Integrated, Exposure-based Treatment of Co-occurring PTSD and Substance Use Disorders

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Outline

I. Background
   • Overview of PTSD
   • Interrelationship of PTSD and SUD

II. COPE Intervention
   • Research to date
   • Clinical components

III. Ongoing and Future Directions
   • Augmentation strategies
     o Pharmacotherapy
     o Technology enhancements
Post-traumatic Stress Disorder (PTSD)

• First included in DSM nomenclature in 1980. “Soldier’s heart” and “Shell shock.”
• A chronic disorder that may occur after exposure to Criterion A event (e.g., actual or threatened death, serious injury, or sexual violence).
• Trauma type examples: combat/military, natural disasters, child abuse, rape, serious car accident.
A. Exposure to a *Criterion A event* (e.g., threatened death, actual or threatened serious injury, sexual violence)

B. Re-experiencing (e.g., intrusive memories, nightmares)

C. Avoidance of trauma-related stimuli (e.g., places, activities, thoughts, feelings)

D. Negative alterations in cognitions or mood (e.g., exaggerated negative beliefs about self and others, shame and guilt)

E. Marked alterations in arousal and reactivity (e.g., hypervigilance, irritable behavior, angry outbursts, sleeping disturbance, self-destructive behaviors)

F. Duration of symptoms > 1 month

G. Significant distress or impairment
PTSD is the most common mental health disorder among Veterans presenting for treatment at VA hospitals (up to ~30% lifetime prevalence).

Kilpatrick et al., 2013; Kessler et al., 1995, 2005; PTSDunited.org; Seal et al., 2007
• Individuals with PTSD are 2 to 5 times more likely to have an SUD.
• Many individuals with co-occurring PTSD/SUD report early childhood traumas, such as childhood physical or sexual abuse.
• Multiple traumas and repeated victimization are the norm.
• As debilitating as PTSD can be, its clinical course is worsened by co-occurring SUD:
  • Poorer physical health
  • Poorer treatment response
  • More inpatient hospitalizations
  • More interpersonal and legal problems

Brown et al., 1998; El-Gabalawy et al., 2018; McDevitt-Murphy et al., 2010; Norman & Hien, 2020; Norman et al., 2007; 2018; Ouimette et al., 2006; Petrakis et al., 2011; Seal et al., 2007; Tate et al., 2007; Vujanovic & Back, 2019
PTSD and Opioids

• **High rates of trauma** (e.g., 92-97%) and **PTSD** (33-54%) among patients with opioid use disorder (OUD).

• Baseline PTSD (hyperarousal/reactivity symptoms) increases risk of developing OUD after exposure to opioid analgesics.

• **Only 12%** of patients with OUD+PTSD receive evidenced-based care for PTSD.

• Treating OUD+PTSD with MAT alone may not resolve underlying mental health conditions that increase risk of opioid use/relapse.

• Integrated treatment that also addresses PTSD may improve retention in treatment (including MAT) and outcomes for veterans.

(Bilevicius et al., 2018; Ecker & Hundt, 2018; Hassan et al., 2017; Meshberg-Cohen et al., 2019; Mills et al., 2005; Peck et al., 2018; Peirce et al., 2009; SAMHSA, 2017; Schacht et al., 2017; Schiff et al., 2015)
Do you believe that your substance use and PTSD symptoms are related?

Almost all (94%) indicate that their substance use and PTSD symptoms are related.

(Back et al., 2014)
If your PTSD symptoms *get worse*, what happens to your substance use?

Most Veterans (85%) indicate that their substance use increases when their PTSD symptoms get worse.

- **Increase**: 85%
- **Stay the Same**: 5%
- **Decrease**: 10%

85% report it increases
Clinical trials for PTSD typically exclude SUD comorbidity

- Out of 156 RCTs, **73.7% excluded participants based on substance use status** (e.g., current, past year, or lifetime diagnosis of SUD).

- Only 7.7% of studies examined substance use related outcomes.

- Importantly, **no studies observed increases in substance use** during PTSD treatment.

*Leeman et al., 2017*
How is Co-occurring PTSD/SUD Treated?

- Historically, the **sequential treatment approach** was the main/only option.

- SUD only treatment first (attain and maintain abstinence), then refer to PTSD treatment.

- Siloed, inefficient, and it is unclear how many patients successfully complete step 1 (SUD) and progress to and complete step 2 (PTSD).
Common Myths

• Talking about the trauma will make patients relapse or use more.
• You can’t start trauma work until patients are “clean” and sober.
• Abstinence is the only option.

*Empirical evidence disconfirms these myths. None are supported by research.
**What is Integrated Psychotherapy?**

- Behavioral intervention or “talk therapy” that integrates evidence-based treatment for both PTSD *and* SUD.

- Conducted by 1 clinician who works with the patient on both conditions *simultaneously* to help them achieve improvement in PTSD *and* SUD.

- Different from *parallel treatment* (e.g., 2 different providers each providing single-focused care) or *sequential treatment* (e.g., complete one single-focused treatment with 1 provider and then move to the next single-focused treatment with another provider).
Why Use Integrated Psychotherapy?

• Untreated PTSD is a risk factor for relapse/use.
• More efficient use of time and resources.
• Reduces potential for patients to “fall through the cracks.”
• Reductions in PTSD symptoms are more likely to lead to reductions in SUD, than the reverse.
• Patients recognize the symptom connection and many prefer integrated treatment.
• Recommended by VA/DOD and other clinical practice guidelines.

(Back et al., 2009; 2014; Brown et al., 1998, Flanagan et al., 2016; Hien et al., 2010; Norman & Hamblen, 2017; Vujanovic & Back, 2019)
Integrated PTSD/SUD Care Model

1. Treat PTSD + SUD Together
2. Manage PTSD symptoms without substances
3. Recovery from PTSD and SUD
4. Long Term Relief
COPE is a 12-session, evidence-based, trauma-focused integrated intervention. Sessions are 90 minutes, delivered once per week, in an individual format.

**Synthesis of two evidence-based treatments:**
- Prolonged Exposure (PE) for PTSD
- Cognitive Behavioral Therapy (CBT) for SUD

**Primary goals:**
- Provide psychoeducation
- Decrease PTSD symptoms via PE
- Decrease substance use using CBT techniques
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Yale Univ.

Drs. Kathleen Brady, Sudie Back, Therese Killeen & Julianne Flanagan
Medical Univ. of South Carolina
Research to date includes 4 RCTs, 2 open-label trials, 2 case reports, 2 ongoing RCTs. Findings show COPE is safe, feasible, and leads to significant reduction in PTSD and SUD (> 500 patients).

<table>
<thead>
<tr>
<th>Lead author, year</th>
<th>COPE Study Description</th>
<th>Civilian or Veteran</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brady et al., 2001</td>
<td>First open-label trial (cocaine and PTSD)</td>
<td>Civilian</td>
</tr>
<tr>
<td>Mills et al., 2012</td>
<td>First RCT (polysubstance drug use and PTSD, Australia)</td>
<td>Civilian</td>
</tr>
<tr>
<td>Back et al., 2012</td>
<td>First case report OEF/OIF Veteran (alcohol and PTSD)</td>
<td>Veteran</td>
</tr>
<tr>
<td>Ruglass et al., 2017</td>
<td>RCT in sub-threshold or full PTSD (polysubstance)</td>
<td>Civilian</td>
</tr>
<tr>
<td>Persson et al., 2017</td>
<td>Open-label trial among women (alcohol and PTSD, Sweden)</td>
<td>Civilian</td>
</tr>
<tr>
<td>Jaconis et al., 2017</td>
<td>First telehealth case (female with alcohol and MST)</td>
<td>Veteran</td>
</tr>
<tr>
<td>Back et al., 2019</td>
<td>First RCT in military Veterans (mostly alcohol and PTSD)</td>
<td>Veteran</td>
</tr>
<tr>
<td>Norman et al., 2019</td>
<td>First comparison of COPE vs. Seeking Safety (alcohol and PTSD)</td>
<td>Veteran</td>
</tr>
<tr>
<td>Mills et al., ongoing</td>
<td>First use of COPE in adolescents (COPE-A, Australia)</td>
<td>Civilians</td>
</tr>
<tr>
<td>Back &amp; Flanagan, ongoing</td>
<td>First combination of COPE + medication (oxytocin)</td>
<td>Veterans</td>
</tr>
</tbody>
</table>
Initial Proof-of-Concept Study

- N = 39 individuals (82.1% women, average age = 34) with cocaine dependence and PTSD
- Average age = 34, 8% married, 51% employed
- 74.4% reported rape, 94.9% reported physical assault

<table>
<thead>
<tr>
<th>Treatment outcome</th>
<th>Pre- to Posttreatment*</th>
<th>M(SD)</th>
<th>M(SD)</th>
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<tbody>
<tr>
<td>IES</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrusion</td>
<td>19.5 (13.0)</td>
<td>9.1 (7.1)*</td>
<td></td>
</tr>
<tr>
<td>Avoidance</td>
<td>20.1 (9.1)</td>
<td>14.6 (8.2)</td>
<td></td>
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<tr>
<td>Total</td>
<td>39.6 (21.4)</td>
<td>23.8 (13.7)</td>
<td></td>
</tr>
<tr>
<td>CAPS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrusion</td>
<td>9.4 (6.3)</td>
<td>3.2 (6.7)**</td>
<td></td>
</tr>
<tr>
<td>Avoidance</td>
<td>19.7 (10.1)</td>
<td>5.8 (8.9)**</td>
<td></td>
</tr>
<tr>
<td>Hyperarousal</td>
<td>16.6 (7.9)</td>
<td>8.7 (11.6)*</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>45.2 (19.8)</td>
<td>15.8 (23.0)***</td>
<td></td>
</tr>
<tr>
<td>MISS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>111.7 (21.9)</td>
<td>83.7 (24.8)*</td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td>12.1 (8.0)</td>
<td>5.7 (7.4)*</td>
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<tr>
<td>ASI</td>
<td>Family</td>
<td>0.28 (0.19)</td>
<td>0.18 (0.16)</td>
</tr>
<tr>
<td></td>
<td>Medical</td>
<td>0.35 (0.37)</td>
<td>0.26 (0.34)</td>
</tr>
<tr>
<td></td>
<td>Employment</td>
<td>0.61 (0.37)</td>
<td>0.57 (0.38)</td>
</tr>
<tr>
<td></td>
<td>Psychiatric</td>
<td>0.46 (0.10)</td>
<td>0.19 (0.17)***</td>
</tr>
<tr>
<td></td>
<td>Legal</td>
<td>0.13 (0.17)</td>
<td>0.07 (0.07)</td>
</tr>
<tr>
<td></td>
<td>Drug</td>
<td>0.20 (0.08)</td>
<td>0.08 (0.07)***</td>
</tr>
<tr>
<td></td>
<td>Alcohol</td>
<td>0.27 (0.22)</td>
<td>0.11 (0.16)***</td>
</tr>
</tbody>
</table>

Positive UDS Tests
At treatment entry = 12.8%
First half of treatment = 12.2%
Second half of treatment = 9.7%

(Brady, Dansky, Back, Foa & Carroll, 2001)
First RCT in Australia

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Sally Hopkins, MSc (Clin)
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Prolonged Exposure Therapy, a Cognitive-behavioral therapy (CBT) involving exposure to memories and reminders of past trauma, has long been regarded as a gold standard treatment for posttraumatic stress disorder (PTSD). Although there are other evidence-based treatments for PTSD, such as eye movement desensitization and reprocessing therapy, there is some empirical evidence for the efficacy of prolonged exposure therapy. However, for any other treatment, it has been standard therapy for PTSD and it has been the mainstay of PTSD treatment in the United States for many years.

Context. There is concern that exposure therapy, an evidence-based cognitive-behavioral therapy for posttraumatic stress disorder (PTSD), may be inappropriate because of the risk of relapse for patients with co-occurring substance dependence. The study compared two groups of PTSD and substance dependence symptom severity compared to usual treatment for substance dependence.

Design, Setting, and Participants. Randomized controlled trial enrolling 105 participants, who met DSM-IV-TR criteria for both PTSD and substance dependence. Participants were recruited from 2007-2009 in Sydney, Australia. Participants were assessed at 9 months postbaseline, with interim measures at 6 weeks and 3 months postbaseline.

Interventions. Participants were randomized to receive COPE plus usual treatment (n=57) or usual treatment alone (n=48). COPE consists of 13 individual 90-minute sessions (60-95) hour with a clinical psychologist.

Main Outcome Measures. Change in PTSD symptom severity as measured by the Clinician Administered PTSD Scale (CAPS), psychological distress as measured by the Impact of Event Scale, and addiction severity as measured by the Addiction Severity Index (ASI). A change in 15 points on the CAPS scale and 1 point on the ASI scale were considered clinically significant.

Results. From baseline to 9-month follow-up, significant reductions in PTSD symptom severity were found for both groups (mean difference, -4.34 (95% CI, -6.71 to -2.34) for the treatment group, and -2.14 (95% CI, -3.57 to -0.74) for the control group. However, the treatment group demonstrated a significantly greater reduction in PTSD symptom severity (mean difference, -6.09 (95% CI, -9.00 to -3.00). No significant differences were found between group differences in relation to changes in substance use, depression, or anxiety.

Conclusions. Among patients with PTSD and substance dependence, the combined use of COPE and usual treatment compared with usual treatment alone resulted in improvement in PTSD symptom severity without an increase in severity of substance dependence.
<table>
<thead>
<tr>
<th>Trauma/PTSD characteristics</th>
<th>N=103</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of first trauma</td>
<td>8 years old</td>
</tr>
<tr>
<td>Childhood trauma (before 15)</td>
<td>76.7%</td>
</tr>
<tr>
<td>Prior PTSD treatment</td>
<td>35.0%</td>
</tr>
<tr>
<td>Number of traumas</td>
<td>6 (2-10)</td>
</tr>
<tr>
<td>Average baseline CAPS</td>
<td>90</td>
</tr>
<tr>
<td><strong>Trauma types</strong></td>
<td></td>
</tr>
<tr>
<td>- Physical assault</td>
<td>93%</td>
</tr>
<tr>
<td>- Threatened or held captive</td>
<td>89%</td>
</tr>
<tr>
<td>- Witnessed injury or death</td>
<td>79%</td>
</tr>
<tr>
<td>- Sexual assault</td>
<td>78%</td>
</tr>
<tr>
<td>- Accident or disaster</td>
<td>66%</td>
</tr>
<tr>
<td>- Torture</td>
<td>24%</td>
</tr>
<tr>
<td>- Combat experience</td>
<td>2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Substance use characteristics</th>
<th>N=103</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Substance use</strong></td>
<td></td>
</tr>
<tr>
<td>History of injection drug use</td>
<td>79.6%</td>
</tr>
<tr>
<td>Prior SUD treatment</td>
<td>93.2%</td>
</tr>
<tr>
<td><strong>Past-month substance use</strong></td>
<td></td>
</tr>
<tr>
<td>- Benzodiazepines</td>
<td>73%</td>
</tr>
<tr>
<td>- Cannabis</td>
<td>69%</td>
</tr>
<tr>
<td>- Alcohol</td>
<td>67%</td>
</tr>
<tr>
<td>- Heroin</td>
<td>45%</td>
</tr>
<tr>
<td>- Amphetamines</td>
<td>42%</td>
</tr>
<tr>
<td>- Cocaine</td>
<td>21%</td>
</tr>
<tr>
<td><strong>Substance of Concern</strong></td>
<td></td>
</tr>
<tr>
<td>- Heroin</td>
<td>21%</td>
</tr>
<tr>
<td>- Cannabis</td>
<td>19%</td>
</tr>
<tr>
<td>- Amphetamines</td>
<td>18%</td>
</tr>
<tr>
<td>- Benzodiazepines</td>
<td>16%</td>
</tr>
<tr>
<td>- Alcohol</td>
<td>12%</td>
</tr>
<tr>
<td>- Cocaine</td>
<td>7%</td>
</tr>
</tbody>
</table>
• Compared COPE + TAU vs. TAU alone.
• Substance use decreased comparably – use did not increase with trauma work.
• COPE+TAU resulted in significantly lower CAPS ($p<.001$) compared to TAU.

*Mills et al., 2012*
Patient Quotes from Australian COPE RCT

• “Overall I thought it was great. No one had ever talked to me about my trauma before. It was good to put a name to my symptoms.”

• “It has changed my life. It was hard going through it but since doing it I have made a lot of positive changes... Doing the imaginal exposure really took the fear away.”

• “I didn’t even realize that PTSD treatment was available...I can now talk about the incident without freaking out.”

• “The imaginal exposure was the hardest part but also the most useful.”
• N = 110 individuals, 64% male
• Average age = 45 years old, 59% African American, 19% Hispanic/Latinx
• 53.6% physical assault, 28.6% sexual assault
• Primary substance = alcohol (45%), cocaine (17%), cannabis (8%), alcohol+stimulants (24%)
• COPE vs. RP vs. Active Monitoring Control Group:
  • Among those with full PTSD, COPE had significantly greater decreases in PTSD severity compared to RP (p<.05). NS among those with sub-threshold.
  • Significant reductions in substance use (end of treatment abstinence = 12.8% in COPE and 14% in RP).
  • Substance use did not increase with exposure work.
  • No differences in retention (# of sessions in COPE = 6 vs. RP = 7).

(Ruglass et al., 2017)
• N = 81, 90.1% male,
• Average age = 40.4 years old, 37% African-American, 4% Hispanic/Latinx
• Military-related index trauma = 81.0%
• 69.7% had physical assault and 24.7% had sexual trauma
• 63% alcohol use disorder, 27% alcohol & drug use disorders, 10% drug use disorder only.
• CAPS baseline = 81 (severe)
• Lifetime SI = 42% and lifetime attempt = 27%
• COPE vs. Relapse Prevention (RP)

(Back, Killeen, Badour, Flanagan, Allan, Santa Ana, Lozano, Korte, Foa & Brady, 2019)
COPE resulted in lower CAPS (\( p < 0.001 \), controlling for baseline) and PCL (\( p = 0.01 \)) scores than RP.

More participants achieved diagnostic remission in COPE vs. RP (ITT sample; 59.3% vs. 22.2%; \( p = 0.002 \); Odds Ratio [OR] = 5.28).

Back et al., 2019
**Substance Use:**
- Both groups had significant and comparable improvement in substance use.
- 40.7% in COPE and 25.9% in RP were abstinent during last 2 weeks of tx.
- At 6 months follow up, significantly lower average number of drinks per drinking day in COPE than RP (4.5 vs. 8.3, p<.05).

**Therapeutic Alliance (TA):**
- Positive therapeutic alliance at session 6 (COPE $M=5.3$ vs. RP $M=5.5$) and 12 (COPE $M=5.2$ vs. RP $M=5.4$).

**Retention**
- No differences in retention (# sessions in COPE = 9 vs. RP = 7).
- Majority of available COPE sessions (73.7%) and RP sessions (61.7%) attended.
Between-Session Habituation of Distress and Craving

- Habituation of fear (*Subjective Units of Distress; SUDS*) within session (W-S) and between sessions (B-S) in PTSD-only patients during PE shows B-S habituation predicts PTSD symptom improvement (Foa & McLean, 2016).

- Key findings from COPE study among PTSD+SUD patients:
  A) **B-S distress habituation** was association with greater reduction in *PTSD symptoms*.
  B) **B-S craving habituation** also associated with improvement in *PTSD symptoms*.
  C) **B-S craving habituation** was associated with greater decrease in *substance use*.

(Badour et al., 2017)
• N = 119
• 89.9% males, average age = 41.6 years old
• Mean number of traumatic events = 8.3
• 84.0% combat trauma (82.4% had physical assault, 23.5% had sexual trauma)

COPE vs. Seeking Safety (SS):
• SS does not include trauma processing or exposure
• Focuses on current symptoms (Taking Back Your Power, Asking For Help, Compassion)
• SS is typically 25 sessions in length – 12 sessions of both treatments used
• Greater reduction in PTSD symptoms and higher rates of PTSD remission in COPE vs. SS ($p < .05$).

• Comparable % days abstinent during COPE (67.5%) and SS (63.1%).

• Overall, 10/12 sessions attended, with fewer sessions in COPE (8.4) than SS (11.4) ($p = .001$).

• COPE led to greater reduction in trauma-related guilt than SS ($p = .04$; Capone et al., 2020).
PTSD and AUD Diagnostic Remission

- Back et al., 2019 (N=81)
  - COPE: 59.3%
  - RP: 22.2%

- Tripp et al., 2020 (N=73)
  - COPE: 51.5%
  - Seeking Safety: 17.2%

- Tripp et al., 2020 (N=73)
  - COPE: 45.5%
  - Seeking Safety: 37.5%

Percent

PTSD Remission

AUD Remission
PTSD and SUD frequently co-occur and are associated with a host of deleterious outcomes.

More effective treatments are needed to address this common comorbidity.

Integrated, exposure-based psychotherapy is safe, feasible, and effective in treating PTSD and SUD simultaneously.

Having a current SUD should not be a barrier to receiving trauma-focused treatment for PTSD.

(Peirce et al., 2020; Roberts et al., 2015; Simpson et al., 2017)
COPE Therapy Components
Techniques To Decrease PTSD and SUD

• **Prolonged Exposure (PE)** including in-vivo & imaginal exposure.

• **CBT techniques for SUD** to manage cravings, thoughts about using, and skills to help reduce/quit use.

• **Psychoeducation**
  - Education about common reactions to trauma (including avoidance and increased substance use)
  - Interrelationship between PTSD symptoms and use
  - Handouts for loved ones

• **Breathing Retraining** technique to manage anxiety and cravings.
<table>
<thead>
<tr>
<th>Session</th>
<th>Prolonged Exposure for PTSD</th>
<th>Relapse Prevention for SUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Introduction and overview of the treatment, psychoeducation regarding the interrelationship between PTSD and SUD, rationale for exposure, goals for therapy, breathing retraining exercise</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Commons reactions to trauma</td>
<td>Awareness of cravings</td>
</tr>
<tr>
<td>3</td>
<td>In vivo hierarchy</td>
<td>Managing cravings</td>
</tr>
<tr>
<td>4</td>
<td>Initiate imaginal exposure, continue in vivo exposures</td>
<td>Copings with cravings skills review</td>
</tr>
<tr>
<td>5</td>
<td>Continue imaginal and in vivo exposures</td>
<td>Planning for emergencies</td>
</tr>
<tr>
<td>6</td>
<td>Continue imaginal and in vivo exposures</td>
<td>Awareness of high-risk thoughts</td>
</tr>
<tr>
<td>7</td>
<td>Continue imaginal and in vivo exposures</td>
<td>Managing high-risk thoughts</td>
</tr>
<tr>
<td>8</td>
<td>Continue imaginal and in vivo exposures</td>
<td>Refusal skills</td>
</tr>
<tr>
<td>9</td>
<td>Continue imaginal and in vivo exposures</td>
<td>Seemingly irrelevant decisions</td>
</tr>
<tr>
<td>10</td>
<td>Continue imaginal and in vivo exposures</td>
<td>Awareness of anger</td>
</tr>
<tr>
<td>11</td>
<td>Continue imaginal and in vivo exposures</td>
<td>Managing anger</td>
</tr>
<tr>
<td>12</td>
<td>Review and termination</td>
<td></td>
</tr>
</tbody>
</table>
What is Prolonged Exposure (PE)?

• Highly effective trauma-focused treatment for PTSD (Foa, Hembree, Rothbaum, & Rauch, 2019) with > 30 yrs of empirical research.

• A best practice intervention supported by clinical guidelines (e.g., VA/DoD, IOM, NIH, SAMHSA).

• **Key components:**
  
  • **In vivo exposure** - the patient directly confronts feared, but safe, situations or places in “real life.”
  
  • **Imaginal exposure** - the patient revisits the memory of the trauma repeatedly during session.
Rationale for Exposure Therapy

- **Avoidance maintains PTSD symptoms.**
  - Normalize attempts to avoid (e.g., not leaving house or going to work, avoiding stores and people).
- But has it worked? Avoidance may be successful in the short-term but maintains PTSD in the long-run.
- Avoiding by using substances can worsen PTSD symptoms (e.g., withdrawal can mimic hyperarousal symptoms; SUD affects mood, cognitions, sleep; decreases ability of executive functioning system and amplifies limbic system, impacts HPA stress system).
Purpose of In Vivo Exercises

• Foster the realization that the avoided situation is safe, disconfirming their belief that the situation is dangerous.
• Patient learns that anxiety does not continue forever.
• Disconfirm the belief that they will not be able to tolerate the distress.
• Enhance sense of self-control and competence.
• Promote engagement in positive activities, hobbies, and relationships, reduces isolation.

❖ With PTSD/SUD clients, it helps them learn they can tolerate these situations without using substances, and that the anxiety goes down all on its own over time, without using (as do cravings).
In Vivo Exposures

- In-between therapy sessions
- Repeated and prolonged (~45 minutes)
- Gradual in nature
- Important that PTSD/SUD patients not use alcohol/drugs before, during, or immediately after to ensure mastery and new learning takes place.
- Select in vivo situations that are safe with regards to substance use.
Safety Behaviors

- Safety behaviors are things that people do or say to temporarily reduce negative feelings or distress.
- They maintain negative emotions and prevent corrective learning (i.e., that the patient can handle the situation without the safety behavior).
- Goal is to identify and remove safety behaviors to optimize effectiveness of in vivo exposure.
- Remind patient to not use any alcohol/drugs before, during, or immediately after the in vivo exercises.
What is Imaginal Exposure?

- Technique to help process traumatic memories.
- Revisit the memory repeatedly for 30-45 minutes followed by 10-15 minutes of processing.

**Purpose of imaginal exposure:**
- Organize the trauma memory, make sense of it, and foster new perspectives.
- Differentiate then vs. now (memory).
- Gain personal mastery and confidence.
- Habituate to anxiety and distressing feelings.
- Learn that will not fall apart or go crazy, and they can manage it without using substances.
The Wave of Anxiety

Anxiety

Time

1st imaginal session
2nd imaginal session
3rd imaginal session
4th imaginal session
5th imaginal session
**SUDS: The Subjective Distress Thermometer**

100 – Highest anxiety/distress that you have ever felt
90 – Extreme anxious/distressed
80 – Very anxious/distressed; can’t concentrate. Physiological signs may be present.
70 – Quite anxious/distressed; interfering with functioning. Physiological signs may be present.
60 – Moderate to strong anxiety or distress
50 – Moderate anxiety/distress; uncomfortable, but can continue to function
40 – Mild to moderate anxiety or distress
30 – Mild anxiety/distress; no interference with functioning
20 – Minimal anxiety/distress
10 – Alert and awake; concentrating well
0 – No distress; totally relaxed

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**Craving Thermometer**

100 – Strongest craving you have ever felt
90 – Extreme craving
80 – Very intense craving, persistent thoughts about using, physiological signs present
70 – Strong craving, interfering with functioning, unable to concentrate, may have physiological signs
60 – Moderate to strong craving
50 – Moderate craving, starting to interfere with functioning and concentration
40 – Mild to moderate craving
30 – Mild craving, thoughts about using, not interfering with functioning
20 – Minimal craving, fleeting thoughts about wanting to use
10 – Fleeting thoughts about alcohol or drugs
0 – No craving
### Craving and SUDS Decrease Over Time

Mean ratings of pre- and post-imaginal craving and distress by session.

<table>
<thead>
<tr>
<th>Session</th>
<th>Craving</th>
<th>Distress</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-imaginal</td>
<td>Post-imaginal</td>
</tr>
<tr>
<td></td>
<td>M (SD)</td>
<td>M (SD)</td>
</tr>
<tr>
<td>4</td>
<td>18.11 (25.99)</td>
<td>23.31 (32.04)</td>
</tr>
<tr>
<td>5</td>
<td>22.08 (30.36)</td>
<td>24.57 (31.61)</td>
</tr>
<tr>
<td>6</td>
<td>16.05 (25.63)</td>
<td>19.05 (25.73)</td>
</tr>
<tr>
<td>7</td>
<td>8.91 (15.95)</td>
<td>10.03 (19.94)</td>
</tr>
<tr>
<td>8</td>
<td>8.44 (16.34)</td>
<td>12.37 (22.87)</td>
</tr>
<tr>
<td>9</td>
<td>10.21 (17.93)</td>
<td>13.75 (25.41)</td>
</tr>
<tr>
<td>10</td>
<td>8.62 (14.69)</td>
<td>6.96 (19.50)</td>
</tr>
<tr>
<td>11</td>
<td>7.78 (16.25)</td>
<td>7.67 (17.33)</td>
</tr>
</tbody>
</table>

Scale is 0 to 100
Cravings typically low

(Jarnecke, Allan, Badour, Flanagan, Killeen & Back, 2019; c.f. Lancaster et al., 2019)
Overview of SUD Components

Primary goals:
• Normalize cravings.
• Identify triggers for cravings (both SUD-related and trauma-related triggers).
• Learn skills to effectively manage cravings.
• Recognize and modify high-risk thoughts about using alcohol/drugs.
• Learn effective coping skills (e.g., drug refusal skills).
Identify Triggers for Cravings

1. **People, places, and things**
   (e.g., being around alcohol/drugs, seeing others using, bars). Trauma cues can trigger cravings.

2. **Negative emotions**
   (e.g., loneliness, boredom, stress). Negative emotions associated with PTSD (e.g., anger, shame, guilt) can trigger cravings.

3. **Thoughts**
   (e.g., focusing on the pleasurable aspects of using without considering the negative aspects). Thoughts about the trauma can lead to cravings.

4. **Physical symptoms**
   (e.g., feeling on edge, restless, jumpy, muscle tension, physical pain, withdrawal symptoms).
What to approach and what to avoid?

• Explain why it is important to approach trauma cues and stay away from SUD cues?
  • Approaching trauma-related memories, thoughts, or situations in the environment that are safe.
  • Avoiding substance-related cues or places in the environment that are not safe and could increase substance use or relapse risk.

What is safe and what is not safe for them?
• Only ~50% identify abstinence as treatment goal.
• Goal of reducing use associated with younger age, employment, served in recent OEF/OIF conflicts, and fewer symptoms of AUD.
• Abstinence is the safest option and is encouraged, but not required.
• Normalize ambivalent feelings, emphasize it doesn’t have to be forever.
Establishing SUD Treatment Goals

Consider the following factors and discuss with the patient:

- **Degree of SUD:** **mild** (2-3 symptoms), **moderate** (4-5), **severe** (6+)

- **Negative consequences from use** (legal problems, incarceration, medical problems, job losses, relationship/child custody issues).

- **Previous SUD treatment outcomes** or attempts to cut back (e.g., longest time without using, history of seizures, detox or hospitalizations).

- **Family history** density or predisposition of SUD.

If goal is to significantly reduce use:

- Be specific about reduction (amount, frequency).
- Aim for having some DAYS with no use (therapy appt, in vivos).
- Revisit goals throughout therapy.
COPE is a trauma-focused treatment that includes PE (both imaginal and in vivo exposure) to reduce PTSD symptoms.

- Exposure therapy components start early (session 3) and are integrated with evidence-based CBT for SUD.
- **SUD component** focuses on teaching skills to manage cravings, thoughts about using, triggers for use, and help patients reduce use/abstain.
- Abstinence is the safest option, but not required to receive treatment.
- **Psychoeducation and breathing retraining** are provided.
- COPE helps patients approach safe, but avoided, trauma related stimuli without using substances, providing new learning.
Ongoing and Future Directions
• Further improve outcomes with pharmacotherapy
• Biometric-driven, virtually guided in vivo exposures
• COPE-A trial for adolescents in Australia
• Combine data from multiple trials to examine effectiveness of different PTSD/SUD treatments and mediators/moderators of outcome

**Project Harmony: A Virtual Clinical Trial (VCT)**

- Alternative group formats of delivery.
- Inpatient settings.

https://www.projectharmonyvct.com/

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Augmentation of COPE with Oxytocin

- Target N = 180 Veterans
- Current PTSD and Alcohol Use Disorders
- Receive oxytocin (40 IU) or placebo prior to each therapy session

Study design overview. Participants randomized to 12 weeks of COPE plus oxytocin (40 IU) or placebo. Weekly visits during weeks 1-12. Follow-up visits at 3- and 6-months post-treatment. Neuroimaging scans at pre- and post-treatment.
Oxytocin

- Hypothalamic 9 amino acid neuropeptide
- Self-administered intranasally
- Short half-life (2-4 hours)
- FDA-approved for women in childbirth (Pitocin via IV)
- Few known contraindications (seizure disorders, pregnancy)
- Highly favorable side effect profile
Oxytocin in Psychiatry

Prosocial Behavior
• OT increases trust, social cognition, affect sharing, empathy, cooperation – factors associated with positive psychosocial outcomes.

Addiction
• Reduces craving, tolerance, withdrawal symptoms, and self-administration.
• Improves corticolimbic connectivity, which is implicated in AUD (and PTSD).
• May reduce stress-induced alcohol consumption via GABAergic transmission in the central nucleus of the amygdala.
• Plasma OT levels increase following abstinence in AUD.

PTSD
• OT enhances fear extinction (purported mechanism of exposure-based treatment).
• Attenuates amygdala reactivity to fear-related cues.
• Pilot data show OT + PE therapy safely and more rapidly reduced PTSD symptoms.

(Flanagan et al., 2018, 2019, 2020; Flanagan & Mitchell, 2019; King et al., 2016; Lee et al. 2016; MacDonald & MacDonald, 2010; MacGregor and Bowen, 2012; Olff et al., 2010; Pederson et al., 2012; Tunstall et al., 2019)
• Examine underlying AUD/PTSD comorbidity and obtain valuable mechanistic insights.
• Prior to first scan, develop personalized imagery scripts for alcohol, trauma, and neutral events using adapted and manualized cue development procedures (Sinha & Tuit, 2012).
• Structural, resting state, and task-activated fMRI at pre- and post-treatment.
Biometric-driven, virtually guided in vivo exposures

- In vivos are key treatment component, but typically “invisible” to the clinician.
- Digital device allows clinician to virtually accompany patients during in vivo exercises.
- Clinician dashboard shows real-time streaming of HR, GSR, and distress ratings – indices of engagement that are used in the moment to optimize the exposure.
- May enhance accountability, effectiveness, and retention.

**Figure 1.** Patient interface consisting of wearables and a software application on a mobile phone that is transmitted to a secure server and can be viewed by the therapist.

Dr. Delisa Brown, Dr. Amber Jarnecke, Mr. Bill Harley, Dr. Robert Adams, Mr. Will Brown, Dr. Sudie Back, Dr. Tanya Saraiya
Integrated, trauma-focused treatment is one option to effectively treat PTSD and SUD. Research among men and women, civilians and Veterans, patients with multiple SUDs and traumas demonstrates COPE is feasible, safe (substance use decreases) and efficacious. Having a current SUD should not be a barrier to receiving evidence-based, trauma-focused treatment. More research is needed to address gaps, such as further improving outcomes with augmentation (e.g., pharmacotherapy, technology, device), reducing attrition, and prevention of PTSD/SUD.

(Hamblen et al., 2019; Peirce et al., 2020; Roberts et al., 2015; Simpson et al., 2017)
Thank you!

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