers et al., 2014
Societal Impact of Negative Perinatal Outcomes

Negative perinatal outcomes

- Infant Death
- Long term neurodevelopmental, behavioral, and medical impairments in the child
- Increased maternal mental health symptoms
- Impaired maternal infant bonding

Anderson et al., 2012; Moster et al, 2008; Saigal & Doyle, 2008
Why should we care about perinatal health outcomes among women Veterans?
The Changing Demographics of Women Veterans

Frayne et al., 2014; Friedman et al., 2011
Women Veterans

More Trauma Exposure

More PTSD

Women Civilians

Katon et al., 2015; Lehavot et al., 2018
Prevalence of Military Sexual Trauma (MST) Among Women Veterans

• Estimates of MST range from 14 - 49% among women Veterans using VHA
What do we know about the role of trauma and PTSD on perinatal outcomes among women Veterans?
Negative Pregnancy Outcomes (e.g., PTB, low infant birthweight)

More Deployments

Pregnancy Occurring During Deployment
Deployment = environmental exposures?
Deployment = changes in health behaviors and mental health?
Deployment = Trauma/Stress?
The Impact of Military Sexual Trauma and Warfare Exposure on Women Veterans’ Perinatal Outcomes

Nillni, Fox, Cox, Paul, Vogt, & Galovski (2021)

*Psychological Trauma: Theory, Research, Practice, and Policy*
Longitudinal Investigation of Gender Health and Trauma (LIGHT) Study

- Ongoing nationwide prospective survey study
- Oversampled for Veterans living in high crime communities and women Veterans
  - N = 3,699
  - 59% high crime
  - 53% women
- Surveyed every 4 months (6 surveys total thus far)
- Assessment of trauma history, warfare exposure, military sexual trauma, and lifetime perinatal history (per pregnancy)

PIs: Tara Galovski and Yael Nillni
Women Who Experienced a Pregnancy Following Entering Into the Military

1,929 Women

911 (47%) women had at least one pregnancy

1,752 pregnancies

Nillni et al., 2021
Demographics of Women Who Had a Pregnancy in LIGHT

Race and Ethnicity
- 58% White
- 12% Hispanic
- 33% Black
- 4% Asian
- 12% Other/Multiracial
- 47.7% Non-Hispanic White

Relationship Status
- 68% are currently in a relationship

Annual Household Income
- 8% < $15,000
- 21% $15,000 - $35,000
- 21% $35,000 - $55,000
- 15% $55,000 – $75,000
- 15% $75,000 - $100,000
- 19% > $100,000

Education
- 6% High School
- 47% Vocational/Associate’s Degree/Some college
- 27% Bachelor’s Degree
- 18% Advanced Degree

Branch of Service
- 51% Army
- 18% Navy
- 23% Air Force
- 6% Marine Corps
- 1% Coast Guard

Deployment Status
- 49% have deployed

Age
- 38.34 (6.94)

Nillni et al., 2021
Lifetime History of Perinatal Outcomes Among Women Who Had a Pregnancy in LIGHT

Rates from ANY pregnancy assessed

- **Preterm Birth (< 37 GA)**
  - 29%

- **Low Birthweight Infant (< 2500 grams)**
  - 9%

- **Postpartum Depression/Anxiety**
  - 45%

Nillni et al., 2021
Association of Warfare Exposure and Military Sexual Trauma and Perinatal Outcomes

Adjusted for age at each pregnancy, minority status, childhood violent trauma exposure, and deployment status

Nillni et al., 2021
Association of Warfare Exposure and Military Sexual Trauma and Perinatal Outcomes

Warfare Exposure

Military Sexual Trauma (MST)

Preterm birth (< 37 wks GA)

Full term birth (> 39 wks GA)

Lower infant birthweight

Postpartum depression and/or anxiety

Adjusted for age at each pregnancy, minority status, childhood trauma exposure, and deployment status

Nillni et al., 2021
MST and Perinatal Depression and Suicidality Among Women Veterans

- Military Sexual Trauma (MST)
  - Perinatal Depression
  - Postpartum depression
  - Suicidal Ideation

- Military Sexual Harassment

Gross et al., 2020
How do the mental health consequences of trauma impact perinatal outcomes?
The Impact of PTSD and Moral Injury on Women Veterans’ Perinatal Outcomes Following Separation From Military Service

Nillni, Shayani, Finley, Copeland, Perkins, & Vogt (2020)

*Journal of Traumatic Stress*
The Veteran Metrics Initiative (TVMI)

- Nationwide prospective cohort study
- N = 9,566
  - 18% women
- Surveyed Veterans within 90 days from separation from active-duty service and followed every 6 months for 3 years (6 surveys)
- Assessment of:
  - PTSD symptoms
  - moral injury symptoms – distress associated with perpetrating, failing to prevent, or witnessing events that contradict deeply held moral beliefs and expectations
  - trauma history
  - perinatal outcomes

PIs: Dawne Vogt, Daniel Perkins, Laurel Copeland, Erin Finley
Impact of PTSD and Moral Injury on Adverse Perinatal Outcomes

9,566 Veterans

1,743 women Veterans

318 became pregnant

Nillni et al., 2020
Demographics of Women Who Became Pregnant Following Separation in TVMI

Race and Ethnicity
- 76% White
- 15% Hispanic
- 17% Black
- 2% Asian
- 13% Other/Multiracial
- 62% Non-Hispanic White

Relationship Status
- 72% married

Annual Household Income
- 14% < $15,000
- 23% $15,000 - $35,000
- 24% $35,000 - $55,000
- 13% $55,000 – $75,000
- 11% $75,000 - $100,000
- 13% > $100,000

Education
- 15% High School
- 48% Vocational/Associate’s Degree/Some college
- 19% Bachelor’s Degree
- 18% Advanced Degree

Age
- 27.99 (5.27)

Branch of Service
- 33% Army
- 23% Navy
- 23% Air Force
- 10% Marine Corps
- 11% National Guard/Reservists

Nillni et al., 2020
Impact of PTSD and Moral Injury on Adverse Perinatal Outcomes

Moral Injury

PTSD

Adverse Perinatal Outcomes (e.g., PTB, emergency c-section, miscarriage, etc.)

Postpartum depression and/or anxiety

Adjusted for age, minority status, SES, and lifetime trauma exposure

Nillni et al., 2020
Current PTSD

Preterm birth, low infant birthweight, gestational diabetes, and preeclampsia

Shaw et al., 2014, 2017
Life Experiences and Pregnancy Research Study (LEAPS)

- Prospective study of pregnant women receiving prenatal care in a large safety net hospital
- N = 161
- Followed through early pregnancy into the early postpartum period
- Regular collection of psychosocial measures, blood samples, medical chart data, and postpartum qualitative interviews

PI: Yael Nillni
Study Population

• Women (aged 18 or older) receiving prenatal care at Boston Medical Center (BMC)

- 33 Trauma-exposed with a diagnosis of full or subthreshold PTSD (PTSD)
- 41 Trauma-exposed with another mental health disorder (Trauma MH)
- 61 Trauma-exposed healthy (Trauma Healthy)
- 30 Non trauma-exposed healthy (Healthy)
Study Design

Baseline: GA 11-23
Follow-up: GA 23-28
Follow-up: GA 32-34
Follow-up: GA 35-38

Can enter the study up to GA 28

Phone call: ≤ 2 wks PP
Follow-up: PP 5-7

Study participation between 18 and 37 weeks
## Demographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total Sample (N = 161)</th>
<th>PTSD (N = 33)</th>
<th>Trauma MH (N = 41)</th>
<th>Trauma Healthy (N = 61)</th>
<th>Healthy (N = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean, SD)</strong></td>
<td>30.5 (6.2)</td>
<td>28.8 (4.0)</td>
<td>29.2 (8.2)</td>
<td>31.8 (5.4)</td>
<td>31.9 (5.8)</td>
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<tr>
<td><strong>Race/Ethnicity</strong></td>
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<tr>
<td>Non-Hispanic White</td>
<td>59 (36.6%)</td>
<td>12 (36.4%)</td>
<td>16 (39.0%)</td>
<td>25 (41.0%)</td>
<td>6 (23.1%)</td>
</tr>
<tr>
<td>Hispanic White</td>
<td>8 (5.0%)</td>
<td>1 (3.0%)</td>
<td>1 (2.4%)</td>
<td>4 (6.6%)</td>
<td>2 (7.7%)</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>47 (29.2%)</td>
<td>13 (39.4%)</td>
<td>13 (31.7%)</td>
<td>15 (24.6%)</td>
<td>6 (23.1%)</td>
</tr>
<tr>
<td>Hispanic Black</td>
<td>7 (4.3%)</td>
<td>2 (6.1%)</td>
<td>3 (7.3%)</td>
<td>2 (3.3%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Asian</td>
<td>11 (6.8%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>5 (8.2%)</td>
<td>6 (23.1%)</td>
</tr>
<tr>
<td>Other/Multiracial</td>
<td>29 (18.0%)</td>
<td>5 (15.2%)</td>
<td>8 (19.5%)</td>
<td>10 (16.4%)</td>
<td>6 (23.1%)</td>
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<tr>
<td><strong>Household income below 25k</strong></td>
<td>63 (39.1%)</td>
<td>23 (69.7%)</td>
<td>19 (46.3%)</td>
<td>13 (22.0%)</td>
<td>8 (30.8%)</td>
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<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
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<tr>
<td>No high school or GED</td>
<td>19 (11.8%)</td>
<td>5 (15.2%)</td>
<td>8 (19.5%)</td>
<td>4 (6.6%)</td>
<td>2 (7.7%)</td>
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<tr>
<td>High School</td>
<td>26 (16.1%)</td>
<td>8 (24.2%)</td>
<td>5 (12.2%)</td>
<td>9 (14.8%)</td>
<td>4 (15.4%)</td>
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<tr>
<td>Some college/associates/vocational</td>
<td>51 (31.7%)</td>
<td>16 (48.5%)</td>
<td>15 (36.6%)</td>
<td>15 (24.6)</td>
<td>5 (19.2%)</td>
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<td>Bachelor’s degree or higher</td>
<td>65 (40.4%)</td>
<td>4 (12.1%)</td>
<td>13 (31.7%)</td>
<td>33 (54.1%)</td>
<td>15 (57.7%)</td>
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<tr>
<td><strong>Relationship Status</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Married or cohabitating</td>
<td>108 (67.1%)</td>
<td>12 (36.4%)</td>
<td>25 (61.0%)</td>
<td>50 (82.0%)</td>
<td>21 (80.8%)</td>
</tr>
<tr>
<td>In a relationship but living separately</td>
<td>29 (18.0%)</td>
<td>12 (36.4%)</td>
<td>7 (17.1%)</td>
<td>8 (13.1%)</td>
<td>2 (7.7%)</td>
</tr>
<tr>
<td>Single</td>
<td>24 (14.9%)</td>
<td>9 (27.3%)</td>
<td>9 (22.0%)</td>
<td>3 (4.9%)</td>
<td>3 (11.5%)</td>
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</tr>
<tr>
<td>Parity</td>
<td>81 (50.3%)</td>
<td>21 (63.6%)</td>
<td>13 (31.7%)</td>
<td>30 (50.8%)</td>
<td>16 (61.5%)</td>
</tr>
<tr>
<td>Psychotropic medication use during pregnancy (e.g., Zoloft)</td>
<td>22 (13.7%)</td>
<td>10 (30.3%)</td>
<td>9 (21.9%)</td>
<td>3 (4.9%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Medication assisted therapy during pregnancy (e.g., suboxone)</td>
<td>15 (9.3%)</td>
<td>7 (21.2%)</td>
<td>5 (12.2%)</td>
<td>3 (4.9%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Cigarette or tobacco use during pregnancy</td>
<td>19 (11.8%)</td>
<td>9 (27.3%)</td>
<td>9 (21.9%)</td>
<td>1 (1.6%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Marijuana use during pregnancy</td>
<td>21 (13.0%)</td>
<td>8 (24.2%)</td>
<td>10 (24.4%)</td>
<td>3 (4.9%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Alcohol use during pregnancy</td>
<td>16 (9.9%)</td>
<td>3 (9.1%)</td>
<td>5 (12.2%)</td>
<td>7 (11.5%)</td>
<td>1 (3.8%)</td>
</tr>
<tr>
<td>Other substance use during pregnancy</td>
<td>14 (8.7%)</td>
<td>7 (21.2%)</td>
<td>5 (12.2%)</td>
<td>2 (3.3%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>
Trauma/Mental Health Group Differences on PTSD Symptoms at 5-7 Weeks Postpartum

Preliminary unpublished data

Adjusted for income, race/ethnicity, and age
Trauma/Mental Health Group Differences on Depressive Symptoms at 5-7 Weeks Postpartum

Preliminary unpublished data

Adjusted for income, race/ethnicity, and age
Trauma/Mental Health Group Differences on Anxiety Symptoms at 5-7 Weeks Postpartum

- PTSD
- Trauma MH
- Trauma Healthy
- Healthy

Preliminary unpublished data

Adjusted for income, race/ethnicity, and age
Trauma/Mental Health Group Differences on Perceived Stress Symptoms at 5-7 Weeks Postpartum

Preliminary unpublished data
Adjusted for income, race/ethnicity, and age
Trauma/Mental Health Group Differences on Adverse Baby Outcomes

Adverse birth outcome: intrauterine growth restriction, preterm delivery (< 37 weeks gestational age), baby admitted to NICU, low infant birthweight (< 2500 grams)

Preliminary unpublished data  Adjusted for income, race/ethnicity, and age
Trauma/Mental Health Group Differences in Trajectories of PTSD

Preliminary unpublished data
Trauma/Mental Health Group Differences in Trajectories of Depression

Preliminary unpublished data
Trauma/Mental Health Group Differences in Trajectories of Anxiety

Preliminary unpublished data
How do trauma-exposed women with PTSD and other mental health conditions experience pregnancy and labor and delivery?
Perinatal PTSD

Experience birth as traumatic

Postpartum PTSD

Ford et al., 2011; Seng et al., 2011
Reported Feeling Isolated During Labor and Delivery (L&D)

Preliminary unpublished data
Reported Perceiving L&D as Dangerous and Feared Infant Death/Injury During L&D

Preliminary unpublished data
Qualitative Experience of Labor & Delivery for Women with PTSD

“I just felt like I was alone. Like I felt like everyone was moving so slow. Like they wasn’t checking on me as much as they should have been checking on me. Because I was in there with no pain medication, you know what I mean, my first baby. Contractions on top of each other. I feel like I was the only one that was trying to make myself feel better. No one else was giving me any tools or tips or you know how to lay or how to breath. I was just kind of left alone.”

”Labor was scary”

Preliminary unpublished data
Summary

• Trauma exposure and/or current PTSD symptoms is associated with negative perinatal outcomes
  • These associations are consistent in Veteran samples

• Current PTSD and other mental health conditions increase perceived danger and fear during labor and delivery
What is the mechanism linking trauma and/or PTSD to negative pregnancy-related outcomes?
Potential Mechanisms

• HPA axis dysregulation
• Inflammation
• Behavioral changes (e.g., increased substance use)
Role of Hormones During Pregnancy and Postpartum
Role of Hormones During Pregnancy and Postpartum

Diagram showing the changes in maternal levels of HCG, Progesterone, and Estrogen over the months after the beginning of the last menstrual period.
Allopregnanolone/Pregnanolone (ALLO)

- ALLO is a neuroactive metabolite of progesterone
- Progesterone $\rightarrow$ 5alphaDHP $\rightarrow$ ALLO
- Positively modulates GABA$_A$ receptors
- Broad Impact
  - Anxiolytic
  - Antidepressant
  - Anticonflict
  - Neuroprotective and neurogenerative
  - Reduces pain
What do we know about ALLO and PTSD?

- Stress exposure and social isolation reduce ALLO levels in animal models of PTSD

Dong et al., 2001; Zhang et al., 2014
What do we know about ALLO and PTSD?

• Block in conversion of ALLO from 5alphaDHP observed among women with PTSD as compared to trauma-exposed healthy women

Rasmusson et al., 2006; Pineles et al., 2018
ALLO as a potential mechanism for preterm birth?

• Blocking ALLO production with finasteride in rats during the final days of pregnancy reduced gestational length

Paris et al., 2011
ALLO may impact preterm birth via multiple pathways
ALLO may impact preterm birth via multiple pathways.

- ALLO decreases expression of HPA-axis and the stress response system in late pregnancy.
- HPA-axis related hormones (e.g., CRH) are elevated in women who deliver preterm babies.

Brunton et al., 2009; McLean et al., 1993
ALLO may impact preterm birth via multiple pathways.

- ALLO reduces inflammation
- ALLO restrains the release of oxytocin

Brunton et al., 2009, Goldenberg et al., 2008; VanLandingham et al., 2007
The role of ALLO in perinatal depression and stress (and PTSD?)

• Low levels of ALLO in late pregnancy and the postpartum period correlate with increased depressive symptoms and stress reactivity

Crowley et al., 2016; Hellgreen et al., 2013; Nappi et al., 2001
PTSD

ALLO Deficit

Negative Pregnancy Outcomes
ALLO Levels by Group (N = 26)

Preliminary unpublished data
ALLO Levels by Group (N = 26)

Preliminary unpublished data
ALLO Levels by Group Postpartum (N = 26)

Preliminary unpublished data

PTSD
Trauma MH
Trauma Healthy
Healthy
ALLO Levels for Those Meeting Postpartum Depression Cut-off

Preliminary unpublished data
### Psychopharmacological Interventions

<table>
<thead>
<tr>
<th>Medication</th>
<th>Perinatal considerations</th>
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</table>
| Sertraline (SSRI)  | • FDA approved for PTSD; recommended by VA/DoD guidelines  
                      • Well studied; favorable safety profile in pregnancy and breastfeeding                           |
| Paroxetine (SSRI)  | • FDA-approved for PTSD; recommended by VA/DoD guidelines  
                      • Well studied; possible increased risk of cardiovascular malformation  
                      (inconsistent across studies, best methodology shows no increased risk)  
                      • Possible increased neonatal discontinuation side effects                                    |
| Fluoxetine (SSRI)  | • Not FDA-approved for PTSD; recommended by VA/DoD guidelines  
                      • Well studied; favorable safety profile in pregnancy  
                      • Side effects in some breastfeeding babies                                                     |
| Venlafaxine (SSNRI)| • Not FDA-approved for PTSD; recommended by VA/DoD guidelines  
                      • Reasonably well studied (less than the other three)  
                      • Favorable safety profile in pregnancy and breastfeeding                                      |

Slide courtesy of Laura Miller
It’s difficult to disentangle the effects of mental health symptoms and psychotropic medication exposure on fetus
Risk of untreated PTSD during pregnancy

Risk of SSRIs during pregnancy
ALLO and Postpartum Depression (and maybe PTSD?)

• Low levels of ALLO in late pregnancy and the postpartum period correlate with increased depressive symptoms and stress reactivity

Crowley et al., 2016; Hellgreen et al., 2013; Nappi et al., 2001
Zulpresso (Brexanolone) for postpartum depression

- 60 hour Brexanolone intravenous infusion vs. placebo for women with moderate to severe PPD
  - Intravenous formulation of ALLO

*Figure 3: Percentage change from baseline in mean HAM-D total score in the integrated BRX90 study population.*

P values were calculated by two-sided t test. BRX90 = brexanolone injection 90 μg/kg. *p<0.05 vs placebo.

Meltzer-Brody et al., 2018
First Drug for Postpartum Depression Released by the FDA March 2019

PHARMACEUTICAL NEWS

ZULRESSO (BREXANOLONE) IS THE FIRST DRUG APPROVED BY THE FDA SPECIFICALLY FOR POSTPARTUM DEPRESSION (PPD)

What is Zulresso?
Zulresso (brexanolone) is a gamma-aminobutyric acid A (GABAA) receptor positive allosteric modulator indicated for the treatment of postpartum depression (PPD).

Brexanolone
1-{3-Hydroxy-10,13-dimethyl-2,3,4,5,6,7,8,9,11,12,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)ethanone
Psychosocial Interventions for Perinatal PTSD

- Very limited research in this area
- Any evidence-based treatment for PTSD!
  - Cognitive Processing Therapy
  - Prolonged Exposure
  - Written Exposure Therapy
Managing Antepartum PTSD Study (MAPS)

• Open trial pilot study examining acceptability, feasibility, and preliminary effectiveness of Written Exposure Therapy for treatment of perinatal PTSD during pregnancy

• Delivered in the context of OBGYN care for pregnant women with comorbid PTSD and SUD

• N = 18 enrolled; N = 10 completed WET

PIs: Yael Nillni and Sarah Valentine
Written Exposure Therapy (WET)

• 5 sessions
• As effective as gold standard treatments for PTSD (e.g., Cognitive Processing Therapy) with fewer drop outs
• Low patient and therapist burden
• Session structure
  • Brief check-in
  • 30 minutes of writing the details and/or impact of the trauma (depending on session)
  • 10-15 minute processing of writing with therapist
# Demographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Intent To Treat (N = 18)</th>
<th>Completed WET (N = 10)</th>
<th>Dropped Out (N = 8)</th>
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</thead>
<tbody>
<tr>
<td><strong>Minority</strong></td>
<td></td>
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<tr>
<td></td>
<td>7 (38.9%)</td>
<td>3 (30%)</td>
<td>4 (50%)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Some high school, no diploma</td>
<td>5 (27.77%)</td>
<td>3 (30%)</td>
<td>2 (25.00%)</td>
</tr>
<tr>
<td>High School</td>
<td>5 (27.77%)</td>
<td>4 (40%)</td>
<td>1 (12.50%)</td>
</tr>
<tr>
<td>Some college/associates degree</td>
<td>8 (44.44%)</td>
<td>3 (30%)</td>
<td>5 (62.50%)</td>
</tr>
<tr>
<td><strong>Relationship Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>6 (33.33%)</td>
<td>3 (30%)</td>
<td>3 (37.50%)</td>
</tr>
<tr>
<td>In a relationship but living separately</td>
<td>9 (50.0%)</td>
<td>7 (70%)</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>Married or cohabitating</td>
<td>3 (16.66%)</td>
<td>0 (0%)</td>
<td>3 (37.50%)</td>
</tr>
<tr>
<td><strong>Living Situation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rent or own house/apartment</td>
<td>4 (22.22%)</td>
<td>1 (10%)</td>
<td>3 (37.50%)</td>
</tr>
<tr>
<td>Live with friend and not paying rent</td>
<td>4 (22.22%)</td>
<td>2 (20%)</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>Substance use residential program</td>
<td>10 (55.6%)</td>
<td>7 (70%)</td>
<td>3 (37.50%)</td>
</tr>
<tr>
<td><strong>Not Employed</strong></td>
<td>14 (77.77%)</td>
<td>7 (70%)</td>
<td>7 (87.50%)</td>
</tr>
<tr>
<td><strong>Household Income</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $15,000</td>
<td>12 (66.66%)</td>
<td>8 (80%)</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>$15,000 - $35,000</td>
<td>5 (27.77%)</td>
<td>2 (20%)</td>
<td>3 (37.50%)</td>
</tr>
<tr>
<td>$35,000 - $45,000</td>
<td>1 (5.55%)</td>
<td>0 (0%)</td>
<td>1 (12.50%)</td>
</tr>
<tr>
<td>Clinical Characteristics</td>
<td>Intent To Treat (N = 18)</td>
<td>Completed WET (N = 10)</td>
<td>Dropped Out (N = 8)</td>
</tr>
<tr>
<td>---------------------------</td>
<td>--------------------------</td>
<td>------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td><strong>Most Frequent Potentially Traumatic Events (PTE)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transportation accident</td>
<td>15 (83.3%)</td>
<td>7 (70.0%)</td>
<td>8 (100.0%)</td>
</tr>
<tr>
<td>Physical assault</td>
<td>17 (94.4%)</td>
<td>9 (90.0%)</td>
<td>8 (100.0%)</td>
</tr>
<tr>
<td>Assault with a weapon</td>
<td>14 (77.8%)</td>
<td>9 (90.0%)</td>
<td>5 (62.50%)</td>
</tr>
<tr>
<td>Sexual assault</td>
<td>15 (83.3%)</td>
<td>9 (90.0%)</td>
<td>6 (75.0%)</td>
</tr>
<tr>
<td>Other unwanted sexual experience</td>
<td>16 (88.9%)</td>
<td>9 (90.0%)</td>
<td>7 (87.5%)</td>
</tr>
<tr>
<td><strong>Perinatal Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal obstetrical medical condition (e.g., hypertension)</td>
<td>9 (50.0%)</td>
<td>7 (70.0%)</td>
<td>2 (25.0%)</td>
</tr>
<tr>
<td>Intrauterine growth restriction</td>
<td>7 (38.9%)</td>
<td>4 (40.0%)</td>
<td>3 (37.50%)</td>
</tr>
<tr>
<td>Pre-term delivery (GA 37 weeks)</td>
<td>4 (22.22%)</td>
<td>2 (20%)</td>
<td>2 (25.0%)</td>
</tr>
<tr>
<td><strong>Stayed engaged in Project RESPECT</strong></td>
<td>15 (83.33%)</td>
<td>9 (90.0%)</td>
<td>6 (75.0%)</td>
</tr>
<tr>
<td>Any relapse during study period</td>
<td>8 (44.4%)</td>
<td>5 (50.0%)</td>
<td>3 (37.5%)</td>
</tr>
<tr>
<td><strong>Number of unique PTEs endorsed</strong></td>
<td>6.87 (1.82)</td>
<td>6.50 (1.78)</td>
<td>6.13 (1.64)</td>
</tr>
<tr>
<td><strong>ACES total score</strong></td>
<td>7.0 (2.03)</td>
<td>6.63 (1.99)</td>
<td>7.50 (2.17)</td>
</tr>
<tr>
<td><strong>Number of unplanned visits to OB clinic</strong></td>
<td>5.72 (2.85)</td>
<td>5.00 (2.36)</td>
<td>6.63 (3.29)</td>
</tr>
</tbody>
</table>
Feasibility and Acceptability

• 56% of women who initiated treatment completed WET
  • Consistent with other first line PTSD treatments/usual care settings
  • Higher than PTSD treatment trials with PTSD/SUD population

• Patients reported high satisfaction with the treatment in both quantitative and qualitative measures

Preliminary unpublished data
Change in PTSD and Depressive Symptoms Pre-Treatment, Post-Treatment, and 6 Months Postpartum Follow-up

Preliminary unpublished data

Percentage Meeting Clinical Cut-Off for PTSD: PCL-5 score \( \geq 33 \)

Percentage Meeting Clinical Cut-Off for Depression: PHQ-9 score \( \geq 10 \)
Interventions for Trauma-Exposed Perinatal Women

• Survivor Moms Companion
  • Psychoeducational program for women who are pregnant or early postpartum with a history of trauma
  • 10-module manualized self-study program supported by weekly phone tutoring sessions with a health professional
  • Improves labor and delivery experiences
  • Improvements in postpartum PTSD, depression, and maternal-infant bonding

• https://survivormoms.org/

Rowe et al., 2014; Seng et al., 2011; Sperlich et al., 2011
CBT Following Delivery of Preterm Infant

• 6-session intervention delivered 1-2 weeks postpartum for moms whose babies were born between 25-35 weeks GA

• Treatment delivered in the NICU

• CBT focus (e.g., psychoeducation, cognitive restructuring, muscle relaxation, trauma narrative)

• Improved PTSD and depressive symptoms compared to usual care

Shaw et al., 2015
Summary

• Trauma history and current PTSD increases risk for a range of negative perinatal outcomes, including preterm birth, low infant birthweight, gestational diabetes, preeclampsia, and postpartum depression

• One potential mechanism explaining increased risk for negative perinatal outcomes is deficient ALLO levels

• Current evidence-based treatments for PTSD, including exposure-based interventions, are acceptable, feasible, and appropriate for treatment of perinatal PTSD