The Intersection of Substance Use Disorders and PTSD: Overview and Advances in Treatment

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Study Collaborators and Staff

Disclosure Statement

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Outline

1. Epidemiology of PTSD/SUD
2. Integrated Treatments
   • Behavioral
   • Pharmacological
3. Summary & Clinical Considerations

Post-Traumatic Stress Disorder (PTSD)

• PTSD can develop after exposure to a “criterion A” event, such as childhood abuse, rape or sexual assault, physical assault, combat, accidents, domestic violence, or natural disasters.

How common is PTSD?

• The majority of people experience at least one “criterion A” event - 75.9% of general population in Canada.
• Approximately 10-20% of trauma-exposed individuals develop PTSD.
• Estimated lifetime prevalence of PTSD:
  • Canada = 9.2%
  • US = 7.8%

(Ameringer et al., 2008; Kilpatrick et al., 2013; Kessler et al., 1995,1998,2005)
PTSD symptoms

1. Intrusions
   - (e.g., distressing thoughts, dreams, flashbacks)

2. Avoidance
   - (e.g., people/places/situations that are reminders of the event)

3. Negative alterations in cognitions and mood
   - (e.g., negative beliefs about self/others, anger, guilt, shame, detached from others)

4. Alterations in reactivity
   - (e.g., difficulty sleeping or concentrating, hypervigilance)

Individuals with (vs. without) PTSD are ~5 to 7 times more likely to develop a substance use disorder (SUD).

SUD treatment-seeking samples:
- 80% - 92% have been exposed to trauma
- 30% - 60% have lifetime PTSD

Veterans serving in Vietnam era or later (N= 1,001,996), 41.4% with an SUD were diagnosed with PTSD.

(Brady et al., 2004; Damsky et al., 1994; Bove et al., 2012; Kessler et al., 1995; Goldstein et al., 2016; Grant et al., 2016; Petrakis et al., 2011; Taylor et al., 2016)
Non-Random Association

PTSD+SUD Negative Outcomes

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., 2000; Barrett et al., 2015; Brady et al., 2009; Killeen et al., 2013; Dunette et al., 2006)
If your PTSD symptoms *get worse*, what happens to your substance use?

Most Veterans (85%) indicate that if their PTSD symptoms increase, their substance use also increases.

85% report it increases

(Bark, Killeen, et al., 2014)

Summary

- PTSD and SUD are common, chronic conditions.
- Frequent co-occurrence and association with negative physical and mental health.
- A critical need to develop more effective treatments.

PTSD/SUD Integrated Behavioral Treatments
PTSD/SUD Treatment Models

1. Sequential Model
   - SUD first, PTSD later

2. Parallel Model
   - SUD and PTSD treated at same time by different clinicians

3. Integrated Model
   - Treat the SUD and PTSD concurrently, same clinician

Exclusion of participants based on substance use status: Findings from randomized controlled trials of treatments for PTSD

Exclusion of participants based on substance use status: Findings from randomized controlled trials of treatments for PTSD

- N=156 randomized controlled trials
- 74% excluded potential participants based on substance use status.
- 70% did not report descriptive characteristics of substance use.
- Only 8% reported substance-related outcomes.
- None reported an increase in substance use during PTSD tx.
- Makes it difficult to evaluate potential benefits of PTSD treatment in comorbid SUD patients.

Why use an integrated model?

- Sequential model deficits

1. Substance Use Treatment

2. PTSD Treatment
Why use an integrated model? cont’d

- More efficient use of time and clinical resources.
- Significant proportion of PTSD/SUD patients prefer an integrated treatment approach:
  - One clinician
  - One treatment episode
- Reductions in PTSD symptoms are more likely to lead to reductions in substance use, than the reverse.

(Back et al., 2009, 2014; Brown et al. 1998; Epstein et al., 1998; Hien et al., 2010; Jacobsen et al., 2001; Kessler et al., 1997; Stewart & Conrod, 2000).

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PTSD severity reduction associated with SUD severity reduction

PTSD treatment responders (vs. non-responders) had significantly fewer:
- Percent days drinking ($p < 0.01$)
- Percent heavy drinking days ($p < 0.01$)
- Average drinks per day ($p < 0.01$)

(Back, Brady, Sonne & Verduin, JNMD, 2006; see also Hien et al., 2010, AJP)

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Minimal evidence of substance use reduction associated with PTSD reduction

No significant differences in Impact of Events Scale or Mississippi Scale by SUD response status.

(Back, Brady, Sonne & Verduin, JNMD, 2006; see also Hien et al., 2010, AJP)
Overview of PTSD/SUD
Integrated Treatment Approach

Treat PTSD + SUD
Manage PTSD symptoms without substances
Recovery from PTSD and SUD
Long Term Relief

Integrated CBT Interventions

• **Non Exposure-Based**
  - **Seeking Safety** – Najavits, 2002; 25 topics. Present focused, coping skills based group therapy. Adding sertraline to SS may help further reduce PTSD (Hien et al., 2015).

• **Exposure-based**
  - **Cognitive Processing Therapy (CPT)** – Kaysen et al., 2014. Chart review of 536 Veterans (43% with SUD) completed 9 sessions of CPT. McCarthy & Petrakis, 2011 – case report of 12 session CPT.
  - **Prolonged Exposure** – In vivo and imaginal exposures (Back et al., 2014; Brady et al., 2001; Foa et al., 2013).

Cochrane Review of Integrated PTSD/SUD Therapies
14 studies included – 1,506 participants
• Evidence that individual trauma-focused therapies delivered alongside SUD intervention are more effective than TAU for (a) PTSD at post-treatment and follow-up (b) drug/alcohol use at follow-up (5–7 months). Note drop out rates high, and effect sizes modest.
• Trauma-focused includes exposure based processing of the memory (e.g., Foa & Rothbaum, 1998; Resick & Schnicke, 1993).
Synthesis of 2 empirically-validated CBT treatments:

1. **Prolonged Exposure (PE)** for PTSD
   (Foa, Hembree, & Rothbaum, 2007)

2. **Relapse Prevention** for SUD
   (Carroll, 1998)

**Primary Goals:**
1. **Educate** patients about the functional relationship between substance use and PTSD.
2. **Decrease PTSD** symptom severity via Prolonged Exposure (in-vivo and imaginal exposure).
3. **Decrease substance use** severity. No requirement of abstinence.

**COPE**
(Concurrent Treatment of PTSD & Substance Use Disorders using Prolonged Exposure)

**COPE Collaborators**

**COPE Therapy Overview**

- 12, individual, 60-90 minute therapy sessions
- Contents:
  - Introduction, psychoeducation about PTSD+SUD, develop treatment goals.
  - Coping with cravings and thoughts about using.
  - Identify triggers for cravings (both trauma- and substance-related triggers).
  - Managing high-risk thoughts (both trauma- and substance-related thoughts)
  - Drink/drug refusal skills.
  - Managing anger (symptom of PTSD, trigger for use)
  - In-vivo exposures (sessions 3-11) and imaginal exposures (sessions 4-11)
  - Session 12 is tx review and next steps.
In Vivo Exercises

- In between therapy sessions
- Repeated (2-3 times each)
- Prolonged (>30-45 min)

Common examples:
- Walmart (or other crowded store)
- Sitting in middle of restaurant
- Baseball game/sporting event
- Driving during rush hour
- Watching or reading the news

Imaginal Exposure

- Repeated revisiting of trauma memory (~30 min per session) leads to extinction.
- Learn to discriminate between past vs. present.
- Learn that thinking about event is not dangerous.
- Trauma memory becomes more organized.
- Maladaptive beliefs are addressed/modified.
- Learn that anxiety (like cravings) behaves like a wave. Comes and goes.

Prolonged Exposure Therapy: The Wave of Anxiety (and Craving)
Positive Urine Drug Screen (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
- N=39
- Mean age = 33.7
- 82.1% female
- Cocaine + PTSD

Pre to post reduction in:
- CAPS (p<.001)
- MISS (p<.05)
- ASI subscales (p<.001)
  - Alcohol
  - Drug
  - Psychiatric

Pilot Study in Sweden
- N = 22
- Average age = 45.5
- Women with PTSD and alcohol use disorder
- Average number of trauma types = 7.3
- Childhood trauma (96.9%)
- Age of first trauma = 9.0 yrs
- Baseline BDI = 30
- Baseline CAPS = 78

Persson et al., 2017
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- Age of first trauma = 9.0 yrs
- Baseline BDI = 30
- Baseline CAPS = 78

(Rossion et al., 2017)

RCT in Australia

Randomized to TAU + COPE or TAU only

<table>
<thead>
<tr>
<th>Substance use characteristics</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of first use</td>
<td>35% (13)</td>
</tr>
<tr>
<td>History of drug use</td>
<td>85%</td>
</tr>
<tr>
<td>Prior substance use treatment</td>
<td>93%</td>
</tr>
<tr>
<td>Past-month substance use</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>7%</td>
</tr>
<tr>
<td>Cannabis</td>
<td>5%</td>
</tr>
<tr>
<td>Heroin</td>
<td>4%</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>4%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>4%</td>
</tr>
<tr>
<td>Main drug of concern</td>
<td>10%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trauma/PTSD characteristics</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of first trauma</td>
<td>85% (42)</td>
</tr>
<tr>
<td>History of childhood trauma</td>
<td>75%</td>
</tr>
<tr>
<td>Prior PTSD treatment</td>
<td>20%</td>
</tr>
<tr>
<td>Number of traumas</td>
<td>6 (1-16)</td>
</tr>
<tr>
<td>Trauma types</td>
<td></td>
</tr>
<tr>
<td>Physical assault</td>
<td>35%</td>
</tr>
<tr>
<td>Threatened or held captive</td>
<td>8%</td>
</tr>
<tr>
<td>Witnessed injury or death</td>
<td>7%</td>
</tr>
<tr>
<td>Sexual assault</td>
<td>7%</td>
</tr>
<tr>
<td>Accident or disaster</td>
<td>8%</td>
</tr>
<tr>
<td>Torture</td>
<td>24%</td>
</tr>
<tr>
<td>Combat exposure</td>
<td>4%</td>
</tr>
<tr>
<td>Median duration of PTSD symptoms</td>
<td>100.7 (17-152)</td>
</tr>
</tbody>
</table>

JAMA Integrated Exposure-Based Therapy for Co-occurring Posttraumatic Stress Disorder and Substance Dependence
RCT in U.S. Military Veterans
Ralph H. Johnson VA, Charleston SC

- N = 81
- Average age = 40.4, 90.1% male
- OEF/OIF service = 63.7%
- Served average of 9.8 yrs
- Military related index trauma = 81.0%
- 83% alcohol use disorder only, 27.2% both alcohol and drugs
- CAPS baseline = 81
- Baseline BDI = 29
- Randomized to 12 sessions of:
  1) COPE
  2) Relapse prevention
COPE improved significantly more than RP on the CAPS and PCL-M. Significant between-group differences observed at end of treatment with COPE participants scoring 26 points lower on the CAPS and 13 points lower on the PCL-M ($SE = 4.8, p < .001, d_{between-group} = 1.09$).

Significantly greater proportion of participants at session 12 in COPE achieved PTSD remission, $p = .004$.

- 77.3% had a reduction in frequency of substance use. No difference by group.
- No increase in substance use with PE treatment.
Mechanisms of Symptom Change

- Direct test of mediation models of symptom change using lagged multilevel mediation

Model 1: Does Change in PTSD mediate change in substance use?

52% of the change in substance use is mediated by change in PTSD symptoms

Model 2: Does change in substance use mediate change in PTSD symptoms?

5% of the change in PTSD symptoms is mediated by change in substance use

RCT in New York City

- N=110
- Average age = 44.8, 62% female
- SUD plus full or subthreshold PTSD
- 75% had multiple trauma types (physical and sexual assault most common)
- 71% alcohol use disorder, 35.7% alcohol and drug use disorder
- Randomized to:
  1) COPE (35.9% subthreshold)
  2) Relapse prevention (32.6% subthreshold)
  3) Active monitoring control group (39.3% subthreshold)

PTSD Outcomes

COPE and RPT showed significantly greater decreases in MPSS-SR scores compared to AMCG, regardless of PTSD diagnostic status (all p-values <0.05). Among participants with full PTSD, COPE also showed significantly greater decreases relative to RPT (COPE-RPT = –21.32, 95% CI: –42.37 to –0.28, p = 0.05).
Substance Use Outcomes

COPE and RP showed significant reductions in past 7 days use by (COPE = –2.31, p < 0.001; RPT = –3.28, p < 0.001), whereas change in the AMCG was nonsignificant. RP had greater decrease (RPT-COPE = –1.10, p = 0.05).

Summary

- Integrated treatments for PTSD/SUD are safe and effective.
- Studies among men and women, civilian and combat-related PTSD, alcohol and drug use disorders, multiple traumas and telemedicine case show similar results.
- Substance use does not increase with PTSD treatment, it decreases.
More Effective Medications Needed

- Pharmacologic studies over the past 2 decades:

<table>
<thead>
<tr>
<th>Study Reference</th>
<th>Treatment</th>
<th>N</th>
<th>Participants</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brady et al., 1995</td>
<td>Sertraline</td>
<td>9</td>
<td>Civilians</td>
<td></td>
</tr>
<tr>
<td>Brady et al., 2005</td>
<td>Sertraline</td>
<td>94</td>
<td>Civilians</td>
<td></td>
</tr>
<tr>
<td>Petrakis et al., 2006</td>
<td>Naltrexone and disulfiram</td>
<td>93</td>
<td>Veterans</td>
<td></td>
</tr>
<tr>
<td>Alderman et al., 2009</td>
<td>Topiramate</td>
<td>29</td>
<td>Veterans</td>
<td></td>
</tr>
<tr>
<td>Petrakis et al., 2012</td>
<td>Antidepressant +/- naltrexone</td>
<td>88</td>
<td>Veterans</td>
<td></td>
</tr>
<tr>
<td>Foa et al., 2013</td>
<td>Naltrexone plus PE</td>
<td>165</td>
<td>Civilians</td>
<td></td>
</tr>
<tr>
<td>Batki et al., 2014</td>
<td>Topiramate</td>
<td>30</td>
<td>Veterans</td>
<td></td>
</tr>
<tr>
<td>Hien et al., 2015</td>
<td>Sertraline plus Seeking Safety</td>
<td>69</td>
<td>Civilians</td>
<td></td>
</tr>
<tr>
<td>Simpson et al., 2015</td>
<td>Prazosin</td>
<td>30</td>
<td>Civilians</td>
<td></td>
</tr>
<tr>
<td>Petrakis et al., 2016</td>
<td>Prazosin</td>
<td>96</td>
<td>Veterans</td>
<td></td>
</tr>
<tr>
<td>Back et al., 2016</td>
<td>N-acetylcysteine</td>
<td>35</td>
<td>Veterans</td>
<td></td>
</tr>
</tbody>
</table>

(See Petrakis & Simpson, 2017; Taylor et al., 2016)

N-acetylcysteine (NAC) - FDA approval since 1963, available over-the-counter, inexpensive, long-established safety record.

- Clinical studies show NAC associated with reduced craving, and cocaine and marijuana use.

- NAC may play a role in oxidative stress, neuro-inflammation, or glutamate dysregulation.

Restoring Choice

(Deepmala et al., 2015; McClure et al., 2014)
**Pilot Study: PTSD Outcomes**

Clinician-Administered PTSD Scale (CAPS) reduced 46% in NAC vs. 25% in placebo group.

PTSD Checklist-Military Version (PCL-M) reduced 32% in NAC vs. 3% in placebo group.

\( p < .05, ** p < .01, *** p < .001 \)

(Back et al., 2018, J Clin Psychiatry)

**Pilot Study: Craving Outcomes**

Craving amount reduced 81% in NAC vs. 32% in placebo group.

Frequency reduced 72% in NAC vs. 29% in placebo group.

\( p < .05, ** p < .01, *** p < .001 \)

(Back et al., 2018, J Clin Psychiatry)

**Table 2: Efficacy of N-Acetylcycteine Treatment on Symptoms of PTSD, Depression, and Craving**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Placebo (n = 14)</th>
<th>N-Acetylcycteine (n = 13)</th>
<th>Between Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Weeks 0</td>
<td>Weeks 4</td>
<td>p-value</td>
</tr>
<tr>
<td>CAPS</td>
<td>41.0 (23.3)</td>
<td>41.9 (23.8)</td>
<td>0.052</td>
</tr>
<tr>
<td>BDI</td>
<td>12.0 (7.0)</td>
<td>12.6 (7.2)</td>
<td>0.12</td>
</tr>
<tr>
<td>UDS</td>
<td>10.0 (6.0)</td>
<td>10.0 (6.0)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

- **BDI** reduced 48% in the NAC group vs. 15% in the placebo group.
- Subjects in both groups significantly reduced substance use. No statistically significant differences between groups in substance use. Trend for NAC to have fewer positive UDS tests than placebo \( p = .07 \).

(Back et al., 2017, J Clin Psychiatry)
The literature on medications for PTSD/SUD is limited and inconclusive. Future research is needed to address the lack of advancement in this area.

Summary

- Integrated treatments for adolescents.
- Integrated treatments for incarcerated populations.
- Ways to enhance retention.
- Better understand mediators/moderators of change.
- Ways to accelerate improvement (e.g., SUD outcomes or rate of reduction in PTSD symptoms).
- Pharmacologic treatments (NAC, doxazosin, oxytocin).
- Neuroimaging pre- and post-treatment to identify treatment targets and predict outcome.

Future Directions

What can you do….today?

- Assess for trauma exposure and PTSD symptoms.

**BRIEF SCREENING MEASURES**

<table>
<thead>
<tr>
<th>Screening Measure</th>
<th>Items</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD Checklist (PCL-5) (Weathers et al., 2013)</td>
<td>20</td>
</tr>
<tr>
<td>Trauma Screening Questionnaire (TSQ) (Brewin et al., 2002)</td>
<td>10</td>
</tr>
<tr>
<td>Primary Care PTSD Screen (PC-PTSD) (Prins et al., 2015)</td>
<td>5</td>
</tr>
</tbody>
</table>

- Provide psychoeducation around common reactions to trauma and the PTSD/SUD interconnection.
- Provide integrative treatment or assist with a referral.
- Provide resources/information – About Face website.
- Never give up hope.
Thank you

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Dr. Dan Gros
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Dr. Kevin Gray
Dr. Robert Malcolm
Dr. Mark Hamner
Dr. Tracy Stocker
Dr. Dave Shirley

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https://www.facebook.com/HelpPTSD/