

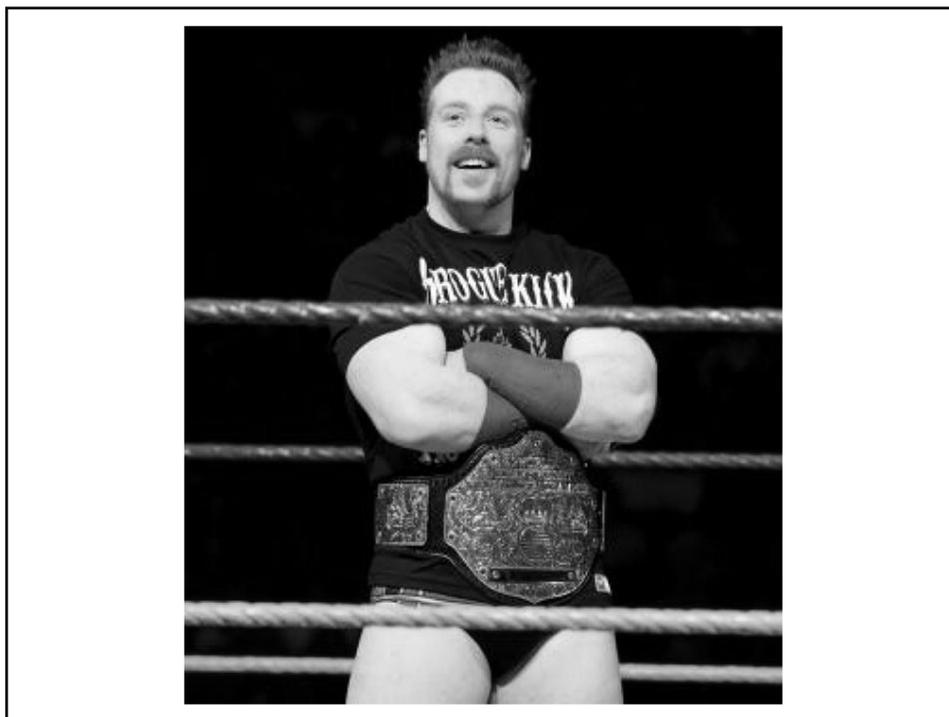
## Trauma/PTSD and SUD: A tangled, interlocking web

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### Acknowledgments/Disclosures

- double-board certified psychiatrist (general and addictions).
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- No financial obligations/conflicts of interest to report

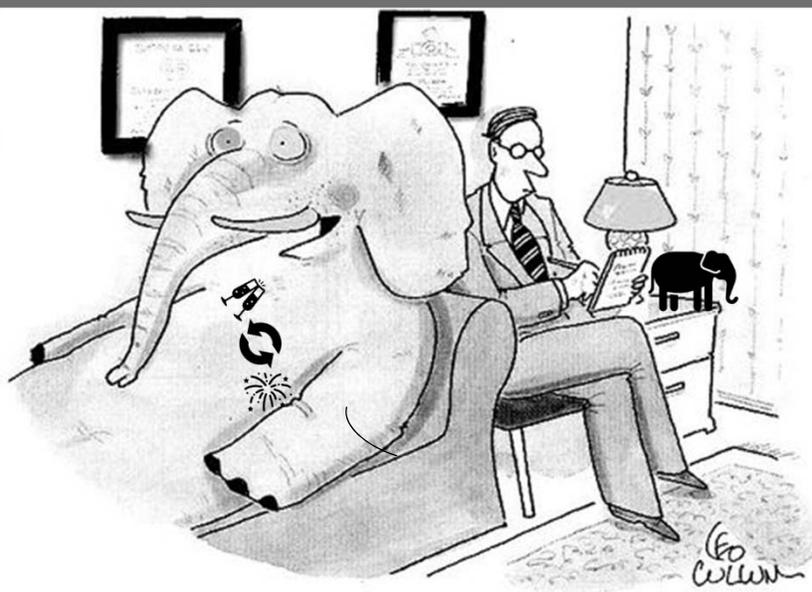




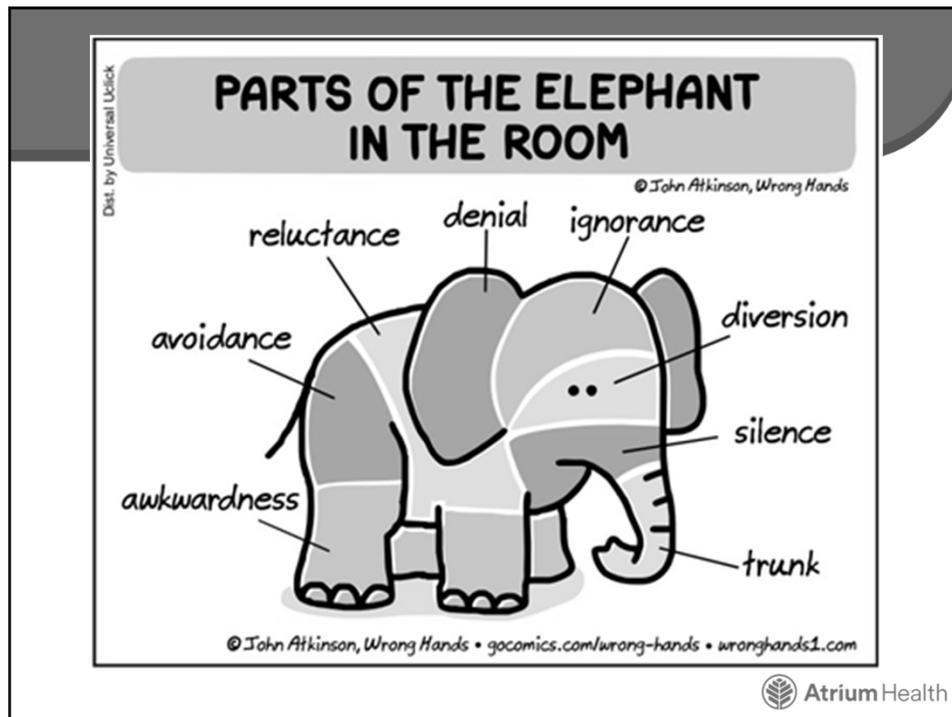
## Objectives

- 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



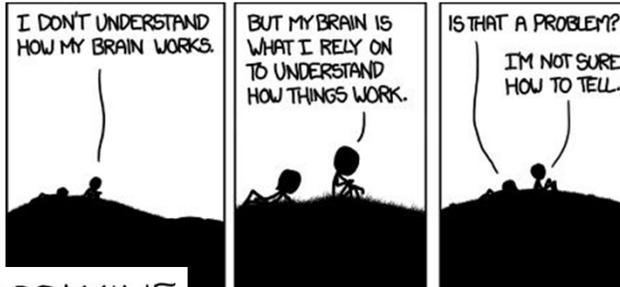
*"I'm right there in the room, and no one even acknowledges me."*



## 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.

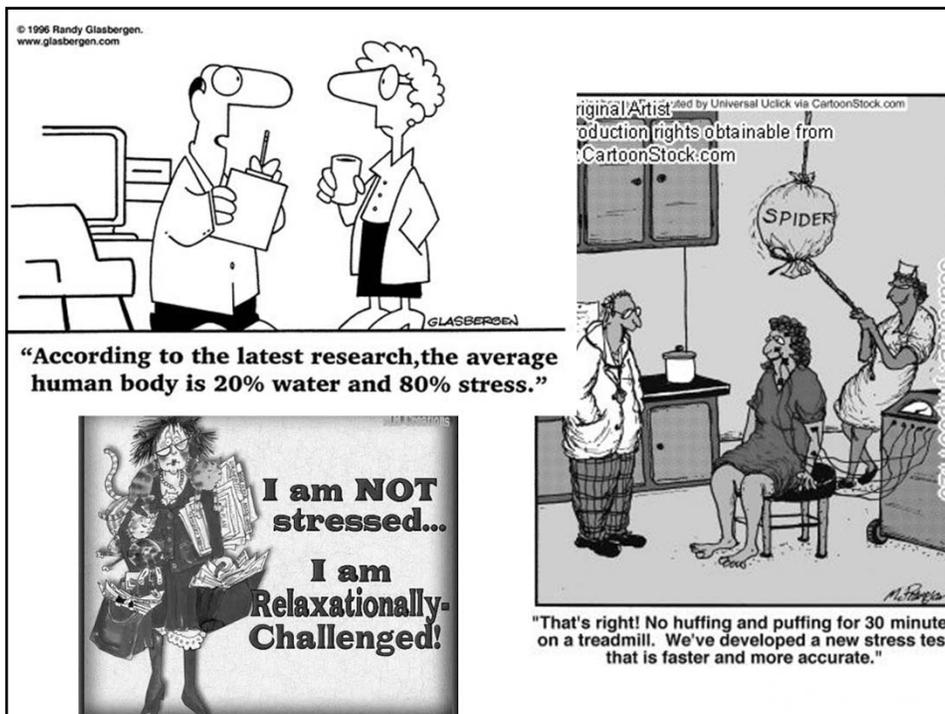
# Neurobiology



## 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



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## 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).

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## 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
  - $\geq 5$  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

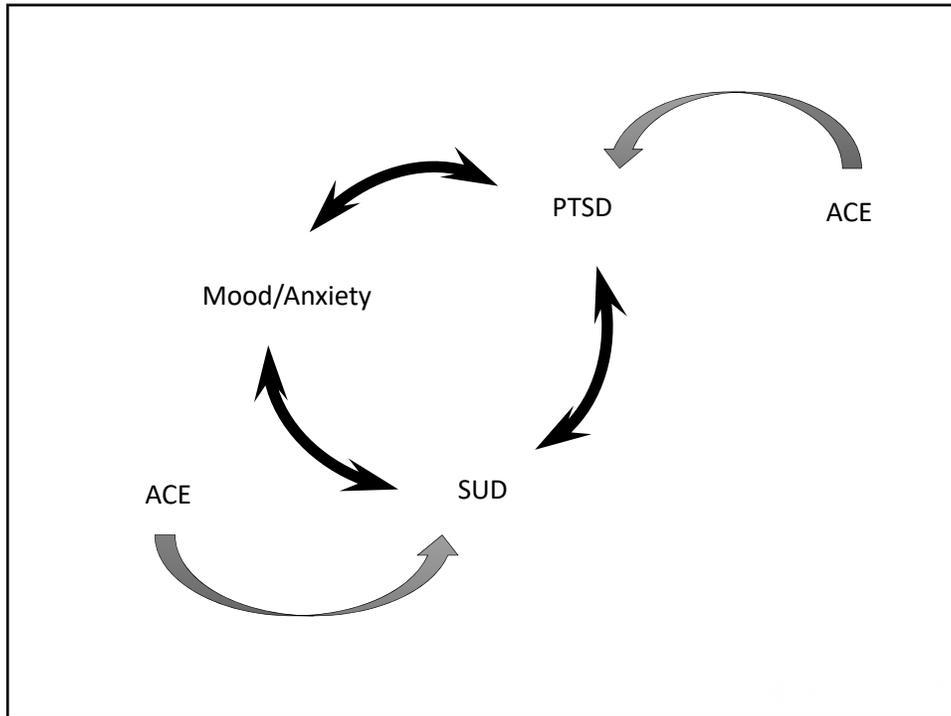


## ACEs everywhere



- 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”
- $\geq 2$  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<sub>A</sub> 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

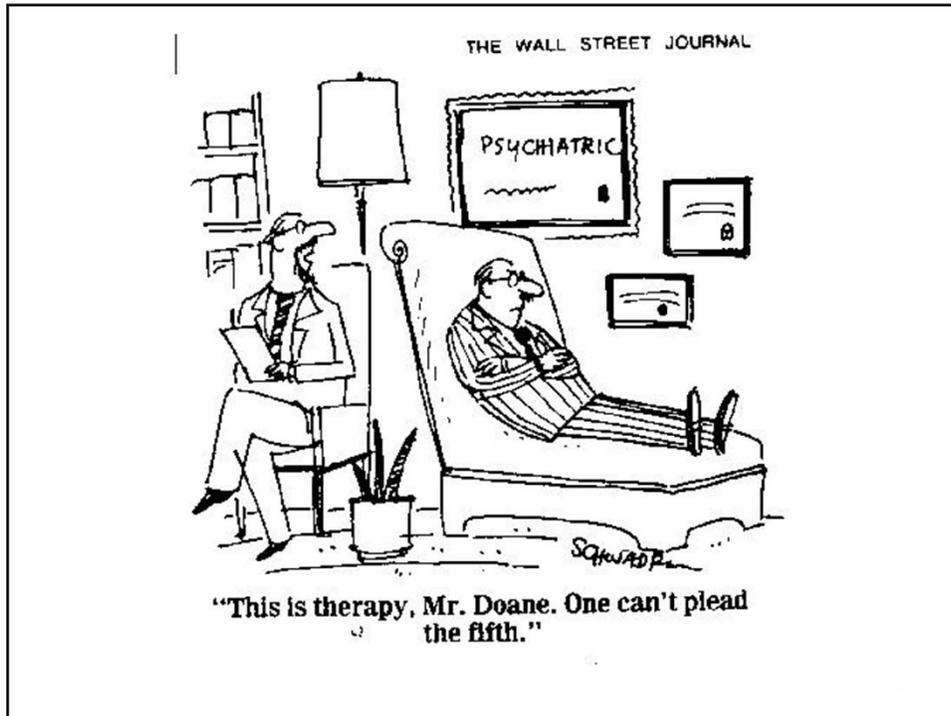
- Currently, *NO* published RTC showing the efficacy of any medication for the combination treatment of PTSD and SUD; therefore, no monopharmacological agent has been proven or FDA-approved for the treatment of both disorders...



"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 1<sup>st</sup> trauma before 1<sup>st</sup> 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?



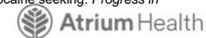
## References

## References

- Dube SR, Felitti VJ, Dong M, Chapman DP, Giles WH, Anda RF. (2003). Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. *Pediatrics*, 111, 564-572.
- Saladin ME, Brady KT, Dansky BS, Kilpatrick DG. (1995). Understanding comorbidity between PTSD and substance use disorders: two preliminary investigations. *Addictive Behaviors*, 20, 643-655.
- Kilpatrick DG. Violence as a precursor of women's substance abuse: the rest of the drugs-violence story. Paper presented at 98<sup>th</sup> Annual Convention of the American Psychological Association, Boston, MA.
- Stasiewicz PR & Maiato SA. (1993). Two-factor avoidance theory: the role of negative affect in the maintenance of substance use and substance use disorders. *Behavior Therapy*, 24, 337-356.
- Ouimette PG, Brown PJ, & Najavits LM. (1998). Course and treatment of patients with both substance use and posttraumatic stress disorders. *Addictive Behaviors*, 23, 785-795.
- Brown PJ, Stout RL, & Mueller T. (1996). Post-traumatic stress disorder and substance abuse relapse among women: a pilot study. *Psychology of Addictive Behaviors*, 10, 124-128.
- Brown PJ & Wolfe J. (1994). Substance abuse and post-traumatic stress disorder comorbidity. *Drug and Alcohol Dependence*, 35, 51-59.
- Najavits LM, Weiss RD, & Shaw SR. (1997). The link between substance abuse and posttraumatic stress disorder in women: a research review. *Am. J on the Addictions*, 6, 273-283.
- Ouimette PC, Ahrens C, Moos RH, & Finney JW. (1997). Posttraumatic stress disorder in substance abuse patients: relationships to 1-year posttreatment outcomes. *Psychology of Addictive Behaviors*, 11, 34-47.
- Ouimette PC, Finney JW, & Moos RH. (1999). Two year posttreatment functioning and coping of patients with substance abuse and posttraumatic stress disorders. *Psychology of Addictive Behaviors*, 13, 105-114.
- Brown PJ, Recupero PR, & Stout R. (1995). PTSD-substance abuse comorbidity and treatment utilization. *Addictive Behaviors*, 20, 251-254.
- Najavits LM, Gastfiend DR, Barber JP, Reif S, Muenz LR, Blaine J, Frank A, Crits-Christoph P, Thase M, & Weiss RD. (1998). Cocaine dependence with and without PTSD among subjects in the National Institute on Drug Abuse Collaborative Cocaine Treatment Study. *Am J of Psychiatry*, 155, 214-219.
- Triffleman EG, Marmar CR, Delucchi KL, & Ronfeldt J. (1995). Childhood trauma and posttraumatic stress disorder in substance abuse inpatients. *J Nervous and Mental Disease*, 183, 172-176.
- Ouimette PC, Ahrens C, Moos RH, & Finney JW. (1998). During treatment changes in substance abuse patients with posttraumatic stress disorder: the influence of specific interventions and program environments. *J Substance Abuse Treatment*, 15, 555-564.

## References

- Brown PJ, Stout RL, & Gannon-Rowley J. (1998). Substance use disorder-PTSD comorbidity: patient's perceptions of symptom interplay and treatment issues. *J Substance Abuse Treatment*, 14, 1-4.
- McFall ME, Mackay PW, & Donovan DM. (1992). Combat-related posttraumatic stress disorder and severity of substance abuse in Vietnam veterans. *J Studies on Alcohol*, 53, 357-363.
- Fairbank JA, Hansen DJ, & Fitterling JM. (1991). Patterns of appraisal and coping across different stressor conditions among former prisoners of war with and without posttraumatic stress disorder. *J Consulting and Clinical Psychology*, 59, 274-281.
- Penk, WE, Peck RF, Robinowitz R, Bell W, & Little D. Coping and defending styles among Vietnam combat veterans seeking treatment for post-traumatic stress disorder and substance use disorder. In M. Galanter (Ed.) *Recent developments in alcoholism* (pp. 69-88). New York: Plenum.
- Sofuoglu M, Rosenheck R, & Petrakis I. (2014). Pharmacological treatment of comorbid PTSD and substance use disorder: recent progress. *Addictive Behaviors*, 39, 428-433.
- Breslau N, David GC, & Schultz LR. (2003). Posttraumatic stress disorder and the incidence of nicotine, alcohol, and other drug disorders in persons who have experience trauma. *Arch Gen Psychiatry*, 60, 289-294.
- Jacobsen LK, Southwick SM, & Kosten TR. (2001). Substance use disorders in patients with posttraumatic stress disorder: a review of the literature. *Am J Psychiatry*, 158, 1184-1190.
- Kerfoot KE, Petrakis IL, & Rosenheck RA. (2011). Dual diagnosis in an aging population: prevalence of psychiatric disorders, comorbid substance abuse, and mental health service utilization in the Department of Veterans Affairs. *J Dual Diagnosis*, 7, 4-13.
- Brady, KT & Sinha R. (2005). Co-occurring mental and substance use disorders: the neurobiological effects of chronic stress. *Am J Psychiatry*, 162,1483-1493.
- Buchmann AF, Laucht M, Schmid B, Wiedemann K, Mann K, & Zimmermann US. (2010). Cigarette craving increases after a psychosocial stress test and is related to cortisol stress response but not to dependence scores in daily smokers. *J Psychopharmacology*, 24, 247-255.
- Bremner JD, Licinio J, Darnell A, Krystal JH, Owens MJ, Southwick SM, et al. (1997). Elevated CSF corticotropin-releasing factor concentrations in posttraumatic stress disorder. *Am J Psychiatry*, 154, 624-629.
- Charmandari E, Tsigos C, & Chrousos G. (2005). Endocrinology of the stress response. *Annual Review Physiology*, 67, 259-284.
- Shaham Y, Funk D, Erb S, Brown TJ, Walker CD, & Stewart J. (1997). Corticotropin-releasing factor, but not corticosterone, is involved in stress-induced relapse to heroin-seeking in rats. *J Neuroscience*, 17, 2605-2614.
- Erb S. (2010). Evaluation of the relationship between anxiety during withdrawal and stress-induced reinstatement of cocaine seeking. *Progress in NeuroPsychopharmacology & Biological Psychiatry*, 34, 798-807.



## References

- Geraciotti TD, Baker DG, Kasckow JW, Strawn JR, Mulchahey J, Dashevsky BA, et al. (2009). Effects of trauma-related audiovisual stimulation on cerebrospinal fluid norepinephrine and corticotropin-releasing hormone concentrations in post-traumatic stress disorder. *Psychoneuroendocrinology*, 33, 416-424.
- Norman SB, Myers US, Wilkins KC, Goldsmith AA, Hristova V, Huang Z, et al. (2012). Review of biological mechanisms and pharmacological treatments of comorbid PTSD and substance use disorder. *Neuropharmacology*, 62, 542-551.
- Sofuoglu M & Sewell RA. (2009). Norepinephrine and stimulant addiction. *Addiction Biology*, 41, 119-129.
- Myers KM, Carlezon WA, & Davis M. (2011). Glutamate receptors in extinction and extinction-based therapies for psychiatric illness. *Neuropsychopharmacology*, 36, 274-293.
- Murphy JG, Yurasek AM, Dennyhardt AA, Skidmore JR, McDevitt-Murphy ME, Mackillop J, et al. (2012). Symptoms of depression and PTSD are associated with elevated alcohol demand. *Drug and Alcohol Dependence*, 127, 129-131.
- Sofuoglu M, Brown S, Babb DA, & Hatsukami DK. (2001). Depressive symptoms modulate the subjective and physiological response to cocaine in humans. *Drug and Alcohol Dependence*, 63, 131-137.
- Sofuoglu M, Dudish-Poulsen S, Brown SB, & Hatsukami DK. (2004). Association of cocaine withdrawal symptoms with more severe dependence and enhanced subjective response to cocaine. *Drug and Alcohol Dependence*, 69, 273-282.
- Logrip ML, Zorrilla Ep, & Koob GF. (2012). Stress modulation of drug self-administration: implications for addiction comorbidity with post-traumatic stress disorder. *Neuropharmacology*, 62, 552-564.
- Coffey SF, Saladin ME, Drobos DJ, Brady KT, Dansky BS, & Kilpatrick DG. (2002). Trauma and substance cue reactivity in individuals with comorbid posttraumatic stress disorder and cocaine or alcohol dependence. *Drug and Alcohol Dependence*, 62, 115-127.
- Brady KT, Sonne S, Anton RF, Randall CL, Back SE, & Simpson K. (2005). Sertraline in the treatment of co-occurring alcohol dependence and posttraumatic stress disorder. *Alcoholism, Clinical and Experimental Research*, 29, 395-401.
- Petrakis IL, Poling J, Levinson C, Nich C, Carroll K, Ralevski E, et al. (2006). Naltrexone and disulfiram in patients with alcohol dependence and comorbid post-traumatic stress disorder. *Biological Psychiatry*, 60, 777-783.
- Petrakis IL, Ralevski E, Desai N, Trevisan L, Gueorguieva R, Rounsaville B, et al. (2012). Noradrenergic vs serotonergic antidepressant with or without naltrexone for veterans with PTSD and comorbid alcohol dependence. *Neuropsychopharmacology*, 37, 996-1004.
- Forget B, Wertheim C, Mascia P, Pushparai A, Goldberg SR, & Le Foll B. (2010). Noradrenergic alpha1 receptors as a novel target for the treatment of nicotine addiction. *Neuropsychopharmacology*, 35, 1751-1760.
- Greenwell Tn, Walker BM, Cottone P, Zorrilla EP, & Koob GF. (2009). The alpha1 adrenergic receptor antagonist prazosin reduces heroin self-administration in rats with extended access to heroin administration. *Pharmacology Biochemistry and Behavior*, 91, 295-302.



## References

- Le AD, Funk D, Juzytch W, Coen K, Navarre BM, Cifani C, et al. (2011). Effect of prazosin and guanfacine on stress-induced reinstatement of alcohol and food seeking in rats. *Psychopharmacology (Berl)*, 218, 89-99.
- Taylor FB, Lowe K, Thompson C, McFall MM, Peskind ER, Kanter ED, et al. (2006). Daytime prazosin reduces psychological distress to trauma specific cues in civilian trauma posttraumatic stress disorder. *Biological Psychiatry*, 59, 577-581.
- Chiamulera C, Tedesco V, Zangrandi L, Giuliano C, & Fumagalli G. (2010). Propranolol transiently inhibits reinstatement of nicotine-seeking behaviour in rats. *J Psychopharmacology*, 24, 389-395.
- Kampman KM, Dackis C, Lynch KG, Pettinati H, Tirado C, Gariti P, et al. (2006). A double-blind, placebo-controlled trial of amantadine, propranolol, and their combination for the treatment of cocaine-dependence in patients with severe cocaine withdrawal symptoms. *Drug and Alcohol Dependence*, 85, 129-137.
- Brunet A, Poundja J, Tremblay J, Bui E, Thomas E, Orr SP, et al. (2011). Trauma reactivation under the influence of propranolol decreases posttraumatic stress symptoms and disorder: 3 open-label trials. *J Clinical Psychopharmacology*, 24, 247-255.
- Hurlermann R, Walter H, Rehme Ak, Kukoja J, Santoro SC, Schmidt C, et al. (2010). Human amygdala reactivity is diminished by the beta-noradrenergic antagonist propranolol. *Psychological Medicine*, 40, 1839-1848.
- Smith RJ & Aston-Jones G. (2011). Alpha(2) adrenergic and imidazoline receptor agonists prevent cue-induced cocaine seeking. *Biological Psychiatry*, 70, 712-719.
- Fox HC, Seo D, Tuit K, Hansen J, Kimmerling A, Morgan PT, et al. (2012). Guanfacine effects on stress, drug craving and prefrontal activation in cocaine dependent individuals: preliminary findings. *J Psychopharmacology*, 26, 958-972.
- Neylan TC, Lenoci M, Samuelson KW, Metzler TJ, Henn-Haase C, Hierholzer RW, et al. (2006). No improvement of posttraumatic stress disorder symptoms with guanfacine treatment. *Am J Psychiatry*, 163, 2186-2188.
- Sofuoglu M, Poling J, Hill K, & Kosten T. (2009). Atomoxetine attenuates dextroamphetamine effects in humans. *Am J Drug and Alcohol Abuse*, 35, 412-416.
- Krupitsky EM, Neznanova O, Masalov D, Burakov AM, Didenko T, Romanova T. (2007). Effect of memantine on cue-induced alcohol craving in recovering alcohol-dependent patients. *Am J Psychiatry*, 164, 519-523.
- Battista MA, Hierholzer R, Khouzam HR, Barlow A, & O'Toole S. (2007). Pilot trial of memantine in the treatment of posttraumatic stress disorder. *Psychiatry*, 70, 167-174.
- Baker DA, McFarland K, Lake RW, Shen H, Toda S, & Kalivas PW. (2003). N-acetyl cysteine-induced blockade of cocaine-induced reinstatement. *Annals New York Academy Sciences*, 1003, 349-351.
- Grant JE, Kim SW, & Odlaug BL. (2007). N-acetyl cysteine, a glutamate-modulating agent in the treatment of pathological gambling: a pilot study. *Biological Psychiatry*, 62, 652-657.



## References

- Knackstedt LA, LaRowe S, Mardikian P, Malcolm R, Upadhyaya H, Hedden S, et al. (2009). The role of cystine-glutamate exchange in nicotine dependence in rats and humans. *Biological Psychiatry*, 65, 841-845.
- McGhee LL, Maani CV, Garza TH, Gaylord KM, & Black IH. (2008). The correlation between ketamine and posttraumatic stress disorder in burned service members. *J Trauma*, 64 (2 Suppl.), S195-198 (Discussion S197-198).
- Alderman CP, McCarthy LC, Condon JT, Marwood AC, & Fuller JR. (2009). Topiramate in combat-related posttraumatic stress disorder. *Annals Pharmacotherapy*, 43, 635-641.
- Saladin ME, Drobos DJ, Coffey SF, Dansky BS, Brady KT, Kilpatrick DG. (2003). PTSD symptom severity as a predictor of cue-elicited drug craving in victims of violent crime. *Addictive Behaviors*, 28, 1611-1629.
- Dansky BS, Saladin ME, Brady KT, Kilpatrick DG, & Resnick HS. (1995). Prevalence of victimization and post-traumatic stress disorder among women with substance use disorder: comparison of telephone and in-person assessment samples. *International J Addictions*, 30, 1079-1099.
- Grice DE, Dustan LR, Brady KT, Malcolm R, & Kilpatrick DG. (1992). Assault, substance abuse, and Axis I comorbidity. *Proceedings of the 145th American Psychiatric Association* (p. 91).
- Triffleman EG, Marmar CR, & Delucchi KL. (1993). Childhood trauma and PTSD in substance abuse inpatients. *Proceedings in Annual College on Problems in Drug Dependence* (p. 89).
- Lancaster CL, Gros DF, Mullarkey MC, Badour CL, Killeen TK, Brady KT, Back SE. (April 23, 2019). Does trauma-focused exposure therapy exacerbate symptoms among patients with comorbid PTSD and substance use disorders? *Behavioral Cognitive Psychotherapy*. Abstract ahead of print.
- Back SE, Killeen TK, Badour CL, Flannagan JC, Allan NP, Santa Ana E, Lozano B, Korte KJ, Foa EB, & Brady KT. (2019). Concurrent treatment of substance use disorders and PTSD using prolonged exposure: a randomized clinical trial in military veterans. *Addictive Behaviors*, 90, 369-377.
- Barrett E, Teeson M, & Mills K. (2014). Associations between substance use, posttraumatic stress disorder and the perpetration of violence: a longitudinal investigation. *Addictive Behaviors*, 39, 1075-1080.
- Grant B, Goldstein R, Saha T, Chou S, Jung J, Zhang H, et al. (2015). Epidemiology of DSM-5 alcohol use disorder: results from the National epidemiologic survey on alcohol and related conditions III. *JAMA Psychiatry*, 72, 757-766.
- Hoge C. (2015). Measuring the long-term impact of war-zone military service across generations and changing posttraumatic stress disorder definitions. *JAMA Psychiatry*, 72, 861-862.
- Kilpatrick DG, Resnick H, Milanak M, Miller M, Keyes K, & Friedman M. (2013). National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. *Journal Traumatic Stress*, 26, 537-547.
- Mills K, Teeson M, Ross J, & Peters L. (2006). Trauma, PTSD, and substance use disorders: findings from the Australian National survey of mental health and wellbeing. *Am J Psychiatry*, 163, 652-658.



## References

- Petrakis IL, Rosenheck R, & Desai R. (2011). Substance use comorbidity among veterans with posttraumatic stress disorder and other psychiatric illness. *Am J on Addictions*, 20, 185-189.
- Simpson T, Lehavot K, & Petrakis I. (2017). No wrong doors: findings from a critical review of behavioral randomized clinical trials for individuals with co-occurring alcohol/drug problems and PTSD. Vol. 41, ACER681-702.
- Stein M, Campbell-Sills L, Gelernter J, He F, Heeringa S, Nock M, et al. (2017). Alcohol misuse and co-occurring mental disorders among new soldiers in the U.S. army. *ACER*, 41, 139-148.
- Teeters JB, Lancaster CL, Brown DG, & Back SE. (2017). Substance use disorders in military veterans: prevalence and treatment challenges. *Substance Abuse and Rehabilitation*, 8, 69-77.
- Back SE, Killeen TK, Teer AP, Hartwell EE, Federline A, Beylotte F, & Cox E. (2014). Substance use disorders and PTSD: an exploratory study of treatment preference among military veterans. *Addictive Behaviors*, 39, 369-373.
- Szafranski DD, Snead A, Allan NP, Gros DF, Killeen TK, Flanagan J, Pericot-Valverde I, Back SE. (2017). Integrated, exposure-based treatment for PTSD and comorbid substance use disorders: predictors of treatment dropout. *Addictive Behaviors*, 73, 30-35.
- Grosso JA, Kimbrel NA, Dolan S, Meyer EC, Kruse MI, Gulliver SB, & Morissette SB. (2014). A test of whether coping styles moderate the effect of PTSD symptoms on alcohol outcomes. *J Traumatic Stress*, 27, 478-482.
- Banducci AN, Bujarski SJ, Bonn-Miller MO, Patel A, & Connolly KM. (2016). The impact of intolerance of emotional distress and uncertainty on veterans with cooccurring PTSD and substance use disorders. *J Anxiety Disorders*, 41, 73-81.
- Bowe A & Rosenheck R. (2015). PTSD and substance use disorder among veterans: characteristics, service utilization and pharmacology. *J Dual Diagnosis*, 11, 22-32.
- Galovski TE, Blain LM, Mott JM, Elwood L, & Houle T. (2012). Manualized therapy for PTSD: flexing the structure of cognitive processing therapy. *J Consulting and Clinical Psychology*, 80, 968-981.
- Garcia HA, Kelley LP, Rentz TO, & Lee S. (2011). Pretreatment predictors of dropout from cognitive behavioral therapy for PTSD in Iraq and Afghanistan war veterans. *Psychological Services*, 8, 1-11.
- Gros DF, Price M, Yuen EK, & Acierno R. (2013). Predictors of completion of exposure therapy in OEF/OIF veterans with posttraumatic stress disorder. *Depression and Anxiety*, 30, 1107-1113.
- Gros DF, Yoder M, Tuerk PW, Lozano BE, & Acierno R. (2011). Exposure therapy for PTSD delivered to veterans via telehealth: predictors of treatment completion and outcome and comparison to treatment delivered in person. *Behavioral Therapy*, 42, 276-283.
- Imel ZE, Laska K, Jakupcak M, & Simpson TL. (2013). Meta-analysis of dropout in treatments for posttraumatic stress disorder. *J Consulting and Clinical Psychology*, 81, 394-404.



## References

- Kelly JF & Moos R. (2003). Dropout from 12-step self-help groups: prevalence, predictors, and counteracting treatment influences. *J Substance Abuse Treatment*, 24, 241-250.
- Lester K, Artz C, Resick PA, & Young-Xu Y. (2010). Impact of race on early treatment termination and outcomes in posttraumatic stress disorder treatment. *J Consulting and Clinical Psychology*, 78, 480-489.
- Marmo A & Weinbaum DF. (1993). Some factors that influence dropping out from outpatient alcoholism treatment facilities. *J Studies on Alcohol*, 54, 92-101.
- McKellar J, Kelly J, Harris A, & Moos R. (2006). Pretreatment and during treatment risk factors for dropout among patients with substance use disorders. *Addictive Behaviors*, 31, 450-460.
- Mertens JR & Weisner CM. (2000). Predictors of substance abuse treatment retention among women and men in an HMO. *Alcoholism: Clinical and Experimental Research*, 24, 1525-1533.
- Milligan Co, Nich C, & Carroll KM. (2004). Ethnic differences in substance abuse treatment retention, compliance, and outcome from two clinical trials. *Psychiatric Services*, 55, 167-173.
- Moos RH & Moos BS. (2003). Long-term influence of duration and intensity of treatment on previously untreated individuals with alcohol use disorders. *Addiction*, 98, 325-337.
- Moos RH, Pettit B, & Gruber V. (1995). Longer episodes of community residential care reduce substance abuse patients' readmission rates. *J Studies on Alcohol*, 56, 433-443.
- Norman SB, Tate SR, Anderson KG, & Brown SA. (2007). Do trauma history and PTSD symptoms influence addiction relapse context? *Drug and Alcohol Dependence*, 90, 89-96.
- Rabinowitz J & Marjefsky S. (1998). Predictors of being expelled from and dropping out of alcohol treatment. *Psychiatric Services*, 49, 187-189.
- Rizvi SL, Vogt DS, & Resick PA. (2009). Cognitive and affective predictors of treatment outcome in cognitive processing therapy and prolonged exposure for posttraumatic stress disorder. *Behavior Research and Therapy*, 47, 737-743.
- Szafranski DD, Gros DF, Meneffee DS, Wanner JL, & Norton PJ. (2014). Predictors of length of stay among OEF/OIF/OND veteran inpatient PTSD treatment noncompleters. *Psychiatry*, 77, 263-274.
- Szafranski DD, Talkovskiy AM, Little TE, Meneffee DS, Wanner JL, Gros DF, & Norton PJ. (2016). Predictors of inpatient PTSD treatment noncompletion among OEF/OIF/OND veterans. *Military Behavioral Health*.
- Tuerk PW, Wangelin B, Rauch SM, Dismuke CE, Yoder M, Myrick H, et al. (2013). Health service utilization before and after evidence-based treatment for PTSD. *Psychological Services*, 10, 401-409.



## References

- van Minnen AA, Arntz AA, & Keijsers GJ. (2002). Prolonged exposure in patients with chronic PTSD: predictors of treatment outcomes and dropout. *Behavior Research and Therapy*, 40, 439-457.
- Zandberg LJ, Rosenfeld D, Alpert E, McLean CP, & Foa EB. (2016). Predictors of dropout in concurrent treatment of posttraumatic stress disorder and alcohol dependence: rate of improvement matters. *Behaviour Research and Therapy*, 80, 1-9.
- Kimerling R, Traffon JA, & Nguyen B. (2006). Validation of a brief screen for Post-Traumatic Stress Disorder with substance use disorder patients. *Addictive Behaviors*, 31, 2074-2079.
- Ouimette PC, Moos RH, & Finney JW. (2003). PTSD treatment and 5-year remission among patients with substance use and posttraumatic stress disorders. *J Consulting and Clinical Psychology*, 71, 410-414.
- Prins A, Ouimette PC, Kimerling R, Cameron RP, Hugelshofer DS, Shaw-Hegwer J, et al. (2004). The primary care PTSD screen: development and operating characteristics. *Primary Care Psychiatry*, 9, 9-14.
- Dworkin ER, Wanklyn S, Stasiewicz PR, & Coffey SF. (2018). PTSD symptom presentation among people with alcohol and drug use disorders: comparisons by substance of abuse. *Addictive Behaviors*, 76, 188-194.
- Back SE, Brady KT, Sonne SC, & Verduin ML. (2006). Symptom improvement in co-occurring PTSD and alcohol dependence. *J Nervous and Mental Disease*, 194, 69-696.
- Chilcoat HD & Breslau N. (1998). Investigations of causal pathways between PTSD and drug use disorders. *Addictive Behaviors*, 23, 827-840.
- Hien DA, Jiang H, Campbell ANC, Hu MC, Miele GM, Cohen LR, et al. (2010). Do treatment improvements in PTSD severity affect substance use outcomes? A secondary analysis from a randomized clinical trial in NIDA's Clinical Trials Network. *Am J Psychiatry*, 167, 95-101.
- Kaysen D, Atkins DC, Moore SA, Lindgren KP, Dillworth T, & Simpson T. (2011). Alcohol use, problems, and the course of posttraumatic stress disorder: a prospective study of female crime victims. *J Dual Diagnosis*, 7, 262-279.
- Khantzian EJ. (1985). The self-medication hypothesis of addictive disorders: focus on heroin and cocaine dependence. *Am J Psychiatry*, 142, 1259-1264.
- Possemato K, Maisto SA, Wade M, Barrie K, McKenzie S, Lantinga JJ, & Ouimette P. (2015). Ecological momentary assessment of PTSD symptoms and alcohol use in combat veterans. *Psychology of Addictive Behaviors*, 29, 894-905.
- Simpson TL, Stappenbeck CA, Luterek JA, Lehavot K, & Kaysen LD. (2014). Drinking motives moderate daily relationships between PTSD symptoms and alcohol use. *J Abnormal Psychology*, 123, 237-247.
- Brady KT, Dansky BS, Back SE, Foa EB, & Carroll KM. (2001). Exposure therapy in the treatment of PTSD among co-morbid cocaine-dependent individuals: preliminary findings. *J Substance Abuse Treatment*, 21, 47-54.



## References

- Breslau N, Davis GC, Andreski P, & Peterson E. (1991). Traumatic events and posttraumatic stress disorder in an urban population of young adults. *Archives Gen Psychiatry*, 48, 216-222.
- Davidson JR & Fairbank JA. (1993). The epidemiology of posttraumatic stress disorder. In J.R. Davidson, & E.B. Foa (Eds.), *Post-traumatic stress disorder: DSM-IV and beyond* (pp. 147-69). Washington, DC: American Psychiatric Press.
- Grant BF, Harford TC, Chou P, Pickering R, Dawson DA, Stinson FS, & Noble J. (1991). Epidemiologic Bulletin No. 27: prevalence of DSM-III-R alcohol abuse and dependence: United States, 1988. *Alcohol Health and Research World*, 15, 91-96.
- Grant BF, Harford TC, Dawson DA, Chou P, Dufour M, & Pickering R. (1994). Prevalence of DSM-IV alcohol abuse and dependence: United States, 1992. *Alcohol Health and Research World*, 18, 243-248.
- Helzer JE, Burnam A, & McElvov LT. (1991). Alcohol Abuse and dependence. In LN Robins & DA Regier (Eds.), *Psychiatric disorders in America: The epidemiological catchment era study* (pp. 81-115). New York: The Free Press.
- Kessler RC, Sonnega A, Bromet E, Hughes M, & Nelson CB. (1995). Posttraumatic stress disorder in the National Co-morbidity Survey. *Arch Gen Psychiatry*, 52, 1048-1060.
- Najavits LM, Weiss RD, Shaw SR, & Munez LR. (1998). "Seeking Safety": Outcome of a new cognitive-behavioral psychotherapy for women with posttraumatic stress disorder and substance abuse. *J Traumatic Stress*, 11, 437-456.
- Kandel DB. (1998). Persistent themes and new perspectives on adolescent substance use: a lifespan perspective. In : Jessor R, ed. *New Perspectives in Adolescent Risk Behavior*. Cambridge, UK: Cambridge University Press: 43-49.
- Hefferman K, Cloitre M, Tardiff K, Marzuk PM, Portera L, Leon AC. (2000). Childhood trauma as a correlate of lifetime opiate use in psychiatric patients. *Addictive Behavior*, 25, 797-803.
- Kendler KS, Bulik CM, Silberg J, Hettema JM, Myers J, Prescott CA. (2000). Childhood sexual abuse and adult psychiatric and substance abuse disorders in women: an epidemiological and cotwin control analysis. *Arch Gen Psychiatry*, 57, 953-959.
- Rohenshow DJ, Corbett R, & Devine D. (1988). Molested children: a hidden contribution to substance abuse? *J Substance Abuse Treatment*, 5, 129.
- Della Femina D, Yeager CA, & Lewis DO. (1990). Child abuse: adolescent records vs. adult recall. *Child Abuse and Neglect*, 14, 227-231.
- Douglas KR, Chan G, Gelernter J, Arias AJ, Anton RF, Weiss RD, Brady KT, Poling J, Farrer L, & Kranzler HR. (2010). Adverse childhood events as risk factors for substance dependence: partial mediation by mood and anxiety disorders. *Addictive Behaviors*, 35, 7-13.
- Chapman DP, Whitfield CL, Felitti VJ, Dube SR, Edwards VJ, & Anda RF. (2004). Adverse childhood experiences and the risk of depressive disorders in adulthood. *J Affective Disorders*, 82, 217-225.
- Dinwiddie S, Heath AC, Dunne MP, Bucholz KK, Madden PA, Slutske WS, et al. (2000). Early sexual abuse and lifetime psychopathology: a twin control study. *Psychological Medicine*, 30, 41-52.



## References

- Dube SR, Anda RF, Felitti VJ, Chapman DP, Williamson DF, & Giles WH. (2001). Childhood abuse, household dysfunction and the risk of attempted suicide throughout the life span: findings from the Adverse Childhood Experiences Study. *JAMA*. 286, 3089-3096.
- Fergusson DM, Boden JM, & Horwood LJ. (2008). The developmental antecedents of illicit drug use: evidence from a 25-year longitudinal study. *Drug and Alcohol Dependence*. 96, 165-177.
- Galaif ER, Stein JA, Newcomb MD, & Bernstein DP. (2001). Gender differences in the prediction of problem alcohol use in adulthood: exploring the influence of family factors and childhood maltreatment. *J Studies on Alcohol Drugs*. 62, 486-493.
- Langeland W, Draijer N, & van den Brink W. (2004). Psychiatric comorbidity in treatment-seeking alcoholics: the role of childhood trauma and perceived parental dysfunction. *Alcohol: Clinical and Experimental Research*. 28, 441-447.
- Molnar BE, Buka SL, & Kessler RC. (2001). Child sexual abuse and subsequent psychopathology: results from the National Comorbidity Survey. *Am J Public Health*. 91, 753-760.
- Nelson EC, Heath AC, Madden PA, Cooper ML, Dinwiddie SH, Bucholz KK, et al. (2002). Associations between self-reported childhood sexual abuse and adverse psychosocial outcomes: results from a twin study. *Arch Gen Psychiatry*. 59, 139-145.
- Penza KM, Heim C, & Nemeroff CB. (2003). Neurobiological effects of childhood abuse: implications for the pathophysiology of depression and anxiety. *Arch Women's Mental Health*. 6, 15-22.
- Pilowsky DJ, Keyes KM, & Hasin DS. (2009). Adverse childhood events and lifetime alcohol dependence. *Am J Public Health*. 99, 258-263.
- Spak L, Spak F, & Allebeck P. (1997). Factors in childhood and youth predicting alcohol dependence and abuse in Swedish women: findings from a general population study. *Alcohol and Alcoholism*. 32, 267-274.
- Widom CS, DuMont K, & Czaja SJ. (2007). A prospective investigation of major depressive disorder and comorbidity in abused and neglected children grown up. *Arch Gen Psychiatry*. 64, 49-56.
- Stein MD, Conti MT, Kenney S, Anderson BJ, Flori JN, Risi MM, & Bailey GL. (2017). Adverse childhood experience effects on opioid use initiation, injection drug use, and overdose among persons with opioid use disorder. *Drug and Alcohol Dependence*. 179, 325-329.
- Afifi TO, Henriksen CA, Asmundson GJ, & Sareen J. (2012). Childhood maltreatment and substance use disorders among men and women in a nationally representative sample. *Can J Psychiatry*. 57, 677-686.
- Anthony JC & Petronis KR. (1995). Early -onset drug use and risk of later dug problems. *Drug Alcohol Dependence*. 40, 9-15.
- Baldwin P, Shrestha R, Potrepka J, & Copenhaver M. (2013). The age of initiation of drug use and sexual behavior may influence subsequent HIV risk behavior: a systematic review. *ISRN AIDS* 97603, 5.



## References

- Chen CY, Storr CL, & Anthony JC. (2009). Early-onset drug use and risk for drug dependence problems. *Addictive Behaviors*. 34, 319-322.
- King KM & Chassin L. (2007). A prospective study of the effects of age of initiation of alcohol and drug use on young adult substance dependence. *J Stud Alcohol Drugs*. 68, 256-265.
- Moseley HF, Fahmy E, Mikhael VS, & El-Sheikh H. (2010). Impact of self-reported life events on the profile of opioid dependence syndrome. *Am J Drug Alcohol Abuse*. 36, 7-12.
- Muhuri PK, Gfroerer JC, & Davies C. (2013). Associations of nonmedical pain reliever use and initiation of heroin use in the United States. *Center Behavioral Health Statistics Quality Review Data*. August.
- Pollini RA, Banta-Green CJ, Cuevas-Mota J, Metzner M, Teshale E, & Garfein RS. (2011). Problematic use of prescription-type opioids prior to heroin use among young heroin injectors. *Substance Abuse Rehabilitation*. 2, 173-180.
- Taplin C, Saddichha S, Li K, & Krausz MR. (2014). Family history of alcohol and drug abuse, childhood trauma, and age of first drug injection. *Substance Use Misuse*. 49, 1311-1316.
- Kessler RC, Davis CG, & Kendler KS. (1997). Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey. *Psychological Medicine*. 27, 1101-1119.
- Grant JD, Sherrer JF, Lynskey MT, et al. (2006). Adolescent alcohol use is a risk factor for adult alcohol and drug dependence: evidence from a twin design. *Psychological Medicine*. 36, 109-118.
- Prescott CA & Kendler KS. (1999). Age at first drink and risk for alcoholism: a noncausal association. *Alcohol Clinical Experimental Research*. 23, 101-107.
- Turner RJ & Lloyd DA. (2003). Cumulative adversity and drug dependence in young adults: racial/ethnic contrasts. *Addiction*. 98, 305-315.
- Bell TM, Raymond J, Vektor A, Mongalo A, Adams Z, Rouse T, & Carroll A. (2019). Long-term prescription opioid utilization, substance use disorders, and opioid overdoses after adolescent trauma. *J Trauma Acute Care Surgery*. Published ahead of print.
- Center for Behavioral Health Statistics and Quality. Behavioral health trends in the United States: results from the 2014 National Survey on Drug Use and Health. *HHS Publication No. SMA 15-4927, NSDUH Series H-50*. <http://www.samsha.gov/data>.
- Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. *Web-based Injury Statistics Query and Reporting System (WISQARS)*. <http://www.cdc.gov/injury/wisqars/>
- McCabe SE, West BT, Teter CJ, & Boyd CJ. (2012). Medical and nonmedical use of prescription opioids among high school seniors in the United States. *Arch Pediatr Adolesc Med*. 166, 797-802.



## References

- Zatzick DF & Grossman DC. (2011). Association between traumatic injury and psychiatric disorders and medication prescription to youths aged 10-19. *Psychiatric Services*. 62, 264-271.
- Chen CY, Storr CL, & JC A. (2009). Early-onset drug use and risk for drug dependence problems. *Addictive Behaviors*. 34, 319-322.
- Grant BF & Dawson DA. (1997). Age at onset of alcohol use and its association with DSM-IV alcohol abuse and dependence: results from the National Longitudinal Alcohol Epidemiologic Survey. *J Substance Abuse*. 9, 103-110.
- Substance Use Prevalence, USA: [https://www.samhsa.gov/data/sites/default/files/report\\_2790/ShortReport-2790.html](https://www.samhsa.gov/data/sites/default/files/report_2790/ShortReport-2790.html)
- USA Population – United States Census Bureau: <https://www.census.gov/programs-surveys/popproj/data.html>



## Image References

- Elephant in the Room Cartoon:
  - <https://i.pinimg.com/474x/6a/1f/d1/6a1fd1701c7caecf26250df8f1bcffca--all-colleges-student-loan-debt.jpg>
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- Sheamus (Stephen Farrelly) Picture
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  - 3<sup>rd</sup>: <http://2.bp.blogspot.com/-VFYp-6HPD1o/UZjfsX55ODI/AAAAAAAAADPI/chbkpoYaAVI/s1600/Sheamus+pointing.jpg>



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- Brain cartoons:
  - <https://i.pinimg.com/474x/ce/37/13/ce3713fc5cbd1a1d41a6c59f00c4343d--the-human-brain-the-brain.jpg>
  - <https://i.pinimg.com/474x/ee/cd/7c/eedc7cb1254883890ecf0162a15581a0--nerd-stuff-funny-stuff.jpg>
- Cards
  - <https://c8.alamy.com/comp/C7A9RF/poker-hand-where-joker-is-wild-with-four-aces-C7A9RF.jpg>
- Stress
  - <https://i.pinimg.com/474x/34/77/bc/3477bc3443fec48fe4f9be6432f80b63--men-vs-women-womens-retreat.jpg>
  - <https://i.pinimg.com/474x/89/af/60/89af60a4eb3df909e9dd156cf0c04e8--stress-fun-quotes.jpg>
  - <https://i.pinimg.com/474x/c8/d4/3b/c8d43b7903d65d77a2f9f230d6ea90df--stress-tests-funny-spider.jpg>
- Running from Negative Affective States;
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- Sitting Man Change My Mind
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- Yelling Pic
  - <https://images.fatherly.com/wp-content/uploads/2017/10/why-i-yelled.jpg?q=65&enable=upscale&w=600>
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- Distracted boyfriend
  - <https://imgflip.com/i/389fq3>
- Flat Earthers
  - <https://images7.memedroid.com/images/UPLOADED907/5bfd7f59f0b92.jpeg>
- No Magic Pill, Process
  - <https://whatcanbegained.com/2017/05/05/falling-in-love-with-the-process-to/>
- Therapy Couch
  - <https://i.pinimg.com/originals/50/30/71/5030719ec35fba7bf728752d078ff430.jpg>
- Oprah
  - <https://imgflip.com/i/389iwo>
- Recommendations
  - [https://s3.amazonaws.com/lowres.cartoonstock.com/medical-exercise-exercising-doctor\\_s\\_recommendation-doctor-gp-aban1105\\_low.jpg](https://s3.amazonaws.com/lowres.cartoonstock.com/medical-exercise-exercising-doctor_s_recommendation-doctor-gp-aban1105_low.jpg)

