

Trauma/PTSD and SUD: A tangled, interlocking web

William F. Wright, MD FAPA
Addiction Psychiatrist, Asst. Professor, Assoc. Clerkship Dir.

Acknowledgments/Disclosures

- double-board certified psychiatrist (general and addictions).
- assistant professor University of North Carolina School of Medicine and core faculty with the Sandra and Leon Levine Psychiatry Residency Program at Atrium Health
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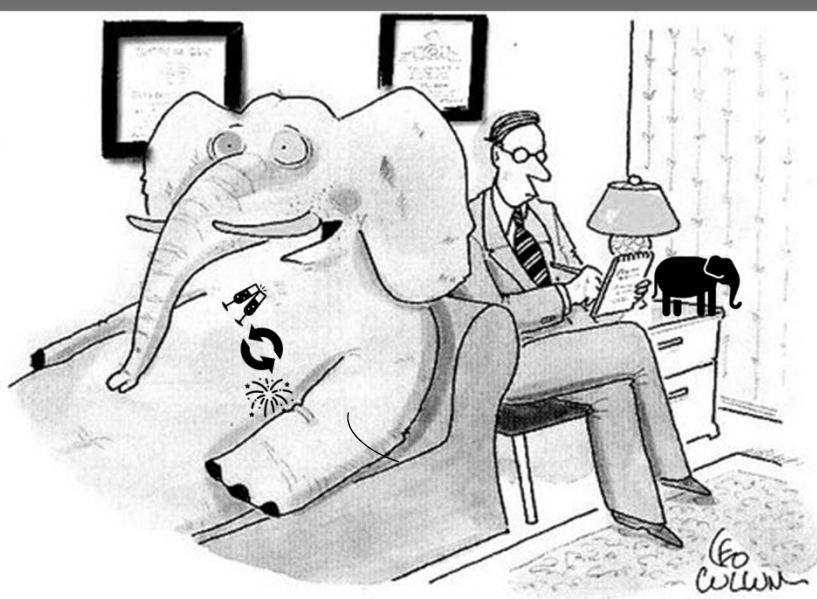




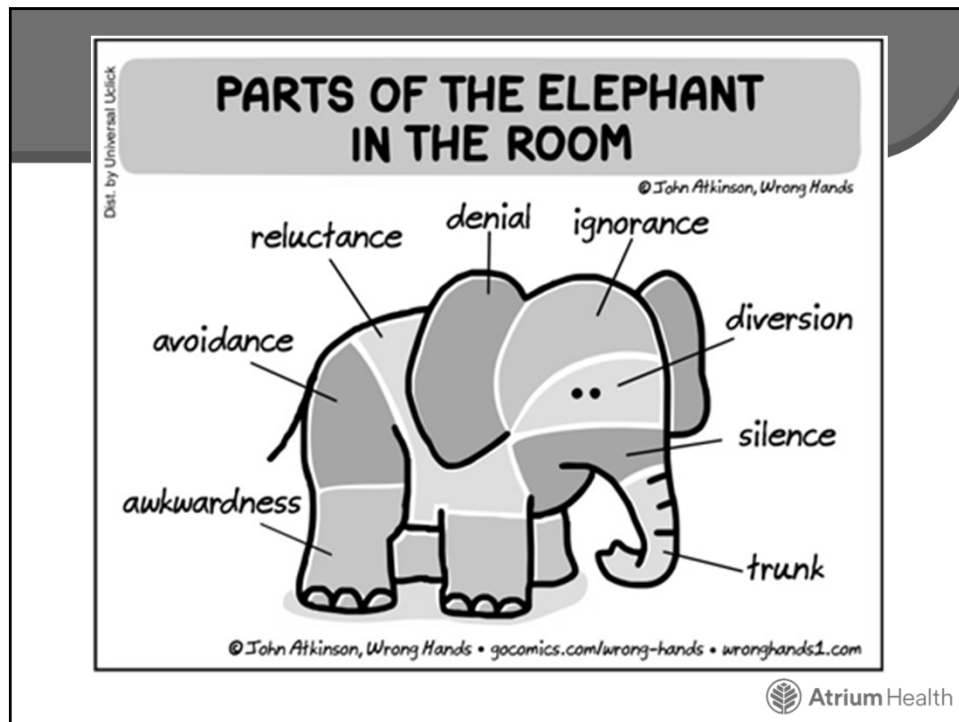
Objectives

- Explore the role of substance use disorders as an underlying predisposing factor for the development of PTSD following traumatic events.
- Learn the prevalence of, basic biological underpinnings of, and psychology of comorbid PTSD and SUD.
- Understand the role of ACEs in the development of both PTSD and SUD.
- Explore the dearth of pharmacological interventions and the new stance on diagnosis priority.
- Discover treatment recommendations.

Background of PTSD/Trauma and SUD



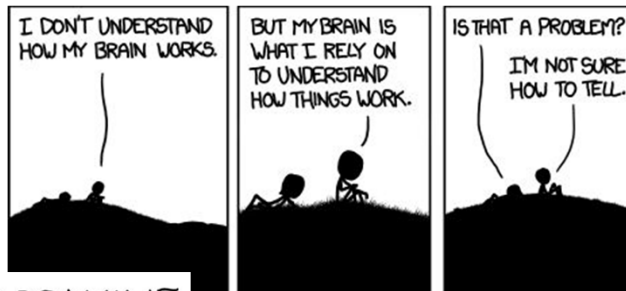
"I'm right there in the room, and no one even acknowledges me."



Prevalence – by the numbers...

- Post-Traumatic Stress Disorder (PTSD) affects ~8% of the United States population (324.5 million) = 26million people.
- 90% or more of the general population will experience a traumatic event in their lifetime; 70% of adults have experienced at least one severe trauma.
- Substance Use Disorders (SUD) affect between 8.1-24.7% of the US Population = 26.2 – 80million people.
- Adults with PTSD are 4.3x more likely to have a SUD, and in a 1-year period, those with PTSD have a 4.9x increased risk of the emergence of an SUD.
- *Conversely*, those with SUDs are 6.5x more likely to have PTSD.
- In the general population of those with PTSD, the prevalence of SUD is 21.6%-43%
 - So...Combination of SUD *AND* PTSD = 5.6 – 11.2 million people.

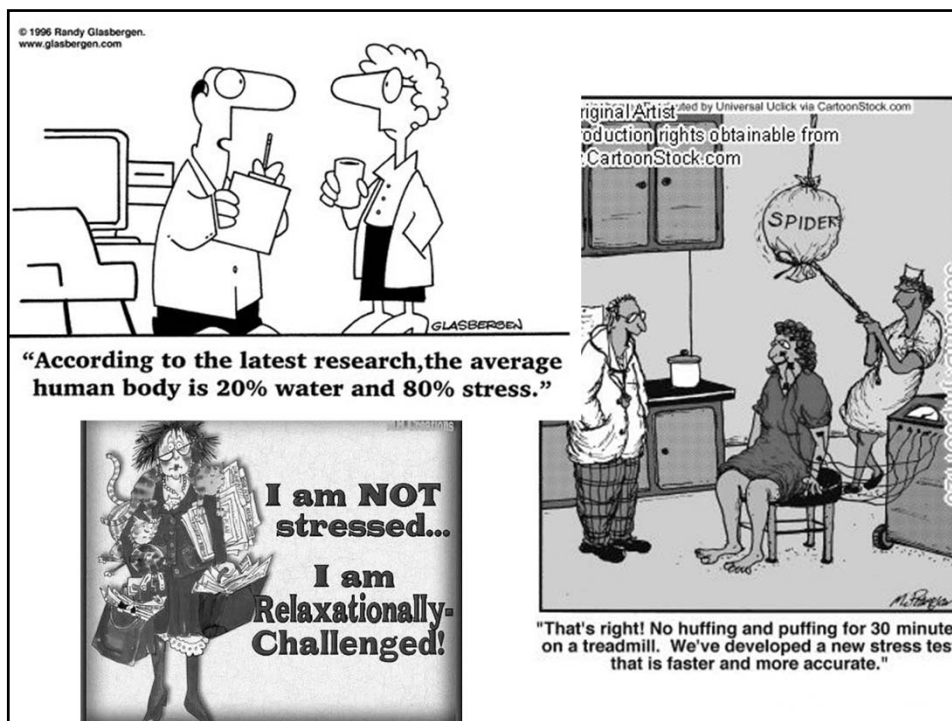
Neurobiology




SEROTONIN & DOPAMINE



Technically, the only two things
you enjoy



Neurobiology

- Physical and psychological stress: facilitates drug self-administration initiation and drug use relapse.
- Stress induction  ↑ cravings and substance use behaviors.



Neurobiology

- Mediators in stress responses include corticotropin releasing hormone (CRH) and norepinephrine (NE)...
- CRH initiates neuroendocrine function/response to stress (PTSD patients have been found to have elevated levels of CRH in their CSF).
- CRH has been found to enhance the pharmacological effects of stimulants and facilitates stress-induced drug-seeking behavior (in rodents).
- NE plays a key factor in stress-induced reinstatement of drug use as well as a role in encoding emotional memories in the amygdala and the PFC (PTSD patients have been found to have elevated NE in CSF indicating ramped up NE activity).



Neurobiology

- GABA and Glutamate Roles:
 - glutamate signaling (through NMDA/AMPA receptors) is a pivotal role in learning and memory
 - GABA is the main inhibitory/braking system in the brain.

Therefore, both stand as targets for potential treatment options.



Neuropsychophysiology



Neuropsychophysiology

- However, in the abstinent/withdrawal states of many substances, a pronounced negative affective state exists with symptoms of:
 - Dysphoria/depressed mood
 - Anxiety
 - Frustration
 - Anger
 - Irritability
 - Leading to attempts at dampening these feelings with continued substance use in those with PTSD; alcohol reduces physiological arousal, increases disinhibition, and gives a temporary cognitive distraction.
- When exposed to cues of their personal trauma, those with PTSD/SUD report an increase in cravings for alcohol and cocaine (regardless of presence of cues for their substance/alcohol).



Psychology

- Hypotheses for the high co-occurrence of PTSD and SUD:

- 1) Shared Vulnerability:
- 2) Susceptibility:
- 3) High-Risk:
- 4) Self-medication:
- 5) Mutual Maintenance:



Psychology

- Hypotheses for the high co-occurrence of PTSD and SUD:

- 1) Shared Vulnerability:
- 2) Susceptibility:
- 3) High-Risk:
- **4) Self-medication:**
- 5) Mutual Maintenance:

- SUD and PTSD patients:

- coping strategies used = emotion-focused >>> problem-focused.





Risk factors and demographics

- Household of origin substance use nearly doubled the risk of a substance dependence (use disorder).
- Those who dropped out of SUD/PTSD treatment (in veterans) were more likely to:
 - Be homeless
 - Obtain more VA disability
 - Higher levels of tolerating uncertainty
 - Lower distress tolerance
 - Poorer treatment outcomes
 - History of accidents/other trauma types (physical assault lowest rate of dropout)
- Treatment dropout demographics for PTSD only pts:
 - Younger age
 - Male
 - African-American
 - Lower education achieved
 - Higher military rank
 - **More comorbid drug use**
 - Lower income
 - Greater disability status/lower social support
 - Higher pretreatment symptom severity

Dealing with the hand that's dealt...



Loaded with ACEs – unfavorably stacking the deck

- **ACE: Adverse Childhood Events**
 - 10 categories: physical abuse, emotional abuse, sexual abuse, physical neglect, emotional neglect, growing up in a household with substance use, household members who were criminals, household members with mental illness, parental discord, and illicit drug use.
- **Each positive ACE criteria met:**
 - Increased the likelihood of early start to substance use 2-4x
 - ≥ 5 ACEs led to 7-10x increase in the likelihood of illicit drug problems, addiction to illicit drug addiction, and IVDU
 - ACE score highly tied with lifetime drug use (higher the score, higher the potential)
 - One of the strongest relationships in drug use behaviors and ACE scores was the inverse relationship with score and early adolescent initiation

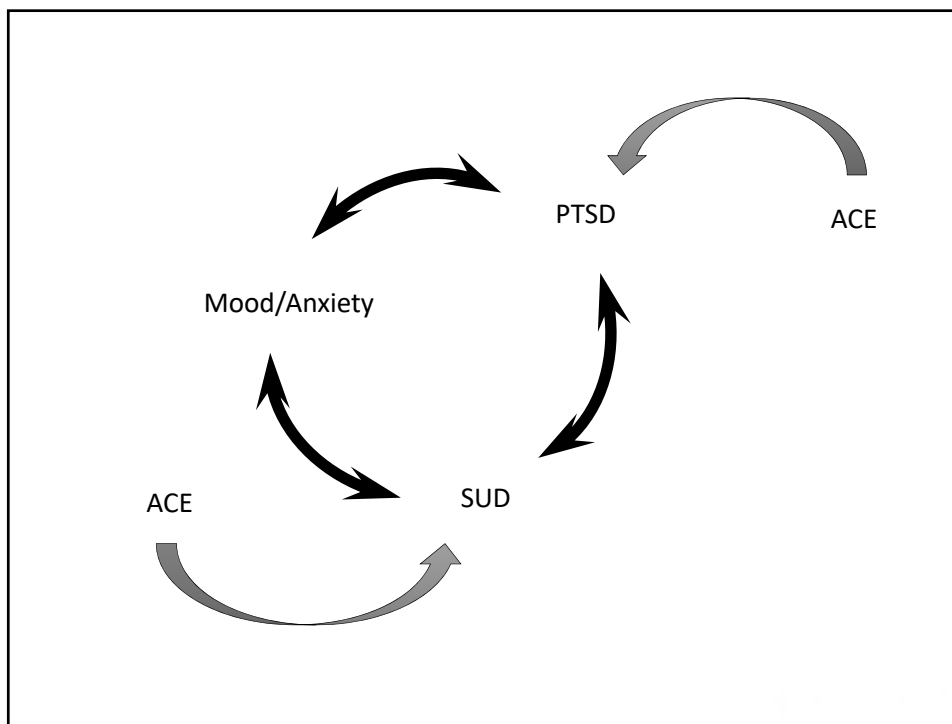


ACEs everywhere



- For every increase in ACE score, 30-40% increase risk for each illicit drug problem –
 - 1) ever having problems
 - 2) ever having a drug use disorder
 - 3) IVDU
- Accounting for one-half to one-third of the serious drug use problems (two-thirds of IVDU attributed to ACEs)
- ACEs are common...2/3 of the study reported 1 or more positive Adverse Childhood Events.
- For each unit increase in ACE numbers, 60% increase in attempted suicides.
- Cumulative lifetime exposure to adverse events is highly associated with drug dependence indicating number of ACEs are more problematic than a single, specific event.





ACE and alcohol

- ACE reports of 1-2...
 - 2-4x more likely to self-report as “alcoholic”
- ≥ 2 ACEs...
 - Odd of alcohol dependence increased by a third.
- Parental divorce is more consistently associated with a lifetime of alcohol dependence (and other psychiatric disorders).

Opioids and ACEs

- ACE scores were inversely associated with the age of first opioid use and with starting any substance use at an earlier age, confers more likelihood of developing an use disorder for that substance.
 - Risk of drug dependence problems is significantly greater for adolescent recent-onset users compared to adult recent-onset users.
 - The rates of lifetime (alcohol) dependence declined from more than 40% age of onset 14 or younger to approx. 10% age of onset 20 and older.
 - Odds of (alcohol) dependence decreased by 14% with each increasing year of age at onset of use, and the odds of abuse decreased by 8%



Opioids and ACEs

- ACE score also linked to opioid dependence and an earlier age of parenteral administration (IVDU).
- ACE scores were associated in a dose-response manner with each behavioral opioid marker studied: age of first use; intravenous drug use, and overdose.
- In typical progression, many injection heroin users began their pattern of use with problematic/misuse of prescription opioids.



Opioids, trauma, and teens...

- In 2014, ½ million 12-17 year-olds use prescription opioids in a non-medical fashion and 170,000 had an Opioid Use Disorder (OUD).
- The CDC reports that over 5million adolescents are treated in the USA annually for injuries.
- 80% of high school students report misusing prescribed opioids given to them first by a physician.
- Per recent data from Indiana...
 - 56% of injured adolescents have an elevated risk of developing an OUD within 3years of their initial injury.
 - 13% had filled >8 opioid prescriptions within 4 years of injury
 - 11% had received an opioid antagonist injection within 5 years of injury
 - 14% had a substance use disorder diagnosis within 5 years of injury
 - Nearly 1 in 10 of the opioid-prescribed injured teens had overdosed within 5 years...



Opioids, Trauma, & Teen demographics

- Teens who later were given a SUD Diagnosis were:
 - older adolescent
 - Male
 - African-American
 - Treated at an adult hospital
 - Had sustained a penetrating or "other" injury type
 - Medicaid/self-pay/other insurance
 - EtOH/drug positive screens
- Teens who later suffered an overdose were:
 - older adolescent
 - African-American
 - Treated at an adult hospital
 - Attained a penetrating-type injury
 - had "unknown insurance" source



Screenings... Not the red carpet kind

The eyes can't see what the mind doesn't know...we can't help what we don't pick up

- Evidence-based screening tools for substance use:
 - <https://www.drugabuse.gov/nidamed-medical-health-professionals/screening-tools-resources/chart-screening-tools> (AUDIT, ORT, TAPS...)
- PC-PTSD: A useful PTSD screen developed within the VA Primary Care setting (like the CAGE for PTSD...) by Prins et al. 2004
 - 1-2 minute self-administered with 4 Yes/No questions
 - Cutoff score of 3 help to improve detection to 90% (has a 91% sensitivity, 80% specificity, 69% PPV, and 95% NPV)

PC-PTSD

- “In your life, have you ever had any experience that was so frightening, horrible, or upsetting that, *in the past month you..*
 - Had nightmares about it or thought about it when you did not want to?
 - Tried hard not to think about it, or went out of your way to avoid situations that reminded you of it?
 - Were constantly on guard, watchful, or easily startled?
 - Felt numb or detached from others, activities, or your surroundings?”



Treatments

Comorbid treatment of SUD/PTSD: Current medications?

- Only 3 RTCs have been conducted studying pharmacological interventions for those patients with combined PTSD and SUD:
 - Sertraline: overall, no better than placebo for EtOH/PTSD reduction but those with less severe AUD and early-onset PTSD showed greater reductions in EtOH use (Brady et al. 2005)
 - Disulfiram and naltrexone: AUD vets -> those with PTSD (36.6%) showed improvement in EtOH outcomes with an active medication component (disulfiram, naltrexone, or both) compared to placebo and overall symptoms of PTSD improved (Petrakis et al. 2006)
 - Paroxetine v desipramine (both with adjunctive NTX): paroxetine = desipramine regarding PTSD symptoms but desipramine > paroxetine regarding study retention and EtOH use outcomes (Petrakis et al. 2012).



Comorbid treatment of SUD/PTSD: Medications on the horizon

- Prazosin (alpha1-adrenergic agonist): reduces cocaine, alcohol, nicotine, and heroin self-administration in rodents; shown to improved emotional response to trauma cues in PTSD -> pending clinical trial of efficacy in PTSD/SUD
- Propranolol (beta-adrenergic antagonist): attenuates stress-induced cocaine and cue-induced nicotine self-administration; shown promise for cocaine treatment especially in high withdrawal severity and promise as a preventative agent for PTSD
- Guanfacine (alpha2-adrenergic agonist): blocks stress- and cue-induced self administration of cocaine and alcohol; showing promise in decreasing cue-induced craving in cocaine users but in a small study has not shown efficacy in PTSD...

None of the above are FDA-approved medications with indication for SUD/PTSD.



Comorbid treatment of SUD/PTSD: Medications on the horizon

- Atomoxetine (NRI): shown efficacy for amphetamine dependence but, but to date, has not been examined for PTSD.
- Memantine (non-competitive NMDA antagonist): shown efficacy in decreasing cue-induced craving for EtOH in AUD patients; small open-label study showing decreasing severity of PTSD symptoms in combat vets; to date, unknown efficacy for AUD/PTSD
- NAC (treatment of acetaminophen overdose): suspected action in normalizing reduced extracellular glutamate levels in NAc by stimulating cystine-glutamate antiporter; small trials for cocaine & nicotine use disorders and gambling with positive results; ongoing study for PTSD treatment

None of the above are FDA-approved medications with indication for SUD/PTSD.



Comorbid treatment of SUD/PTSD: Medications on the horizon

- Ketamine (NMDA receptor antagonist): OIF/OEF soldiers with burns who received ketamine during operation were less likely to develop PTSD than those not receiving; currently undergoing RCT for rapid treatment of PTSD
- Acamprosate (NMDA and GABA receptor modulator): FDA approved for AUD; not currently tested for PTSD/SUD
- Topiramate (GABA_A receptor agonist, AMPA/kainite-subtype Glu receptor antagonist, carbonic anhydrase inhibitor): open-label study showing safety and potential efficacy for PTSD/AUD (in male combat vets)

None of the above are FDA-approved medications with indication for SUD/PTSD.



Comorbid treatment of SUD/PTSD: Medications on the horizon

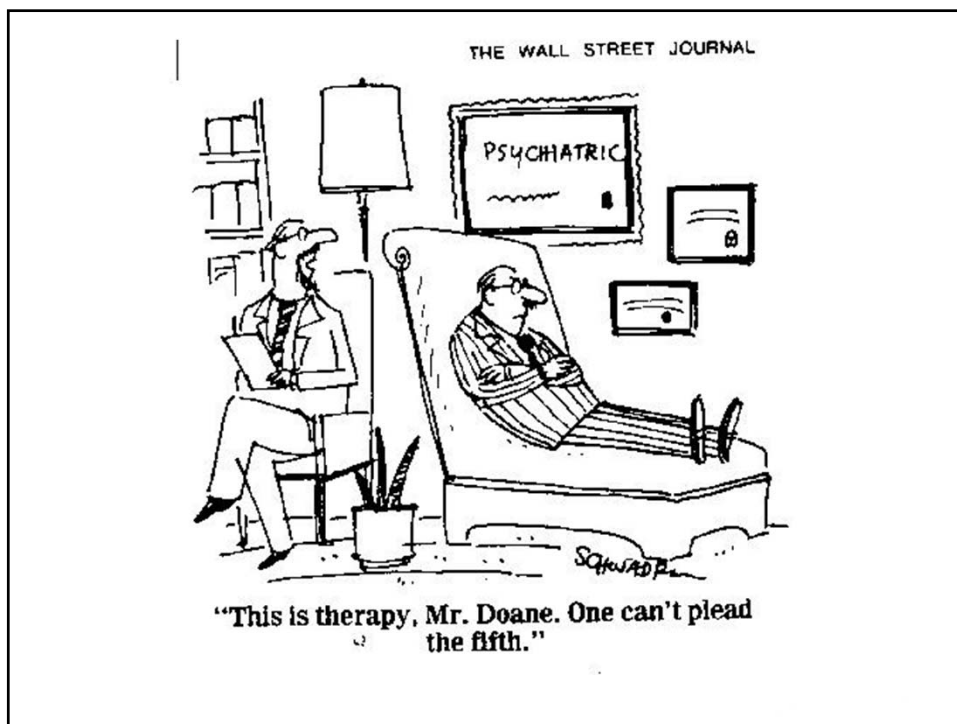
- Currently, *NO* published RTC showing the efficacy of any medication for the combination treatment of PTSD and SUD; therefore, no monopharmacological agent has been proven or FDA-approved for the treatment of both disorders...



"THERE'S NO
MAGIC PILL,
BUT THERE
IS A MAGICAL
PROCESS."

-JIM KWIK-

@CheeseGirlPA



Psychotherapeutic Treatments

- Increasing evidence showing trauma-focused, exposure-based therapy does NOT increase the risk of symptom exacerbation (PTSD or SUD) relative to non-exposure-based therapy.
- Vets: No differences in retention between COPE (Concurrent treatment of PTSD and Substance Use Disorders Using Prolonged Exposure) and Relapse Prevention (RP)
 - COPE showed significantly greater reductions in severity and higher PTSD diagnostic remission
 - both showed significant reduction in SUD severity.
- COPE completers: 83% no longer met PTSD criteria.
- Greatest reductions in COPE but RP also had improvement in PTSD (22% remission) ->
 - likely CBT skills in RP could generalize to PTSD-related symptoms BUT COPE did NOT show significantly greater decrease in SUD outcomes (compared to RP) as participants in COPE also received ~50% of RP intervention coping skills.



Psychotherapeutic Treatments

- **Findings:** integrated, exposure-based treatment is effective in decreasing SUD and PTSD severity from multiple trauma types (including military-related)
- Integrated SUD/PTSD treatment resulted in as much reduction in SUD severity as EBM SUD-only treatment while added benefit of reducing PTSD severity (2 birds with one stone: 2 Dx in same time frame).
- Comorbid pts receiving PTSD treatment are 3.7x more likely to achieve long-term substance remission compared to those with untreated PTSD.
- Remission from PTSD confers better SUD outcomes but remission from SUD is NOT as associated with improved PTSD outcomes.



Why does it matter?

Why should we care? What's in the way?

- >1/2 of all crime victims had their 1st trauma before 1st EtOH intoxication or other substance use.
- PTSD renders SUD pts more vulnerable to poor outcomes and negative consequences of having PTSD/SUD more so than other psychiatric diagnoses and continues to intensify over time.
- Comorbid SUD/PTSD associated with significant psychiatric comorbidity, medical problems, job problems, and increased violence.

Why should we care? What's in the way?

- Worsening PTSD symptoms tied with an increase in substance use (85.3%); conversely, improved PTSD then showed a decrease in substance use (61.8%).
- (In 1998), SUD-PTSD pts with ~\$6,000 more/year in substance-related treatment costs than those with SUD alone (with inflation rate, now would be >\$12,000)
- Barriers to treatment:
 - clinicians: lack of awareness, downplaying trauma effect, discomfort in asking about trauma/PTSD, lack of resources, belief in primacy of substance use problems in other psychiatric issues
 - patients: emotional pain (76%), shame (60%), and self-blame (67%), ~40% believed talking about trauma would make it worse, lack of trust in clinicians, and fear of discovery by others of their trauma



Recommendations



Recommendations – what should we do?

1. All SUD pts should be appropriately screened for trauma/PTSD; all PTSD pts should be appropriately screened for SUD.
2. Comorbid SUD/PTSD should be given referrals for trauma treatment
3. SUD/PTSD should be offered more intense SUD counseling (more sessions)
4. SUD/PTSD should be referred to self-help groups and family therapy/treatment (when indicated/feasible)
5. Understand that "the popular practice of treating SUDs before treating any comorbid disorder is suboptimal"
6. All veterans with SUD should be evaluated for PTSD and given integrated, exposure-based treatment
7. PTSD treatment should NOT be delayed until abstinence achieved

Recommendations – what should we do?

(To combat functional difficulties)

8. Incorporate measures fostering completion of treatment
9. Engender/facilitate other support sources or provide support themselves (i.e. telephone check-ins between sessions or alternative support systems like telepsychiatric appointments)
10. Incorporate vocational and social skill training into programs



Recommendations – what should we do?

(With Child and Adolescent Physical trauma Population)

11. Evaluate adolescents with high ACE scores as a marker for at risk early opioid initiation
12. With at risk child/adolescents, spend more time discussing risks of opioids at discharge with the family/adolescent (i.e. what are use disorders as well as problems with misuse)
13. Talk with caregiver regarding guidelines
14. Secure a mental health appointment for and during the post-acute injury period



Questions?



YOU!! In the front row?



In the back?



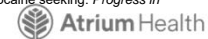
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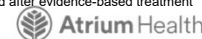
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Image References

- Elephant in the Room Cartoon:
 - <https://i.pinimg.com/474x/6a/1f/d1/6a1fd1701c7caecf26250df8f1bcffca--all-colleges-student-loan-debt.jpg>
- Parts of the Elephant in the Room Cartoon:
 - <https://qph.fs.quoracdn.net/main-qimg-6f0bfaa00c9eb5d98ef8c5bf22105244>
- Opie Taylor (Ron Howard) Picture:
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- Ron Weasley (Rupert Grint) Picture:
 - https://upload.wikimedia.org/wikipedia/en/thumb/5/5e/Ron_Weasley_poster.jpg/220px-Ron_Weasley_poster.jpg
- Sheamus (Stephen Farrelly) Picture
 - 1st: <http://www.profightdb.com/img/wrestlers/thumbs-600/b797247d72sheamus.jpg>
 - 2nd: <https://i.pinimg.com/236x/70/7c/11/707c1191dbc4392ea227bdf2622a748--sheamus-guilty-pleasure.jpg>
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Image References

- Brain cartoons:
 - <https://i.pinimg.com/474x/ce/37/13/ce3713fc5cbd1a1d41a6c59f00c4343d--the-human-brain-the-brain.jpg>
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Image References

- Yelling Pic
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