Alcohol Withdrawal and Craving at Treatment Entry Prospectively Predict Alcohol Use Outcomes During Outpatient Treatment

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BACKGROUND

Alcohol misuse and Alcohol Use Disorder (AUD) are significantly associated with adverse consequences and global disease burden (Griswold et al., 2018). Although there are efficacious treatments for AUD, treatment failure and high relapse rates remain a significant issue in AUD treatment (Sinha, 2011).

- Recent initiatives (e.g., Litten et al., 2015; Witkiewitz et al. 2019) aimed at improving personalized treatment of AUD emphasize the need:
  - To Identify AUD clinical features that increase risk for treatment failure
  - To develop treatments specifically targeted for those who are at risk for relapse
- Early alcohol abstinence in AUD is associated with:
  - Altered stress and reward brain neurocircuitry (e.g., Koob, 2003; Seo et al., , 2013)
  - Disrupted prefrontal-striatal and HPA axis function (Blaine et al., 2020)
  - Clinical symptomology: alcohol withdrawal (AW), craving, depression, anxiety, and sleep difficulties (Fox et al., 2007; Sinha et al., 2011; Milivojevic and Sinha, 2018)

Despite evidence of treatment failure risk in those showing such stress pathophysiology, research to specifically assess whether these clinical features of AUD significantly impact alcohol use outcomes in outpatient treatment has lagged behind.

Thus, we examined whether alcohol withdrawal (AW) symptoms, craving, and additional symptoms of depression, anxiety, and sleep difficulties in AUD patients entering outpatient treatment predict subsequent alcohol use outcomes in outpatient treatment.

METHOD

Participants were 80 AUD treatment-seeking community adults with current moderate to severe AUD (38.8% female; 42.5% White; aged 20-60 years; Mage = 36.6, SD = 11.24) who were prospectively followed while they participated in weekly behavioral counseling utilizing the manualized 12-Step Facilitation and Relapse Prevention Therapy for 8 weeks.

Initial visits and baseline assessments at intake:

- Demographic information (sex, age, race, and SES)
- Clinical Institute of Withdrawal Assessment for Alcohol (CIWA-Ar, Sullivan et al., 1989)
- Alcohol Urge Questionnaire (AUQ; Bohn, Krahn and Staehler, 1995)
- Hamilton Anxiety Scale (HAS; Maier et al., 1988)
- Beck Depression Inventory (BDI; Beck et al., 1961)
- The Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1988)
- 90-day Substance Use Calendar (SUC; Miller and Del Boca, 1994)

Weekly behavioral counseling and assessments:

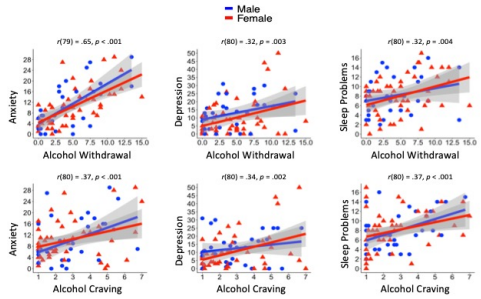
- 1x week treatment session using 12-Step and Relapse Prevention as outlined in the NIAAA Project MATCH manuals (Kadden et al., 1994; Nowinski, Baker and Carroll, 1994)
- Timeline follow-back assessments using the 7-day SUC

Daily ecological momentary assessment (EMA):

- Brief surveys administered in a smartphone application (MetricWire, Inc.)
  - Daily morning and evening prompts (compliance rate: approx. 69%)
  - Total number of drinks consumed (beer, wine, and liquor)

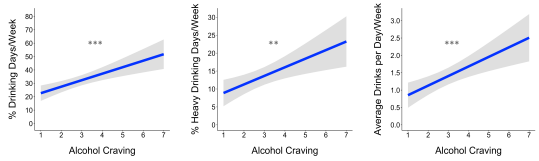
RESULTS

Correlations between Alcohol Withdrawal (AW), Craving, and Other Abstinence Symptoms



Pretreatment AW and craving were moderately to strongly associated with depression, anxiety, and sleep difficulties at treatment entry (mean value $|r|$ = .42; range .32 to .65; all p's < .05), but these associations did not vary systematically between men and women.

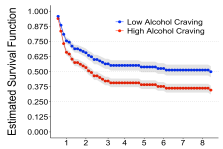
Alcohol Craving Predicting Treatment Response



Significant main effects of craving on drinking days per week (DD; p < .001), heavy drinking days per week (HDD, p < .009), and average drinks per week (AvgD; p < .001) during treatment. *Covariate Adjustment*: # abstinence days, past alcohol use, age, sex, race, and SES.

Alcohol Craving Predicting Relapse

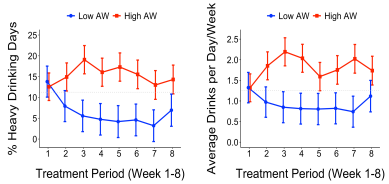
HR: 1.20; 95% CI [1.00-1.44], p = .049



Pretreatment alcohol craving (continuous scores) predicted risk of relapse to heavy drinking during treatment. Covariate Adjustment: # abstinence days, past alcohol use, age, sex, race, and SES.

Each one-unit increase in craving at treatment entry was associated with a 20% increase in the risk of subsequent relapse to heavy drinking day during treatment.

Alcohol Withdrawal (AW) Predicting Treatment Response



Significant interaction of baseline AW with treatment week on HDD (p < .018) and AvgD (p < .004) *Covariate Adjustment*: # abstinence days, past 90-day alcohol use, age, sex, race, and SES.

CONCLUSIONS

- Higher levels of pretreatment alcohol craving consistently predicted higher levels of alcohol intake during treatment and higher risk of relapse to heavy drinking.
- Pretreatment levels of alcohol withdrawal predicted different trajectories in treatment response throughout the treatment period, such that treatment was effective for patients with little or no withdrawal symptoms, but it did not benefit patients with high levels of withdrawal at treatment entry.
- Pretreatment symptoms of depression, anxiety, and sleep difficulties did not predict any drinking-related outcome during treatment.
- Predictive effects of alcohol withdrawal and craving on treatment response held up even after controlling for drinking history and alcohol intake levels prior to treatment entry.
- Assessment of alcohol withdrawal and craving at intake is critical for understanding the heterogeneity of AUD treatment responses to improve and develop AUD treatments targeted at reducing acute withdrawal-related distress and stress-induced craving.

REFERENCES

Blaine et al. (2020) *Association of Prefrontal-Striatal Functional Pathology with Alcohol Abstinence Days at Treatment Initiation and Heavy Drinking after Treatment Initiation*, Am J Psychiatry, 177, 1048–1059
Fox et al. (2007) *Stress-induced and alcohol cue-induced craving in recently abstinent alcohol-dependent individuals*, Alcohol Clin Exp Res, 31, 395–403
Griswold et al. (2018) *Alcohol use and burden for 195 countries and territories, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016*, The Lancet, 392,1015–1035
Koob (2003) *Alcoholism: Allostasis and Beyond*, Alcohol Clin Exp Res, 27, 232–243
Litten et al. (2015) *Heterogeneity of alcohol use disorder: Understanding mechanisms to advance personalized treatment*, Alcohol Clin Exp Res, 39, 579–584
Milivojevic & Sinha (2018) *Central and Peripheral Biomarkers of Stress Response for Addiction Risk and Relapse Vulnerability*, Trends Mol Med, 24, 173–186
Seo et al. (2013) *Disrupted ventromedial prefrontal function, alcohol craving, and subsequent relapse risk*, JAMA Psychiatry, 70, 727-739.
Sinha (2011) *New findings on biological factors predicting addiction relapse vulnerability*, Curr Psychiatry Rep, 13, 398–405
Witkiewitz et al. (2019) *Advancing Precision Medicine for Alcohol Use Disorder: Replication and Extension of Reward Drinking as a Predictor of Naltrexone Response*, Alcohol Clin Exp Res, 43, 2395–2405

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