

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



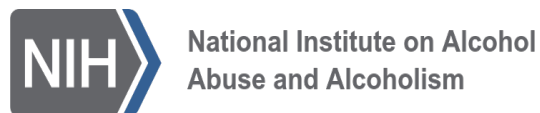
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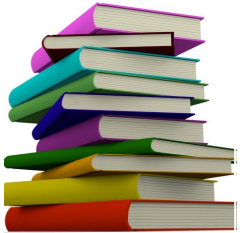
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Disclosure Statement

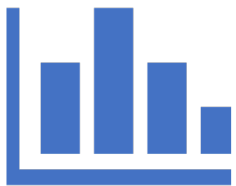
The COPE trials have been sponsored by NIDA and NIAAA (R01 DA030143; PI: Back and R01 AA02811; PIs: Back & Flanagan) and the therapy manuals are published through Oxford University Press.

Outline



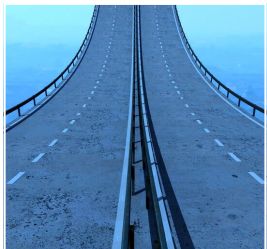
I. Background

- Overview of PTSD
- Interrelationship of PTSD and SUD



II. COPE Intervention

- Research to date
- Clinical components



III. Ongoing and Future Directions

- Augmentation strategies
 - Pharmacotherapy
 - Technology enhancements

Post-traumatic Stress Disorder (PTSD)

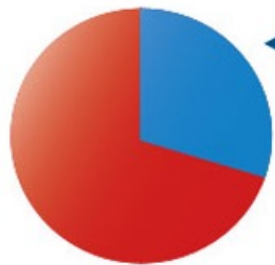
- First included in DSM nomenclature in **1980**. “Soldier’s heart” and “Shell shock.”
- A chronic disorder that may occur after exposure to *Criterion A event* (e.g., actual or threatened death, serious injury, or sexual violence).
- Trauma type examples: combat/military, natural disasters, child abuse,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



DSM-5 Criteria for PTSD

- 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 \geq 1 month
- G. Significant distress or impairment

How common is PTSD?



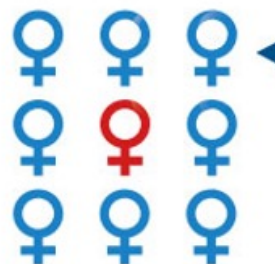
70% of adults in the U.S. have experienced some type of traumatic event at least once in their lives.



Up to 20% of these people go on to develop PTSD.



An estimated 8% of Americans – 24.4 million people – have PTSD at any given time. That is equal to the total population of Texas.



An estimated one out of every nine women develops PTSD, making them about twice as likely as men.

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

Trauma, PTSD, and SUD Comorbidity

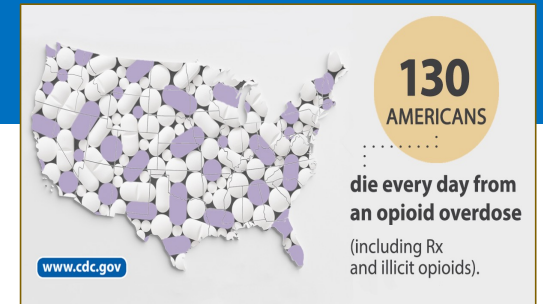
- Individuals with PTSD are **2 to 5 times** more likely to have an SUD.
- Many individuals with co-occurring PTSD/SUD report **early childhood traumas**, such as childhood physical or sexual abuse.
- **Multiple traumas** and repeated victimization are the norm.
- As debilitating as PTSD can be, its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

Higher rates of attempted suicide
Higher rates of suicidal ideation

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

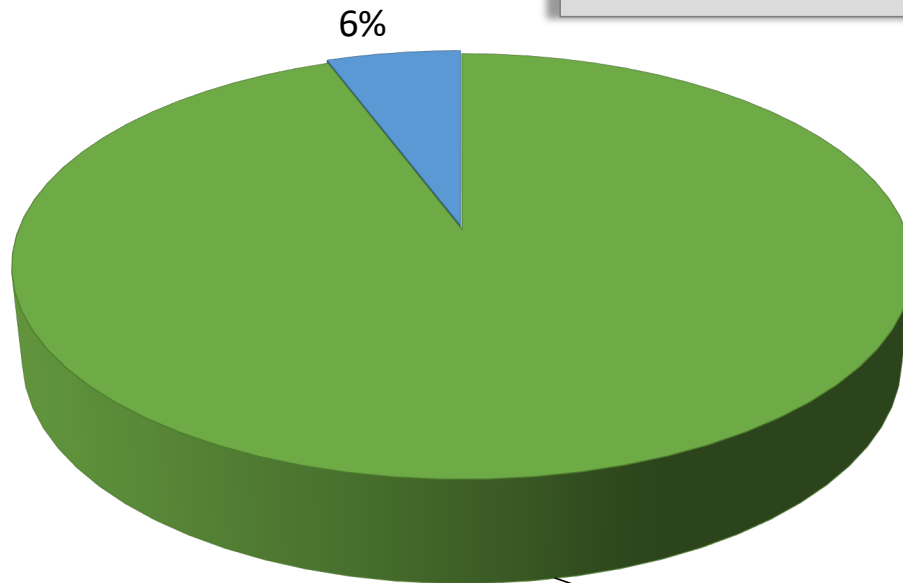
- **High rates of trauma** (e.g., 92-97%) and **PTSD** (33-54%) among patients with opioid use disorder (OUD).
- Baseline PTSD (hyperarousal/reactivity symptoms) increases risk of developing OUD after exposure to opioid analgesics.
- **Only 12%** of patients with OUD+PTSD receive evidenced-based care 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.



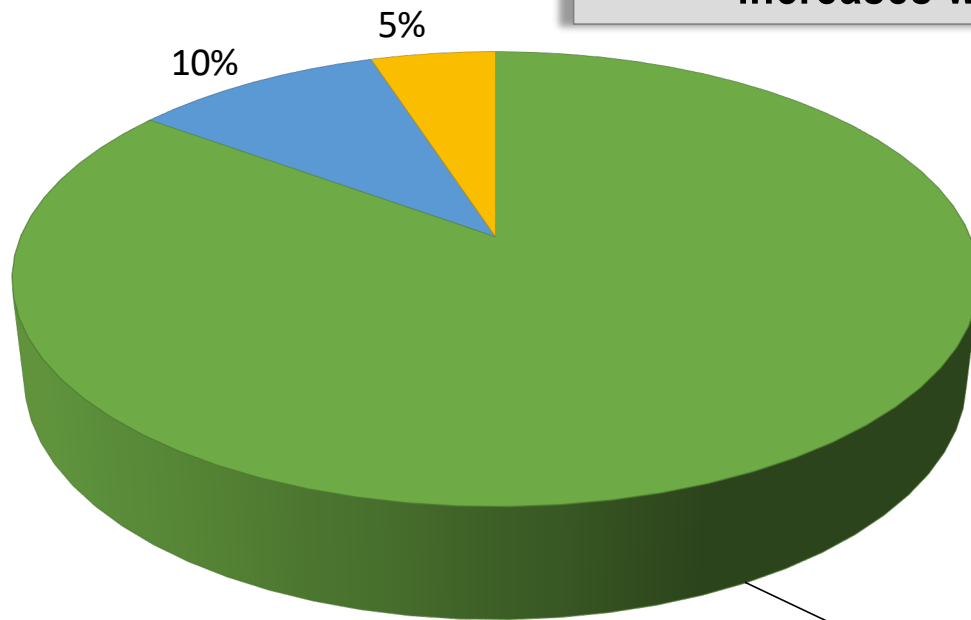
■ Related ■ Unrelated

94% say they 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.

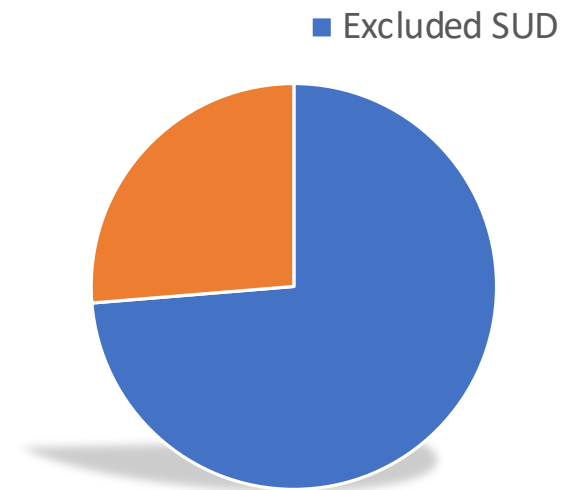


■ Increase ■ Stay the Same ■ Decrease

85% report it increases

Clinical trials for PTSD typically exclude SUD comorbidity

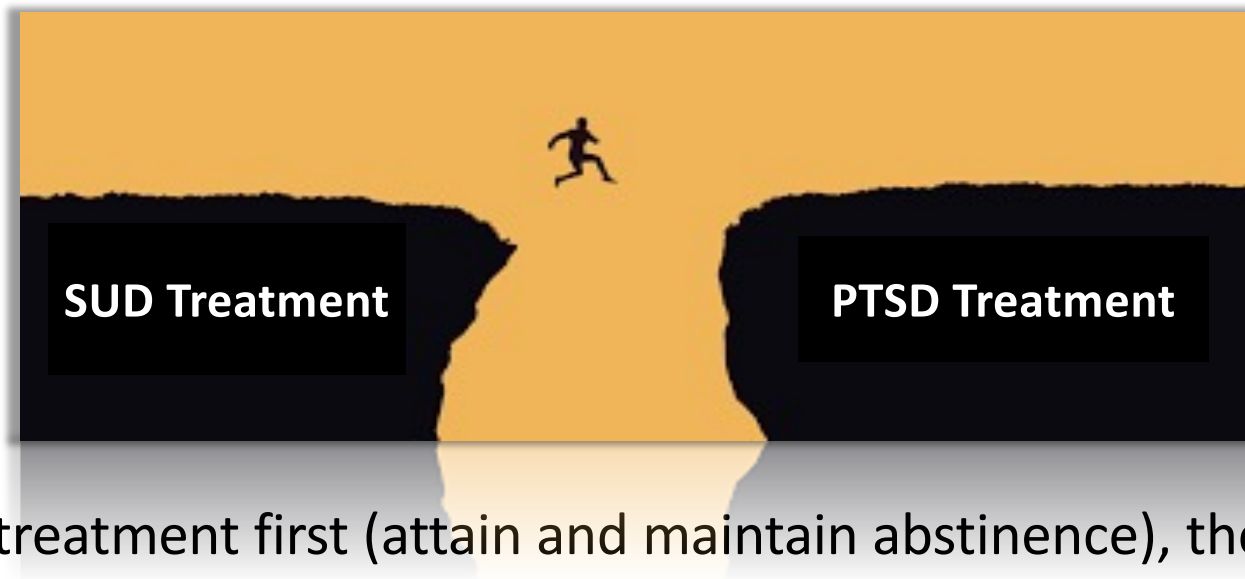
- Out of 156 RCTs, **73.7% excluded participants based on substance use status** (e.g., current, past year, or lifetime diagnosis of SUD).
- Only 7.7% of studies examined substance use related outcomes.
- Importantly, **no studies observed increases in substance use** during PTSD treatment.



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).

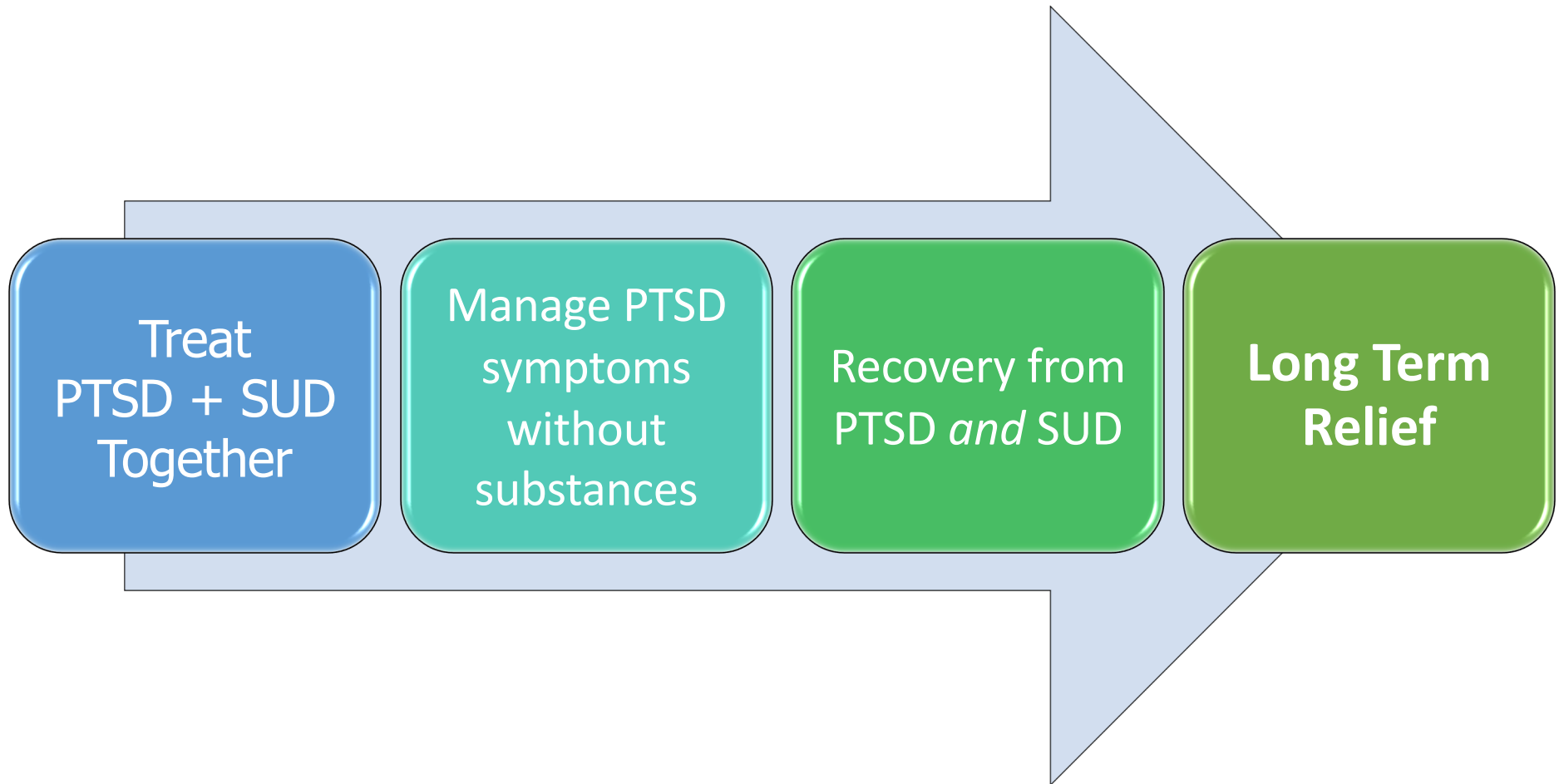
Why Use Integrated Psychotherapy?



- 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



Concurrent Treatment of PTSD and SUD Using Prolonged Exposure (COPE)

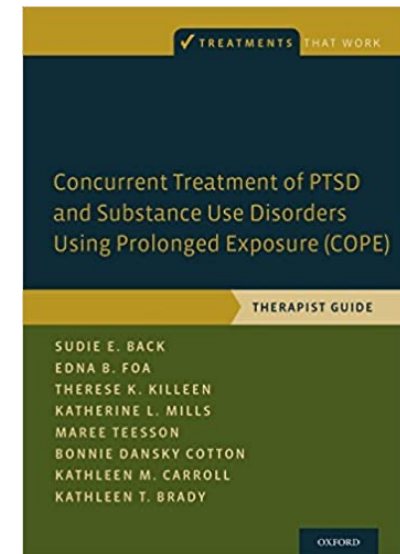
- COPE is a 12-session, evidence-based, trauma-focused integrated intervention.
- Sessions are 90 minutes, delivered once per week, in an individual format.

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



COPE Collaborators



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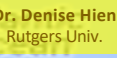
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COPE Studies to Date

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).

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

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



Dr. Kathleen Brady

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

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)



Dr. Katherine Mills

First RCT in Australia

JAMA

The Journal of the American Medical Association

August 15, 2012



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www.jama.com



ORIGINAL CONTRIBUTION

Integrated Exposure-Based Therapy for Co-occurring Posttraumatic Stress Disorder and Substance Dependence A Randomized Controlled Trial

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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 more empirical evidence for the efficacy of prolonged exposure than for any other treatment.¹ Indeed, the International Consensus Group on Depression and Anxiety recommends prolonged exposure as the most appropriate form of psychotherapy for PTSD,² and it was the only treatment for PTSD endorsed in a US Institute of Medicine study as evidence based.³ The efficacy of prolonged exposure in reducing PTSD symptom severity has been demonstrated among persons from a number of populations who have been exposed to a wide variety of trauma types.⁴ There is, however, a notable absence of research examining the

Context There is concern that exposure therapy, an evidence-based cognitive-behavioral treatment for posttraumatic stress disorder (PTSD), may be inappropriate because of risk of relapse for patients with co-occurring substance dependence.

Objective To determine whether an integrated treatment for PTSD and substance dependence, Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE), can achieve greater reductions in PTSD and substance dependence symptom severity compared with usual treatment for substance dependence.

Design, Setting, and Participants Randomized controlled trial enrolling 103 participants who met DSM-IV-TR criteria for both PTSD and substance dependence. Participants were recruited from 2007-2009 in Sydney, Australia; outcomes were assessed at 9 months postbaseline, with interim measures collected at 6 weeks and 3 months postbaseline.

Interventions Participants were randomized to receive COPE plus usual treatment (n=55) or usual treatment alone (control) (n=48). COPE consists of 13 individual 90-minute sessions (ie, 19.5 hours) with a clinical psychologist.

Main Outcome Measures Change in PTSD symptom severity as measured by the Clinician-Administered PTSD Scale (CAPS; scale range, 0-240) and change in severity of substance dependence as measured by the number of dependence criteria met according to the Composite International Diagnostic Interview version 3.0 (CIDI; range, 0-7), from baseline to 9-month follow-up. A change of 15 points on the CAPS scale and 1 dependence criterion on the CIDI were considered clinically significant.

Results From baseline to 9-month follow-up, significant reductions in PTSD symptom severity were found for both the treatment group (mean difference, -38.24 [95% CI, -47.93 to -28.54]) and the control group (mean difference, -22.14 [95% CI, -30.33 to -13.95]); however, the treatment group demonstrated a significantly greater reduction in PTSD symptom severity (mean difference, -16.09 [95% CI, -29.00 to -3.19]). No significant between-group difference was found in relation to improvement in severity of substance dependence (0.43 vs 0.52; incidence rate ratio, 0.85 [95% CI, 0.60 to 1.21]), nor were there any significant between-group differences in relation to changes in substance use, depression, or anxiety.

Conclusion Among patients with PTSD and substance dependence, the combined use of COPE plus usual treatment, compared with usual treatment alone, resulted in improvement in PTSD symptom severity without an increase in severity of substance dependence.

Trial Registration isrctn.org Identifier: ISRCTN12908171
JAMA. 2012;308(7):690-699

www.jama.com

efficacy of prolonged exposure among individuals with co-occurring PTSD and substance dependence.




Epidemiologic and clinical research has demonstrated that trauma exposure among individuals with substance dependence is almost universal, and up to 62% experience comorbid PTSD.^{5,6} Similarly,

up to 65% of patients with PTSD have been found to have a comorbid substance use disorder.^{7,8} Although PTSD is perva-





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See also p 714 and Patient Page.

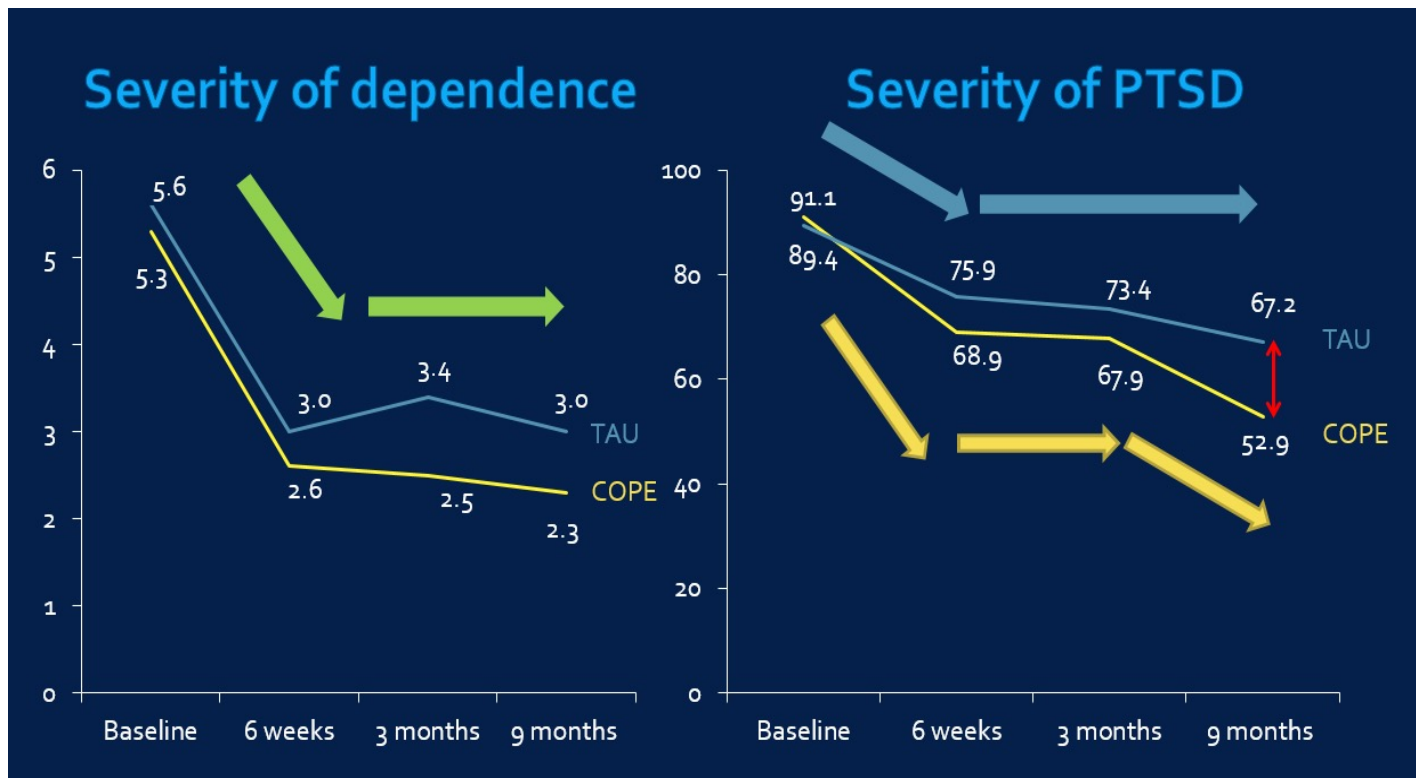
Trauma/PTSD characteristics

| Trauma/PTSD | N=103 |
|---|-------------|
| Age of first trauma  | 8 years old |
| Childhood trauma (before 15) | 76.7% |
| Prior PTSD treatment | 35.0% |
| Number of traumas  | 6 (2-10) |
| Average baseline CAPS  | 90 |
| <u>Trauma types</u> | |
| - Physical assault | 93% |
| - Threatened or held captive | 89% |
| - Witnessed injury or death | 79% |
| - Sexual assault | 78% |
| - Accident or disaster | 66% |
| - Torture | 24% |
| - Combat experience | 2% |

Substance use characteristics

| Substance use | N=103 |
|---|-------|
| History of injection drug use  | 79.6% |
| Prior SUD treatment | 93.2% |
| <u>Past-month substance use</u> | |
| - Benzodiazepines | 73% |
| - Cannabis | 69% |
| - Alcohol | 67% |
| - Heroin | 45% |
| - Amphetamines | 42% |
| - Cocaine | 21% |
| <u>Substance of Concern</u> | |
| - Heroin  | 21% |
| - Cannabis  | 19% |
| - Amphetamines  | 18% |
| - Benzodiazepines | 16% |
| - Alcohol | 12% |
| - Cocaine | 7% |

- 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.



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.*”



COPE in Full vs. Subthreshold PTSD

Psychother Psychosom 2017;86:150–161

- 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).



Dr. Lesia Ruglass



Dr. Denise Hien

(Ruglass et al., 2017)

RCT in Military Veterans

Ralph H. Johnson VA, Charleston SC

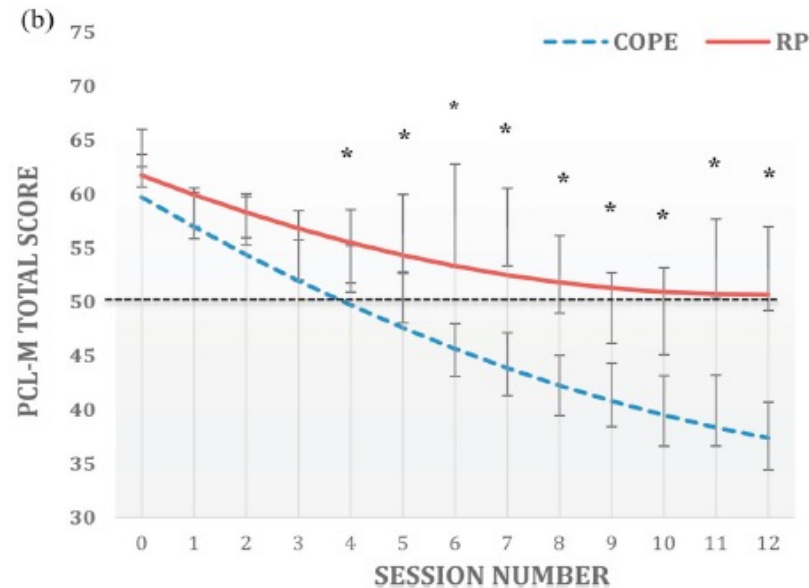
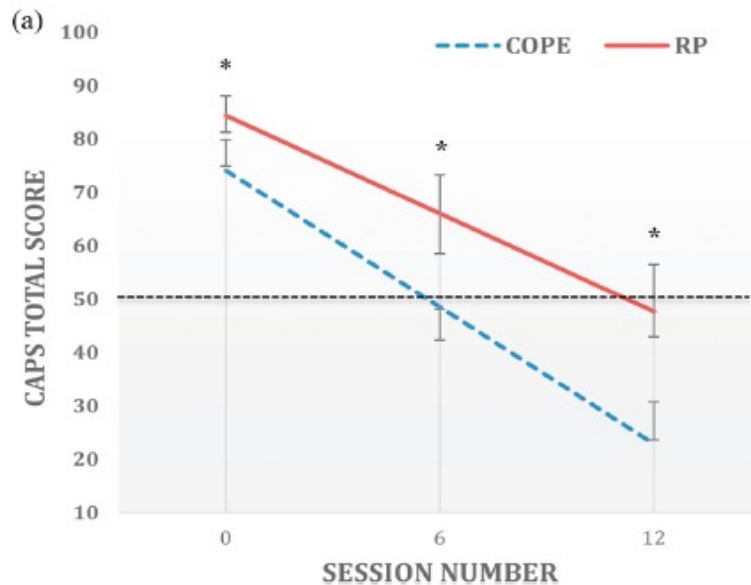
Addictive Behaviors 90 (2019) 369-377

- 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)

PTSD Symptom Improvement: COPE vs. Relapse Prevention



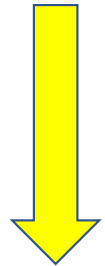
Dr. Christal Badour

- COPE resulted in lower CAPS ($p < .001$, controlling for baseline) and PCL ($p = .01$) scores than RP.
- More participants achieved diagnostic remission in COPE vs. RP (ITT sample; 59.3% vs. 22.2%; $p = .002$; Odds Ratio [OR] = 5.28).

Results cont'd

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 $M=5.4$).



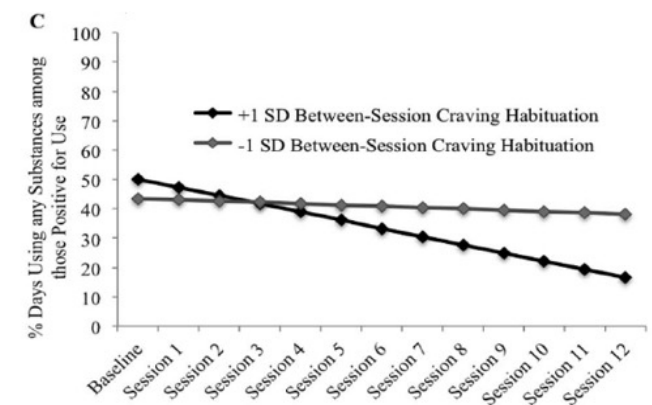
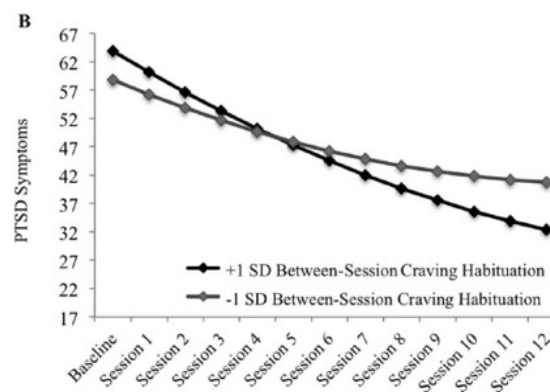
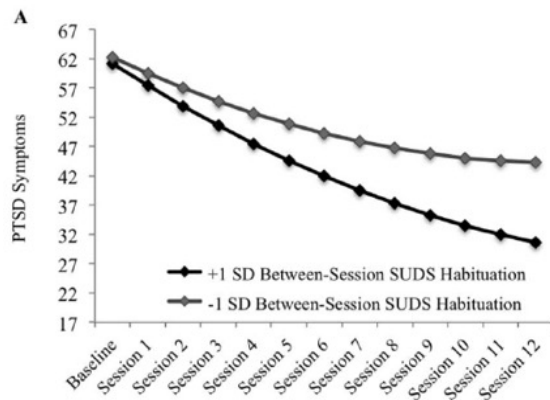
Retention

- 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 associated 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)

JAMA Psychiatry | Original Investigation

Efficacy of Integrated Exposure Therapy vs Integrated Coping Skills Therapy for Comorbid Posttraumatic Stress Disorder and Alcohol Use Disorder

A Randomized Clinical Trial

JAMA Psychiatry. doi:10.1001/jamapsychiatry.2019.0638
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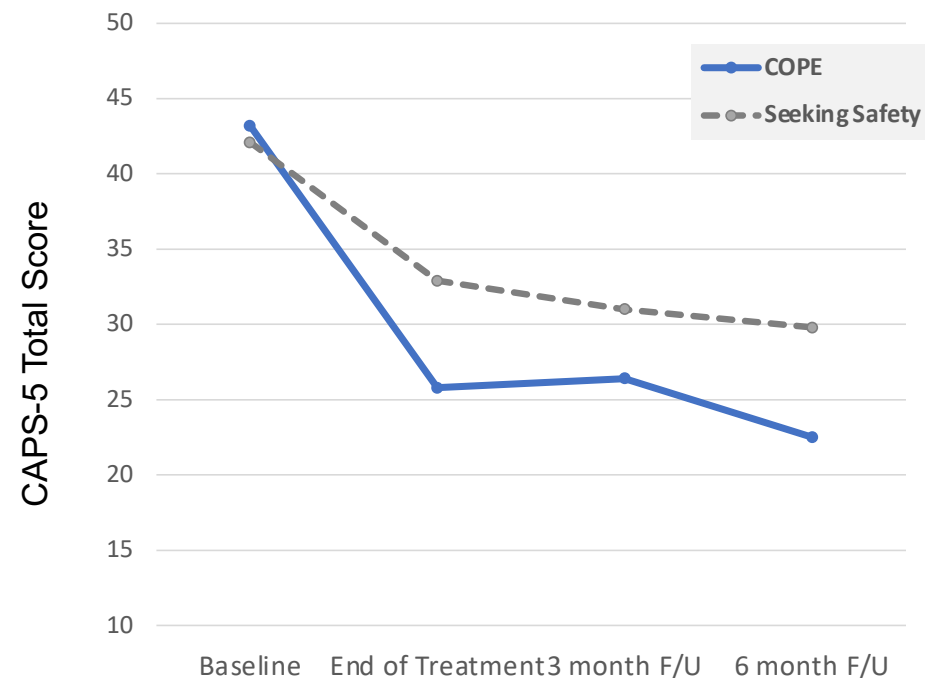
- N = 119
- 89.9% males, average age = 41.6 years old
- Mean number of traumatic events = 8.3
- 84.0% combat trauma (82.4% had physical assault, 23.5% had sexual trauma)

COPE vs. Seeking Safety (SS):

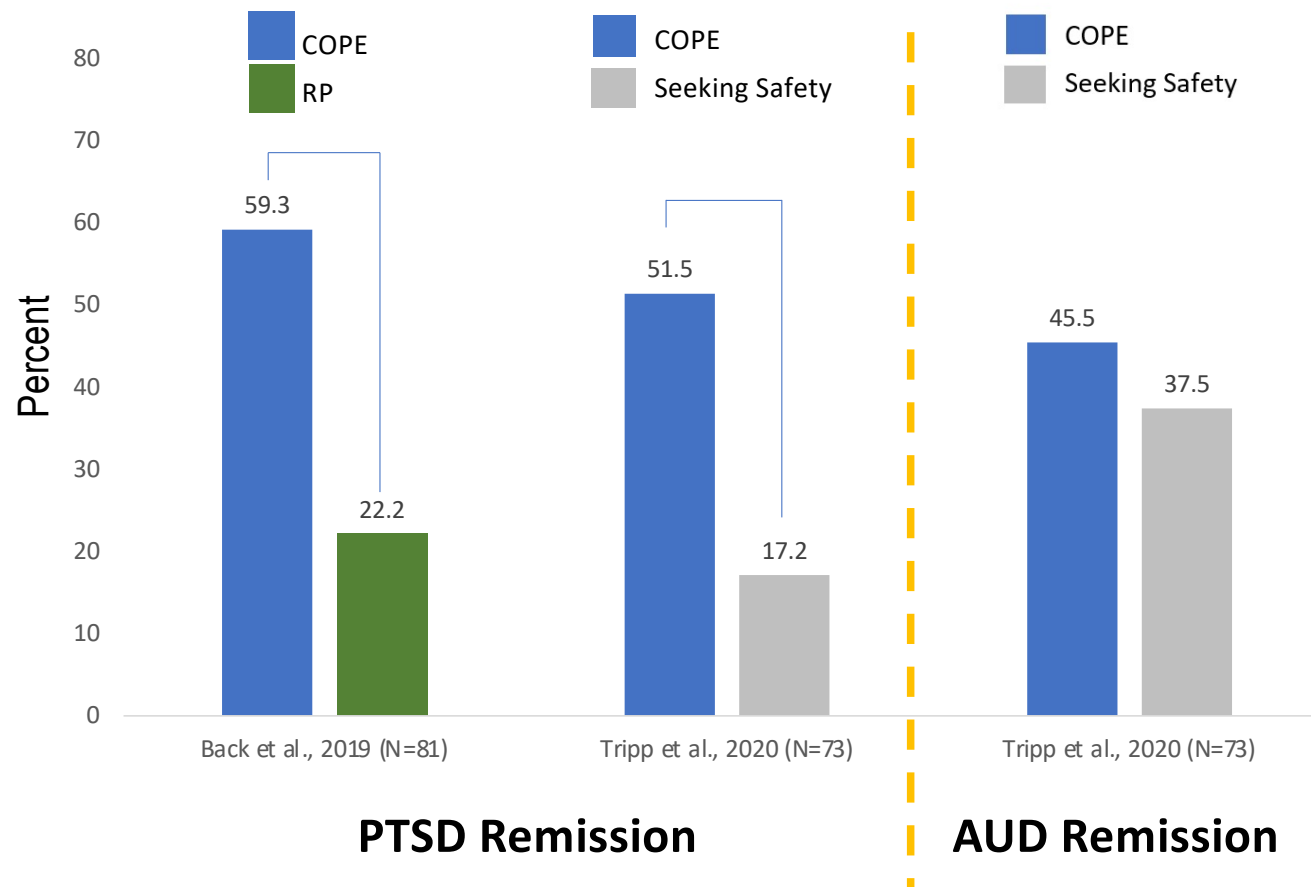
- SS does not include trauma processing or exposure
- Focuses on current symptoms (Taking Back Your Power, Asking For Help, Compassion)
- SS is typically 25 sessions in length – 12 sessions of both treatments used

PTSD Symptom Improvement: COPE vs. Seeking Safety

- 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



Summary – Part I

- 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 1. Table of Contents – COPE Therapy Sessions

| Session | Prolonged Exposure for PTSD | Relapse Prevention for SUD |
|----------------|--|-------------------------------------|
| 1 | Introduction and overview of the treatment, psychoeducation regarding the interrelationship between PTSD and SUD, rationale for exposure, goals for therapy, breathing retraining exercise | |
| 2 | Commons reactions to trauma | Awareness of cravings |
| 3 | In vivo hierarchy | Managing cravings |
| 4 | Initiate imaginal exposure, continue in vivo exposures | Copings with cravings skills review |
| 5 | Continue imaginal and in vivo exposures | Planning for emergencies |
| 6 | Continue imaginal and in vivo exposures | Awareness of high-risk thoughts |
| 7 | Continue imaginal and in vivo exposures | Managing high-risk thoughts |
| 8 | Continue imaginal and in vivo exposures | Refusal skills |
| 9 | Continue imaginal and in vivo exposures | Seemingly irrelevant decisions |
| 10 | Continue imaginal and in vivo exposures | Awareness of anger |
| 11 | Continue imaginal and in vivo exposures | Managing anger |
| 12 | Review and termination | |

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.



The image shows the homepage of the PEWeb website. At the top left is the MUSC logo (Medical University of South Carolina) with the text 'National Center for Veterans Research & Treatment Center'. To the right is the PE logo (Prolonged Exposure Emotional Processing Therapy) and a circular diagram. A navigation bar contains links for 'Register', 'Login', 'Introduction', 'Resources', 'About', and 'My Account'. The main heading reads 'PEWeb' in a stylized font, followed by 'A web-based learning course for PROLONGED EXPOSURE FOR PTSD'. A central image shows a soldier in camouflage holding a black helmet. To the right is a list of course topics: Basics, Assessment, Treatment Components, Rationale & Trauma Interview, Psychoeducation, In Vivo Exposure, Imaginal Exposure, Processing, Hotspots, Homework, Special Issues, Special Populations, and Telehealth. At the bottom, there are three small images: a soldier, a tank, and a soldier in a helmet. The footer includes the text 'A Strategy for Healing' and 'System Requirements | Home', along with a copyright notice: 'Copyright © 2013-2014 Medical University of South Carolina'.

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.**

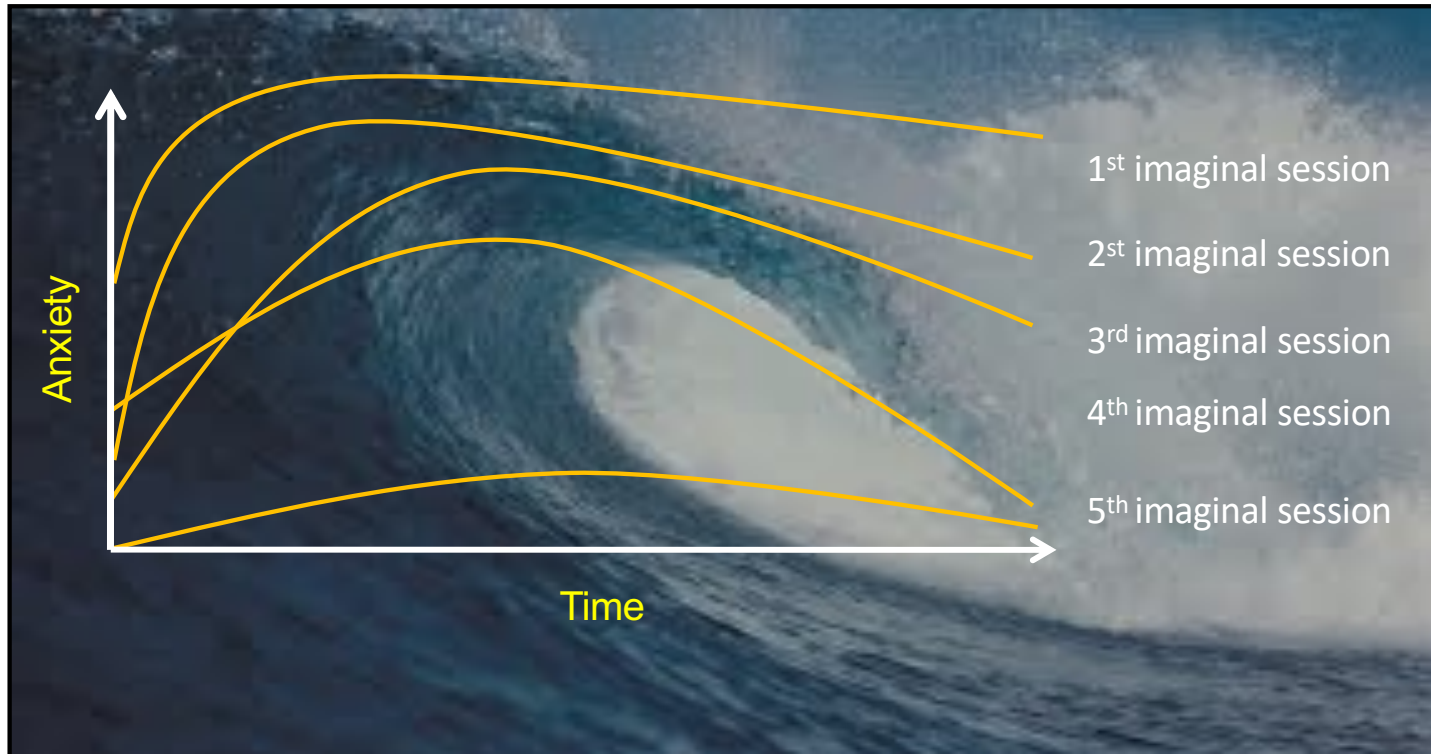


What is Imaginal Exposure?

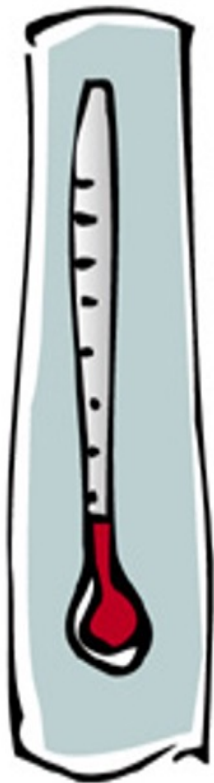
- Technique to help process traumatic memories.
- Revisit the memory repeatedly for 30-45 minutes followed by 10-15 minutes of processing.
- Purpose of imaginal exposure:
 - ❖ Organize the trauma memory, make sense of it, and foster new perspectives.
 - ❖ Differentiate then vs. now (memory).
 - ❖ Gain 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

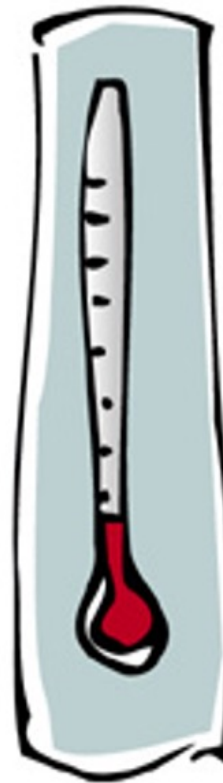


SUDS: The Subjective Distress Thermometer



- 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

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.

Scale is 0 to 100
Cravings typically low

| Session | Craving | | Distress | |
|---------|---------------|---------------|---------------|---------------|
| | Pre-imaginal | Post-imaginal | Pre-imaginal | Post-imaginal |
| | M (SD) | M (SD) | M (SD) | M (SD) |
| 4 | 18.11 (25.99) | 23.31 (32.04) | 52.05 (24.03) | 58.13 (27.10) |
| 5 | 22.08 (30.36) | 24.57 (31.61) | 41.35 (28.12) | 50.22 (26.51) |
| 6 | 16.05 (25.63) | 19.05 (25.73) | 41.03 (26.88) | 42.44 (25.54) |
| 7 | 8.91 (15.95) | 10.03 (19.94) | 35.30 (24.97) | 38.64 (24.73) |
| 8 | 8.44 (16.34) | 12.37 (22.87) | 28.59 (23.29) | 36.72 (26.32) |
| 9 | 10.21 (17.93) | 13.75 (25.41) | 33.83 (24.94) | 35.70 (27.65) |
| 10 | 8.62 (14.69) | 6.96 (19.50) | 21.38 (19.77) | 28.28 (24.50) |
| 11 | 7.78 (16.25) | 7.67 (17.33) | 25.37 (22.31) | 27.78 (19.18) |



Dr. Amber Jarnecke

(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?

THE AMERICAN JOURNAL ON ADDICTIONS

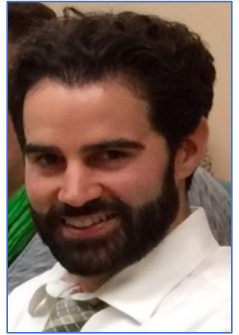
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ISSN: 1055-0496 print / 1521-0391 online
DOI: 10.1111/ajad.12263

To Reduce or Abstain? Substance Use Goals in the Treatment of Veterans With Substance Use Disorders and Comorbid PTSD

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Maryanne Jaconis, MA,² Francis M. Beylotte III, MA,² Stephen Boyd, MA,²
Sudie E. Back, PhD^{1,2}**

¹Ralph H. Johnson Veterans Affairs Medical Center, Charleston, South Carolina

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Dr. Brian Lozano

- 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.

Summary – Part II

- 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

Ongoing Studies

- **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)**

<https://www.projectharmonyvct.com/>

- Alternative group formats of delivery.
- Inpatient settings.

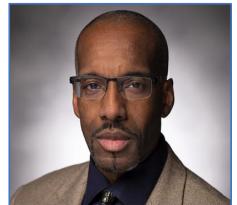
Dr. Julianne Flanagan



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Dr. Denise Hien



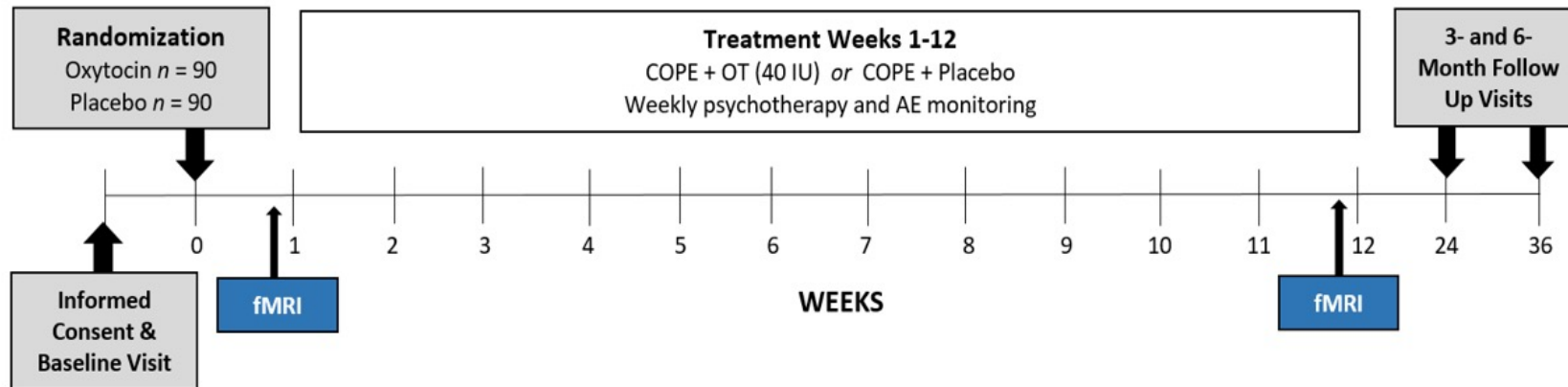
Augmentation of COPE with Oxytocin



Dr. Julianne Flanagan

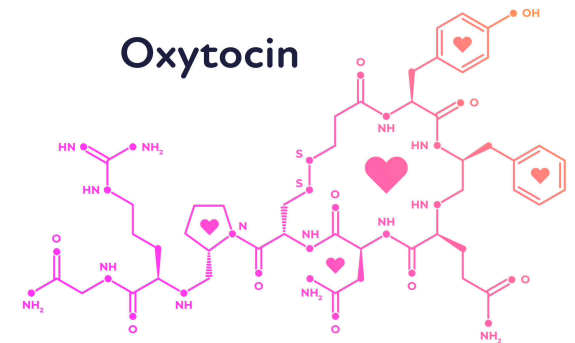
- Target N = 180 Veterans
- Current PTSD and Alcohol Use Disorders
- Receive oxytocin (40 IU) or placebo prior to each therapy session

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.

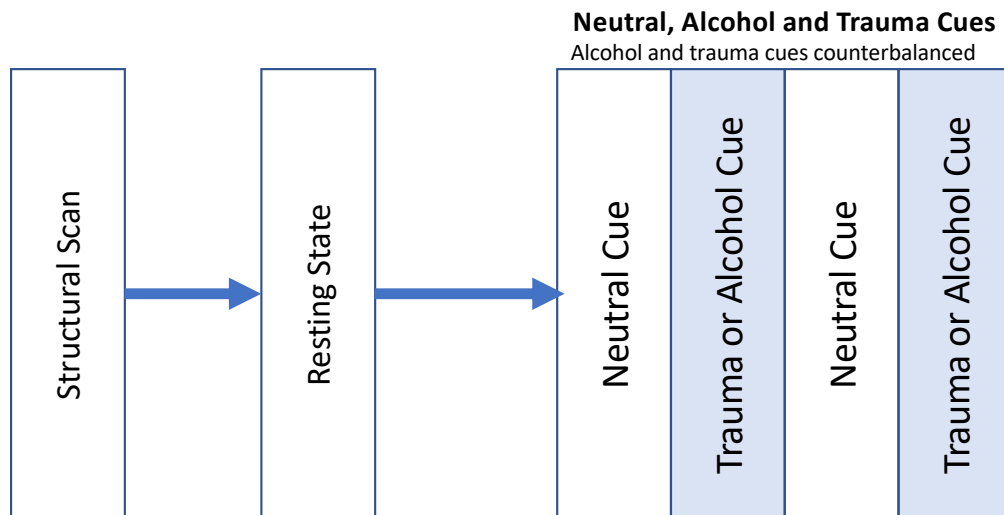
How oxytocin helps make social interactions rewarding PAGE 173



(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)

Neuroimaging Component

- 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.



Dr. Jane Joseph



MUSC Center for Biomedical Imaging (CBI) Staff -
Siemens 3T Prisma MRI

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.

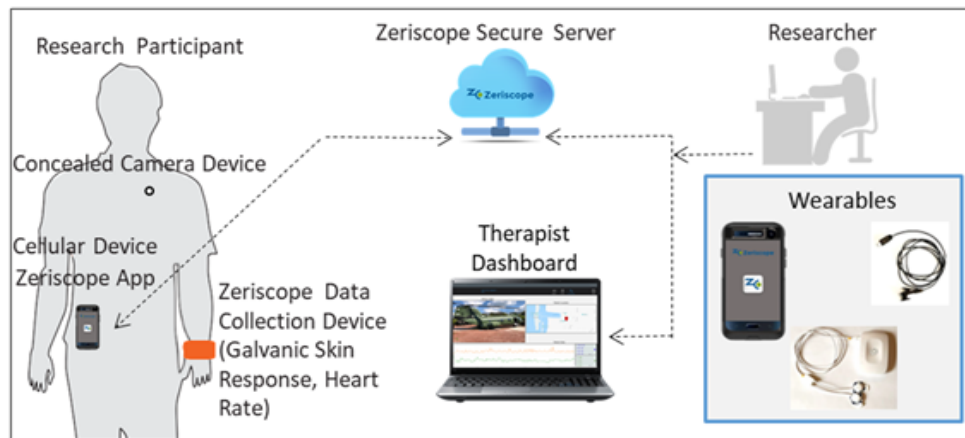
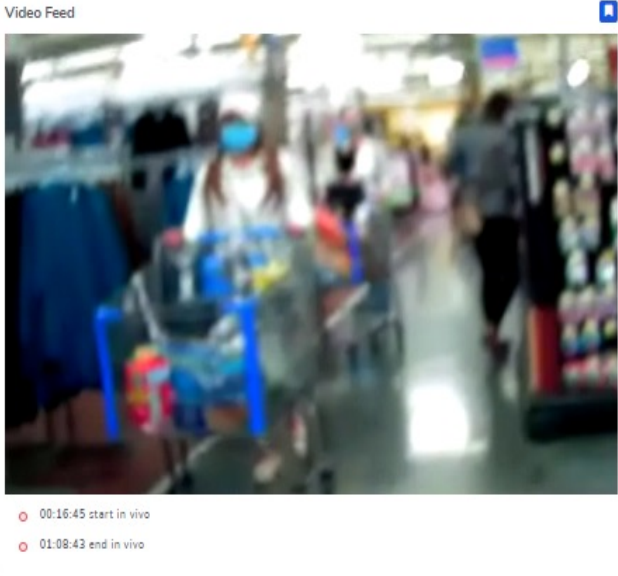
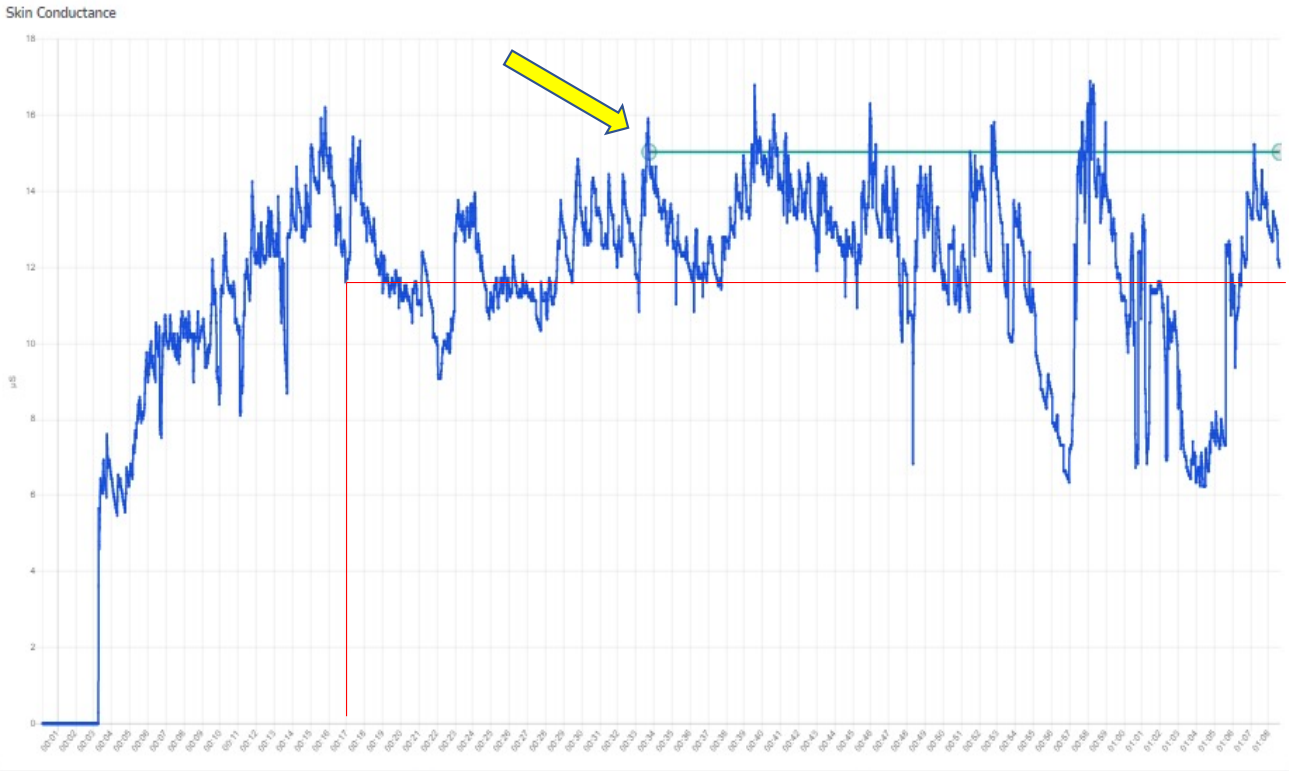


Figure 1. Patient interface consisting of wearables and a software application on a mobile phone that is transmitted to a secure server and can be viewed by the therapist.



Dr. Delisa Brown, Dr. Amber Jarnecke, Mr. Bill Harley, Dr. Robert Adams, Mr. Will Brown, Dr. Sudie Back, Dr. Tanya Saraiya

Lozano Patient IVE



| | |
|-----|-------|
| GSR | 15.04 |
| HR | 95 |

SUDs/Map

SUDs Map

20 - 2:59:40 PM

Microsiemens

15.04 µS

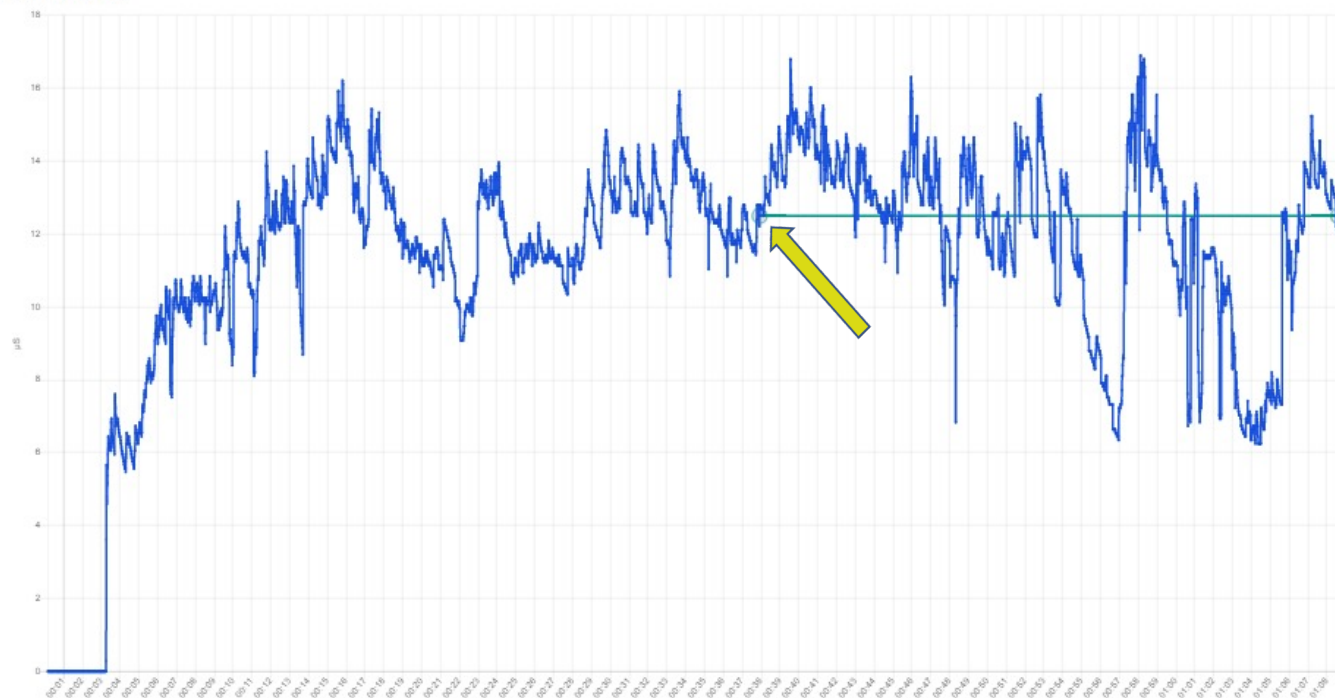
| | |
|--------------------|----------|
| Minimum | 0.29 µS |
| Maximum | 16.21 µS |
| Difference Min.Max | 15.92 µS |

Heart rate

95 bpm

| | |
|--------------------|---------|
| Minimum | 41 bpm |
| Maximum | 121 bpm |
| Difference Min.Max | 80 bpm |

Skin Conductance



Video Feed



00:16:45 start in vivo
01:08:43 end in vivo

SUDs/Map

SUDs Map

20 - 2:59:40 PM

Microsiemens

12.50 µS

Minimum 0.29 µS
Maximum 16.21 µS
Difference Min.Max 15.92 µS

Heart rate

82 bpm

Minimum 41 bpm
Maximum 121 bpm
Difference Min.Max 80 bpm

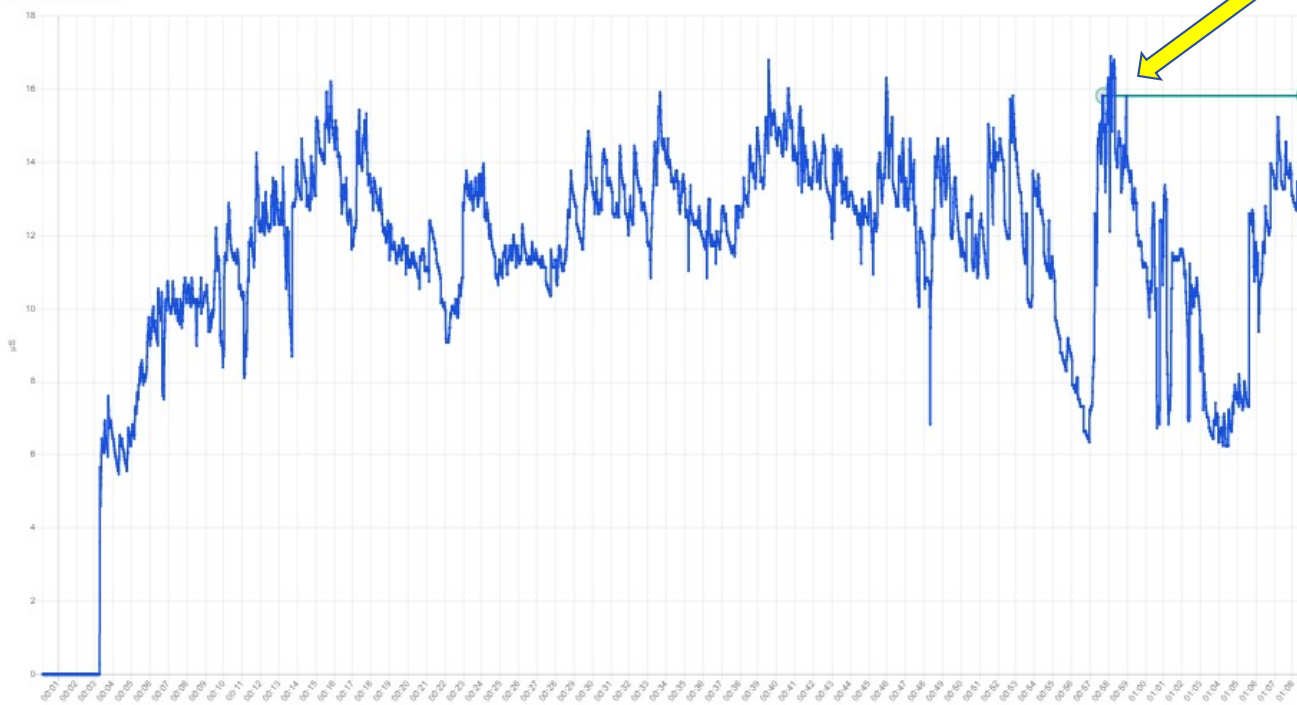
GSR 15.04

HR 95

GSR 12.50

HR 82

Skin Conductance



Video Feed



- 00:16:45 start in vivo
- 01:08:43 end in vivo

SUDs/Map

SUDs Map

20 - 2:59:40 PM

Microsiemens

15.82 μ S

Minimum 0.29 μ S
 Maximum 16.80 μ S
 Difference Min_Max 16.50 μ S

Heart rate

94 bpm

Minimum 41 bpm
 Maximum 121 bpm
 Difference Min_Max 80 bpm

| | |
|-----|-------|
| GSR | 15.04 |
| HR | 95 |

| | |
|-----|-------|
| GSR | 12.50 |
| HR | 82 |

| | |
|-----|-------|
| GSR | 15.82 |
| HR | 94 |

Summary

- 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)



Welcome to the
Ralph H. Johnson VA Medical Center



Thank you!

Sudie Back, PhD

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