

The Association between Alcohol Dependence, Post-traumatic Stress Disorder,
and Aggression

by

Jared Bollinger

Thesis submitted to the Faculty of the
Clinical Psychology Graduate Program
Uniformed Services University of the Health Sciences
In partial fulfillment of the requirements for the degree of
Doctor of Philosophy 2019



UNIFORMED SERVICES UNIVERSITY, SCHOOL OF MEDICINE GRADUATE PROGRAMS
Graduate Education Office (A 1045), 4301 Jones Bridge Road, Bethesda, MD 20814

November 15, 2017

APPROVAL SHEET

Title of Masters: **"The Association between Alcohol Dependence, Post-Traumatic Stress Disorder, and Aggression"**

Name of Candidate: **Jared Bollinger**, Master of Science ,

11/15/17

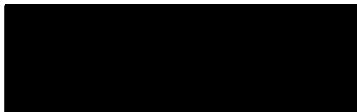
THESIS AND ABSTRACT APPROVED:

DATE:



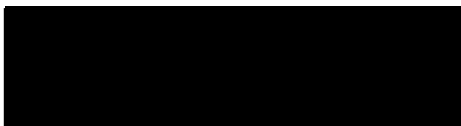
11/15/17

Andrew J. Waters
DEPARTMENT OF
Thesis Advisor



11/15/17

David Riggs
DEPARTMENT OF
Committee Member



11/15/2017

Marjan Holloway
DEPARTMENT OF
Committee Member

ACKNOWLEDGMENTS

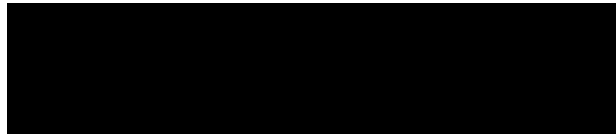
I want to acknowledge my research advisor, Andrew Waters, for his help in preparing my thesis.

DEDICATION

I want to dedicate this thesis for my mom, dad, brothers, and girlfriend, Grace, for all their support over the years.

COPYRIGHT STATEMENT

The author hereby certifies that the use of any copyrighted material in the thesis manuscript entitled: The Association between Alcohol Dependence, Post-traumatic Stress Disorder, and Aggression is appropriately acknowledged and, beyond brief excerpts, is with the permission of the copyright owner.



Jared Bollinger

[Month Day, Year of BOR meeting, check
thesis and dissertation manual for dates]

DISCLAIMER

The views presented here are those of the author and are not to be construed as official or reflecting the views of the Uniformed Services University of the Health Sciences, the Department of Defense, or the U.S. Government.

ABSTRACT

The Association between Alcohol Dependence, Post-traumatic Stress Disorder, and Aggression

Jared W. Bollinger, B.S., 2017

Thesis directed by: Andrew J. Waters, Professor, Department of Medical and Clinical Psychology

Aggression imparts a tremendous burden on society through violence, abuse, and damage to property and life. Alcohol dependence (AD) has been shown to be associated with increased aggression, although this has been explored in relatively few studies. Post-traumatic Stress Disorder (PTSD) has also been shown to be associated with aggression, and alcohol use or dependence may mediate the association between PTSD and aggression. In this study, two groups with AD (non-treatment-seeking participants and inpatient treatment-seeking) were compared to healthy controls on a measure of self-reported aggression. In addition, within the inpatients, a mediation model tested whether the association between PTSD and aggression was mediated by severity of alcohol dependence. Consistent with our hypothesis, the results suggested that AD is associated with self-reported aggression. Individuals with AD reported higher levels of self-reported aggression than those without AD. Moreover, within inpatients with AD, severity of AD was positively associated with self-reported aggression. Within inpatients with AD, severity of AD partially mediated the association between PTSD and aggression. In sum, AD is robustly associated with aggression, and severity of AD may mediate the association between PTSD and aggression. Implications from this study suggest that

aggression may be a treatment target with individuals with AD. In addition, co-occurring PTSD may be predictive of greater aggression in AD populations.

TABLE OF CONTENTS

LIST OF TABLES	ix
LIST OF FIGURES	x
CHAPTER 1: INTRODUCTION	1
ALCOHOL AND SOCIETY	1
ALCOHOL MISUSE & HEALTH.....	1
ALCOHOL ADDICTION	2
ALCOHOL AND VIOLENCE.....	2
Alcohol Consumption and Aggression	3
Alcohol Administration and Aggression	4
Alcohol Dependence and Aggression.....	6
Alcohol Dependence and Co-occurring Disorders	8
PTSD, AGGRESSION, AND ALCOHOL.....	8
Alcohol Misuse and PTSD.....	9
PTSD & Aggression	10
CHAPTER 2: SPECIFIC AIMS	11
STUDY RATIONALE	11
STUDY AIMS	11
Specific Aim 1	11
Hypothesis 1.1.....	12
Hypothesis 1.2.....	12
Hypothesis 1.3.....	12
Specific Aim 2	12
Hypothesis 2.1.....	12
Hypothesis 2.2.....	12
CHAPTER 3: METHODS.....	13
Participants.....	13
Procedure	13
Measures	14
Psychiatric Diagnosis.....	14
Alcohol Dependence Severity.....	15
Aggression	15
Drinks per day	16
Demographic Variables	16
DATA ANALYSIS.....	16

CHAPTER 4: RESULTS.....	21
Aim 1	21
Aim 2	22
CHAPTER 4: DISCUSSION.....	25
LIMITATIONS.....	29
STRENGTHS	31
CONCLUSION.....	31
FUTURE DIRECTIONS	32
REFERENCES	47

LIST OF TABLES

Table 1.	Literature Review: Aggression in Alcohol Dependence.....	34
Table 2.	Assessments by Protocol.....	35
Table 3.	Participant Characteristics	36
Table 4.	Inpatient Alcohol Dependent Characteristics.	38
Table 5.	Regression Results for Mediation Models	39

LIST OF FIGURES

Figure 1.	Diagram of the comorbidity between AUD/SUD and PTSD	40
Figure 2.	Specific Aim 1, Hypothesis 1.1 Results: Total Aggression	41
Figure 3.	Specific Aim 1, Hypothesis 1.2 Results: Physical Aggression	42
Figure 4.	Specific Aim 1, Hypothesis 1.2 Results: Verbal Aggression	43
Figure 5.	Specific Aim 1, Hypothesis 1.2 Results: Anger	44
Figure 6.	Specific Aim 1, Hypothesis 1.2 Results: Hostility	45
Figure 7.	Mediation Model using Baron and Kenny's (1986) terminology	46

CHAPTER 1: INTRODUCTION

Aggression imposes a tremendous burden on society through violence, abuse, damage to property, and loss of life. Alcohol dependence (AD) has been shown to be associated with increased aggression, although this has been explored in relatively few studies. Post-traumatic stress disorder (PTSD) has also been shown to be associated with aggression. The current study examines the pattern of associations between PTSD, AD, and aggression.

The organization of the introduction will be as follows. First, there will be an overview of the consequences of chronic alcohol use, focusing then on aggression-related outcomes. Second, the literature on the association between PTSD and alcohol misuse will be reviewed. Third, the literature on the association between PTSD and aggressive behavior will be reviewed, and mechanisms of this association explored.

ALCOHOL AND SOCIETY

It is estimated that overuse of alcohol costs the United States (US) \$223 billion each year in terms of loss of life, productivity, health, and crime (Sacks et al., 2015). Persons who overuse alcohol tend to live shorter lives, thereby resulting in loss of productivity. Medical costs include: treating alcohol-related injuries in emergency rooms, chronic health conditions on inpatient wards, and other health deficits in general medical settings. Most notably for this paper, alcohol use often precipitates aggressive behavior (Maldonado-Molina et al., 2010), which also results in great costs to society.

ALCOHOL MISUSE AND HEALTH

Excessive alcohol use is associated with a wide range of physical health problems. Alcohol drinking is implicated in development of fatty liver, stenosis, alcoholic

hepatitis, fibrosis, and cirrhosis (Gao & Bataller, 2011). Excessive alcohol use is also associated with increased prevalence of over two hundred types of cancer, most notably of the esophagus and stomach (World Health Organization, 2015). Chronic alcohol abuse is also a causal factor in debilitating neurological conditions such as alcohol-induced dementias and Korsakoff's syndrome (Thomson, Guerrini, & Marshall, 2012). Excessive acute doses of alcohol also have effects on short-term physiological functioning. Overconsumption of alcohol can lead to deficits in immune system functioning (Crews et al., 2015) and the release of endotoxins into the blood (Bala et al., 2014). In extreme cases, excessive alcohol consumption can result in overdose and death.

ALCOHOL ADDICTION

Alcohol addiction has been defined medically as the syndromes of Alcohol Abuse (AA) and Alcohol Dependence (AD); DSM-IV-TR; American Psychiatric Association [APA], 2000), now jointly called Alcohol Use Disorder (AUD, DSM-5; APA, 2013). AD, AA, and AUD are prevalent mental health disorders. There were approximately 17 million cases of AUD in the US in 2012 (Substance Abuse Mental Health Services Administration, 2012). Estimates of the current and lifetime prevalence of AUD are 13.9% and 29.1% based on studies using structured psychiatric interviews (Grant et al., 2015). Addiction to alcohol is thought to result from chronic stimulation of dopaminergic cells in the ventral tegmental area and the nucleus accumbens in the human brain (Koob & LeMoal, 1997). Alcohol's effects on the brain are diverse and complex. Alcohol increases gamma-aminobutyric acid (GABA) activity, stimulates opioid receptors, and at some doses enhances transmission of norepinephrine. Of particular interest for this study is that it has been posited that the neurotransmitter mechanisms of

aggression include serotonin depletion and dopamine stimulation, the later which occurs during alcohol intoxication (Seo, Patrick, & Kennealy 2008).

ALCOHOL AND VIOLENCE

Most pertinent to the current study, alcohol use is associated with various forms of violence. It has been estimated that 86% of homicides and 37% of assaults are carried out by perpetrators under the influence of alcohol (National Institute on Alcohol Abuse and Alcoholism, 1997). In one study of 1887 homicide offenders, 50% reported consuming more alcohol than usual and being under the influence of alcohol during the crime (Wieczorek, Welte, & Abel, 1990). It is also estimated that 50% of sexual assaults are committed under alcohol intoxication (Abbey et al., 2011). Alcohol consumption also increases the chances of domestic violence and its intensity (World Health Organization factsheet, n.d.). In a study of 508 suicides in Slovenia, approximately 75% of the autopsies indicated the presence of alcohol (Bilban & Skibin, 2005).

There is a large social and economic burden of alcohol-related aggression. Of the \$223.5 billion cost of alcohol abuse (Sacks et al., 2015), \$5.9 billion is directly attributable to violence and property crimes. Another analysis indicated even greater costs of alcohol-related violence, yielding an estimate of \$85 billion in costs due to alcohol-related crime (Miller, Levy, Cohen, & Cox, 2006).

ALCOHOL CONSUMPTION AND AGGRESSION

Increased levels of alcohol consumption have been associated with increased levels of anger and aggression in the general population (Barrett, Mills & Teesson, 2013). Degree of alcohol consumption has been positively correlated with scores on the Buss-Perry Questionnaire (BPAQ; Tremblay & Ewart, 2005), a validated self-report measure of aggression. This is true for not only for males, but also females (Newberry, Williams,

& Caulfield, 2013). In another sample, increased alcohol use disorder symptoms were associated with the BPAQ physical aggression subscale score (Bacskai, Czobor, & Gerevich, 2008). In a study in veterans, alcohol misuse as well as trauma history indicated higher risk for aggression (Gobin, Green, & Iverson, 2015).

Alcohol use could cause aggression, and/or aggressive individuals could be more likely to drink more alcohol. Data regarding the directionality between aggression and alcohol use are mixed. Several longitudinal studies have measured aggression and alcohol use in samples of adolescents growing into adulthood. Some studies have found that early aggressive behavior predicts later alcohol use (White, Brick, & Hansell, 1993). Similarly, another study found that negative emotionality (including aggression) at 17 was a significant predictor of AUD three years later (Elkins et al., 2006). Other studies have found that aggression predicted future alcohol use and also that alcohol use predicted future aggression (Xue, Zimmerman, & Cunningham, 2009).

In one of the largest longitudinal studies surveying over 10,000 adolescents followed into early adulthood (age 26), alcohol use, and not self-reported aggression at baseline, doubled the chances of future self-reported aggression (Maldonado-Molina et al., 2010). In a large study of twins and adoptees followed up for over 8 years, alcohol use initiation was found to increase several negative emotions, most pronouncedly aggressive emotionality (Blonigen et al., 2015). However, there are some findings that do not support the hypothesis that alcohol use predicts future aggression (e.g., White & Hansell, 2009).

ALCOHOL ADMINISTRATION AND AGGRESSION

The acute effects of alcohol on aggression have been examined using laboratory-behavioral measures of aggression. Aggression is commonly measured in laboratory

settings using the Taylor Aggression Paradigm (TAP; Taylor, 1967). In this task, a participant administers shocks to a sham participant during a faux competitive reaction-time task. Aggression is operationalized by the frequency and intensity of the shocks the participant gives to their confederate opponent. When participants are administered alcohol before the TAP, they deliver significantly more severe and larger numbers of shocks to sham participants than participants administered a nonalcoholic beverage (Lau, Pihl, & Peterson, 1995).

Self-report measures of aggression such as the BPAQ may predict laboratory measures of aggression when participants are under intoxication. In social drinkers, BPAQ scores predicted aggression assessed with the TAP when participants received alcohol, but not when performing the task without alcohol (Miller, Parrott, & Giancola, 2009). There are also other findings that indicate that more problematic drinking may be associated with higher aggression during the TAP. Participants who were classified as heavy episodic drinkers had higher aggression assessed with the TAP than regular social drinkers (Parrott & Giancola, 2006).

Alcohol is a powerful central nervous system depressant. As such, its suppression of decision making centers of the brain impairs judgment. It has been hypothesized that these biological changes affect cognition in a way that promotes aggression. In the most popular version of this theory, the attention allocation model (AAM), alcohol is thought to impair attentional redirecting processes. Therefore, when provocations occur under intoxication, the aggressor is unable to divert attention to non-threatening, less salient stimuli or to consider potential consequences (Giancola et al., 2009). In one well-known test of this hypothesis, participants were administered alcohol before an aggression task

while simultaneously being required to complete a sustained attention task. The sustained attention task asked participants in different conditions to hold either 2, 4, or 8 digits in working memory. In line with the AAM, participants whose attention was diverted to non-threatening stimuli (in this case during the sustained attention task) showed substantial decreases in aggression, although only at the level of the 4 digit condition (Giancola & Corman, 2007).

ALCOHOL DEPENDENCE AND AGGRESSION

Although many studies have examined the association between alcohol use and aggression in non-dependent populations, relatively few studies have examined the association between AD and aggression. In a large cross-sectional study, AD was associated with a three times higher risk of violence than a control group without AD (Coid et al., 2006), suggesting greater aggression. Persons with AD also score higher on laboratory tasks measuring aggression (Kose et al., 2015). In addition, a majority of studies comparing ADs to controls support that conclusion that self-reported aggression is elevated in AD (see Table 1).

In a study of 330 detoxified inpatients undergoing treatment for AD in Hungary, scores on all four aggression subscales (physical aggression, verbal aggression, hostility, and anger) of the BPAQ (Buss & Perry, 1992) were significantly higher than those of the non-dependent group (Gerevich et al., 2007). These results were replicated in an additional sample of 101 inpatients with AD and 212 controls from Hungary (Bácskai et al., 2011). In a study from Turkey, 94 AD inpatients also had significantly higher scores on the BPAQ (and all four BPAQ subscales) than the 63 control participants (Bozkurt et al., 2013). Thus, the link between AD and self-report aggression has been demonstrated across cultures. However in one study from Germany that surveyed 258 AD inpatients

and then compared the sample to the questionnaire's normative group on a self-reported measure of aggression, the authors found no significant differences (Mann et al., 1995). However, the authors note that their AD sample may have been lower on aggression due to their eligibility criteria (e.g., requirement of either a job or family support before entering treatment).

To the best of the author's knowledge, no study has examined the association between alcohol dependence and self-reported aggression in a US sample. One review has noted differences in drinking patterns between U.S. and European samples (Bloomfield et al., 2003). This suggests that one cannot assume that associations between alcohol dependence and aggression-related variables observed in European samples seamlessly generalize to U.S. samples. In the countries where studies have been conducted comparing aggression between AD and controls (reviewed above), alcohol consumption differed from the United States. The World Health Organization (2014) found the rate of alcohol use was: 11.8 liters of pure alcohol per capita in Germany, 13.3 liters of pure alcohol per capita in Hungary, and 2.0 liters of pure alcohol per capita in Turkey. The United States drinks on average 9.2 liters of pure alcohol per capita (WHO, 2014). In addition, it has also been noted that: "Levels and patterns of alcohol consumption vary widely between countries...Similarly, levels of violence differ between countries" (WHO, 2006). However, it was also noted that: "Even where estimates of alcohol's role in violence are available, methodological differences between studies complicate direct comparisons between countries" (WHO, 2006). Therefore, it appears that further cross-cultural comparisons, using standardized measures of aggression, are warranted.

ALCOHOL DEPENDENCE AND CO-OCCURRING DISORDERS

AD and AUD often co-occur with mental health disorders. The National Comorbidity Survey (NCS) demonstrated that AUD overlaps significantly with major depression, bipolar, drug use, borderline personality disorder, and antisocial personality disorder (Grant et al., 2015). Other associations were found for panic, specific phobia, and generalized anxiety disorder. These results were largely drawn from data using DSM-IV-TR criteria for AD. In a previous iteration of the NCS, AD was associated with depression, anxiety, and personality disorders (Hasin et al., 2007). The current DSM also indicates that alcohol can have a causal role in the development of several disorders including alcohol-induced psychosis, mania, and depression (American Psychiatric Association, 2013). Most pertinent for the current study is the high comorbidity between AD and PTSD (National Center for PTSD, 2016).

PTSD, ALCOHOL, & AGGRESSION

PTSD is a psychiatric disorder that occurs in response to an extreme stressor or stressors known as trauma (American Psychiatric Association, 2013). PTSD is also associated with several psychiatric disorders and symptoms including depression, panic attacks, and impulse control problems such as problematic substance use (Grant et al., 2015).

AD and PTSD are commonly associated (see Figure 1 for conceptual diagram for the association). Approximately 7.7% of persons with AD have PTSD (Petrakis, Gonzalez, Rosenheck, & Krystal, 2002), whereas approximately 4% of persons without a substance use disorder (including AD) have PTSD. Approximately 20% of persons with PTSD have a substance or alcohol use disorder (Petrakis et al., 2011), whereas approximately 14% of persons without PTSD have AD or another substance use disorder.

Overall, persons with PTSD have AD at a rate four times higher than persons without PTSD (Kresler et al., 1995). The rate of having both of these disorders over a lifetime has been estimated as 1.59% (Blanco et al., 2013). It has also been found that having comorbid PTSD and AD was associated with worse outcomes than having either disorder alone.

PTSD AND ALCOHOL MISUSE

It is not hard to imagine that some sufferers of PTSD resort to alcohol to assuage their symptoms. In a longitudinal study of firefighters, PTSD diagnosis, not solely trauma exposure, increased the risk for developing alcohol abuse (Mcfarlane, 1998). There is also evidence from ecological momentary assessment (EMA) studies that emergent symptoms of PTSD, specifically negative affect-related symptoms, predicted subsequent alcohol drinking (Kaysen et al., 2014). Overall, a review and recent study on the literature showed that PTSD and alcohol use has bi-directional relationship (Read, Wardell, & Colder, 2013).

PTSD AND AGGRESSION

PTSD may be associated with increased aggression. PTSD in veterans has been found to be associated with both self and family member ratings of physical aggression (Van Voorhees et al., 2016). Among persons with PTSD, up to 7.5% (versus 2% of participants without PTSD) report being involved in a physical fight or serious trouble with the law over the past year (Corrigan & Watson, 2005). Other evidence has shown AD inpatients with co-occurring PTSD have higher aggression than inpatient ADs without PTSD (Sells et al., 2016).

In a sample of 1090 veterans of post-9/11 wars, PTSD and combat exposure were also associated with increased physical aggression and violence. However, when PTSD

and alcohol misuse were present, the rate of violence tripled. Furthermore, persons with PTSD without alcohol misuse were not significantly more prone to violence than participants without PTSD (Elbogen et al., 2014). The pathway they suggest to why aggression is elevated in PTSD in the presence of alcohol use was: “Use of alcohol could exacerbate PTSD hyperarousal symptoms such as anger...higher PTSD could lead to increasing use of alcohol...increase disinhibition” (Elbogen et al., 2014).

PTSD may be associated with aggression through multiple pathways. First, PTSD may promote alcohol use that in turn leads to aggression. Second, PTSD may promote aggression through a pathway that is independent of alcohol use. For example, PTSD may promote arousal (Aebi et al., 2017) and sleep disturbances (LaMotte et al., 2017) that may in turn increase aggression independently of alcohol. There is also evidence that hyperarousal symptoms of PTSD in particular result in increased aggression found in PTSD (Watkins et al., 2017; Aebi et al., 2017).

Few studies have examined the specific mechanisms of the relationships linking PTSD, alcohol dependence, and aggression. This is a focus of the current study. First, we wanted to confirm that aggression is indeed elevated in AD compared to control (i.e., non-AD) participants. Second, we sought to examine if the increased aggression we expected to find in participants with PTSD is mediated by AD severity.

CHAPTER 2: SPECIFIC AIMS

STUDY RATIONALE

The rationale for the study is as follows. First, as noted earlier, relatively few studies have examined the association between AD (or severity of AD) and aggression. In

addition, no study has examined this association in a U.S. sample. Therefore, the current study can contribute to this literature by examining whether an association is present in a U.S. sample.

Second, relatively few studies have examined the mechanisms linking PTSD, AD, and aggression. This study will examine whether the relationship between PTSD and aggression is mediated by severity of AD.

STUDY OVERVIEW

The current study will examine a large sample of inpatients with AD, non-treatment seeking ADs, and controls recruited from three screening protocols for the intramural program of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) at the National Institutes of Health's Clinic Center. Treatment-seeking participants with AD (henceforth referred to as Inpatient ADs), non-treatment-seeking participants with AD (henceforth referred to as Non-treatment seeking ADs), and a healthy control group (including social, light, and non-drinkers; henceforth referred to as Controls) were recruited to participate in NIAAA screening protocols to determine eligibility for clinical trials and human participant studies. Assessments included psychiatric interviews, aggression questionnaires, and assessments of alcohol dependence, severity of AD symptoms and alcohol consumption.

STUDY AIMS

Specific Aim 1

To examine if AD and AD severity are associated with aggression.

Hypothesis 1.1: Participants with AD will self-report greater levels of total aggression on the Buss-Perry Aggression Questionnaire than controls.

Hypothesis 1.2: Participants with AD will self-report higher levels of physical aggression, verbal aggression, hostility, and anger on the Buss-Perry Aggression Questionnaire than controls.

Hypothesis 1.3. Alcohol Dependence Symptoms assessed using the Alcohol Dependence Scale will be associated with greater aggression on the Buss-Perry Aggression Questionnaire.

Specific Aim 2

Alcohol dependence severity will mediate the relationship between PTSD and aggression within treatment-seeking AD participants (data on the AD severity was not available for a majority of the Non-treatment seeking ADs or Controls).

Hypothesis 2.1: In treatment-seeking AD participants, alcohol dependence severity will mediate the relationship between PTSD diagnosis and total aggression.

Hypothesis 2.2: In treatment-seeking AD participants, alcohol dependence severity will mediate the relationship between PTSD diagnosis and physical aggression.

CHAPTER 3: METHODS

Participants

Participants ($N=1218$) were recruited across the Washington, D.C. area at the NIAAA's Laboratory of Clinical and Translational Studies. NIAAA recruits healthy controls, non-treatment-seeking participants with AD, or participants seeking inpatient treatment for AD. All data for this study were collected during in-person screenings that occurred in the NIAAA's outpatient or inpatient clinics. The screening is used to determine if eligibility requirements are met before enrollment into experimental protocols. Several studies that recruited from the screening protocols have been published elsewhere (Schwandt et al., 2013, Spagnolo et al., 2014, Kwako et al., 2015a, Kwako et al., 2015, Lee et al., 2015; Sells et al., 2016).

Procedure

Participants were invited to an in-person screening visit after a phone screening. The phone screenings were conducted by research assistants or a social worker. The phone screening included assessments for daily drinking, medical history including current medications, psychiatric history, treatment-seeking status, and demographic variables. Participants were invited to the in-person screening visits based on inclusion/exclusion criteria for studies that were active at the time of the screening. Of note, criteria varied over time due to different protocols being active.

During the in-person screening, participants were assessed for medical conditions, psychiatric diagnosis, alcohol dependence, aggression, and other measures (see Table 2 for differences between non-treatment seeking and treatment-seeking protocols).

Visits for non-treatment seeking participants (with and without AD) lasted approximately 8 hours in an outpatient clinic of the NIAAA. During this visit, participants met with a research nurse to be screened for suicidality, psychopathology, and alcohol withdrawal (these data were not included in this study). Participants then completed self-report measures on a computer. A physical examination was also conducted to provide investigators with information on eligibility for future research participation. A structured psychiatric interview was also administered by a trained research assistant, nurse, or staff psychiatrist. Non-treatment-seeking ADs or controls were allowed to leave the clinic after the screening visit.

Similar procedures were followed for treatment-seeking participants with AD. However, in many cases detoxification was required before research assessments. Inpatients began the screening protocol during or after detoxification. Inpatients typically entered a treatment evaluation study or a clinical trial after screening.

Because of differences in protocols, certain questionnaires and measures were added to the screening protocols over time. Most pertinent here, the Alcohol Dependence Scale (ADS) was not administered for a majority of the Non-treatment seeking ADs or Controls.

Measures

Psychiatric Diagnosis

Each participant was given the Structured Clinical Interview for Axis I Disorders (SCID-I). This interview screened for Axis I Disorders based on DSM-IV-TR criteria (APA, 2000). This interview has good to excellent inter-rater reliability (Lobbestael, Leurgans, & Arntz, 2011). Each patient was given modules for substance, alcohol use,

anxiety, depressive, bipolar, psychosis, eating, body dysmorphic, post-traumatic stress, and obsessive compulsive disorders. The SCID was administered by nurses for inpatient ADs. The SCID was administered to Non-treatment-seeking ADs and Controls by trained research assistants. The diagnoses were verified by a licensed psychiatrist or clinical psychologist.

Alcohol Dependence Severity

The Alcohol Dependence Scale (ADS) is a 25-item self-report measure that assesses the AD severity as a continuous variable. The total score is then used to suggest treatment intensity based on the American Society of Addiction Medicine's treatment level (I-IV) recommendations for AD.

The ADS has been observed to have adequate reliability and validity in assessing AD in treatment-seeking populations (Doyle & Donovan, 2009). The ADS has a three-factor structure reflecting loss-of-control drinking, withdrawal, and obsessive-compulsive drinking (Doyle & Donovan, 2009).

The ADS also yields a total composite score ranging from 0-47. This total score can be used to guide treatment based on the American Society of Addiction Medicine's treatment placement criteria. Scores of 0 correspond to no evidence of alcohol dependence, scores of 1-13 correspond to low levels of alcohol dependence, 14-21 to intermediate level of alcohol dependence, 22-30 to substantial and physical dependence, and 31-47 to severe dependence with likely medical and psychiatric comorbidity. Each range maps on to a recommended intervention from advice to inpatient medical management of alcohol-related illnesses.

Aggression

Aggression was assessed using the Buss-Perry Aggression Questionnaire (BPAQ; Buss & Perry, 1992). The BPAQ measures total aggression and also includes four subscales of aggression: physical aggression, verbal aggression, hostility, and anger. The BPAQ has 29 items and asks participants to: “indicate how uncharacteristic or characteristic each of the following statements is in describing you” on a 5-point likert scale (Buss & Perry, 1992). Normative data are available from the authors (Buss & Perry, 1992). The Buss-Perry has been used extensively to assess aggression in psychopathology, including alcohol dependence (Gerevich et al., 2007; Bácskai et al., 2011; Bozkurt et al., 2013) (See Table 1). BPAQ has been shown to correlate with other measures of aggression including history of violence in federal offenders and aggression measured during laboratory-based tasks (Diamond, 2006; Miller, Parrott, & Giancola, 2009).

Drinks per day

Alcohol consumption was assessed with a 90-day computerized version of the Time Line Follow back (TLFB; Sobell & Sobell, 1992). The TLFB is a calendar form that asks participants to report their best estimate of the number of standardized drinks consumed in each of the previous 90 days. To maximize validity of the measure, a research assistant explained the quantity of a typical standard drink before the TLFB was administered. In addition, a key was available to participants throughout the task on how to calculate standardized drinks.

Demographic Variables

Age, gender, and race were obtained through computerized self-report questionnaires.

DATA ANALYSIS

SPSS version 20 was used for analyses. All tests used $\alpha = .05$ and were 2-tailed.

Three groups of patients were examined in the study: Controls; Non-treatment-seeking ADs; and Inpatient ADs. These groups were determined by their SCID diagnosis and the participant's decision to be volunteer for either a treatment-seeking or non-treatment seeking screening protocol at NIAAA.

To examine between-group differences in demographic variables, Pearson Chi Squared tests (categorical variables) or 1-way between-subject ANOVA (continuous variables) were used. Age, gender, and race were used as covariates in analyses testing study hypotheses due to chi-squared and ANOVA tests revealing significant differences between the three groups for these variables.

Hypothesis 1.1: Participants with AD will self-report greater levels of total aggression on the Buss-Perry Aggression Questionnaire than Controls.

To address Hypothesis 1.1, a one-way ANOVA was conducted with total aggression as the dependent variable and Group (3 levels: Controls, Non-treatment seeking ADs, and Inpatient ADs) as the independent variable. An ANCOVA, controlling for age, gender, and race was also performed due to significant differences in these variables between the three participant groups (Table 3; Controls, Non-treatment seeking ADs, and Inpatient ADs). In addition, ANCOVAs (controlling for age, gender, and race group) were performed for two planned contrasts: Controls vs. Non-treatment seeking ADs; Controls vs. Inpatient ADs.

Hypothesis 1.2: Participants with AD will self-report higher levels of physical aggression, verbal aggression, hostility, and anger on the Buss-Perry Aggression Questionnaire than Controls.

To address Hypothesis 1.2, the same methods as used above for Hypothesis 1.1 were used, with the exception that the dependent variable was scores on each of the four subscales (rather than the total score).

Hypothesis 1.3. Alcohol Dependence Symptoms assessed using the Alcohol Dependence Scale will be associated with higher aggression on the Buss-Perry Aggression Questionnaire.

To address Hypothesis 1.3, multiple linear regression was used. The dependent variable was overall aggression (BPAQ total score), and the primary independent variable was alcohol dependence severity (ADS score). Consistent with analyses for Hypotheses 1.1 and 1.2, age, gender, and race were included as covariates. These analyses used data from AD inpatients only, because the ADS was routinely administered to this group only.

Hypothesis 2.1: In treatment-seeking AD participants, alcohol dependence severity will mediate the relationship between PTSD diagnosis and total aggression.

For mediation analysis (Hypothesis 2.1) three separate methods were used to evaluate if ADS mediated the relationship between PTSD and Aggression in AD Inpatients: I) The causal steps approach described by Baron and Kenny (1986); II) Sobel's (1982) test of indirect effects; and III) The bootstrapping method to generate confidence intervals for the indirect effect. The Sobel and bootstrapping tests were conducted using software provided by Preacher and Leonardelli (2001) and Hayes (2015) respectively.

All mediation analysis included age, gender, and race as covariates. Race was coded using two dummy variables (Dummy variable 1: 0 = white, 1 = black, other race = 0; Dummy variable 2: 0 = white, 0 = black, 1 = other race). The Other race category

collapses the following racial groups: Multiracial, Native Hawaiian or Other Pacific Islander, Unknown Race Unanswered, American Indian/Alaska Native Asian. PTSD diagnosis was a binary variable (0 = no diagnosis, 1 = positive diagnosis). For Hypothesis 2.1, total aggression was the dependent variable.

For the Baron and Kenny (1986) method, simultaneous linear regressions were run. For the/se analyses, PTSD was designated as the independent variable, X, total aggression was the dependent variable, Y, and ADS score was the mediator, M. (As noted above, age, gender, and race were included as covariates in all models.) For the “c path,” termed the “total effect,” PTSD was entered as the predictor, and total aggression was the dependent variable. For the “a path,” PTSD diagnosis was entered as the predictor, and ADS was the dependent variable. For the “b path,” ADS and PTSD were entered as predictors, and total aggression was the dependent variable. For the “c’ path,” the “direct effect,” PTSD was evaluated when controlling for the mediator (ADS). The product of the a and b paths represents the indirect effect (a.b). The Baron and Kenny (1986) method is widely used, but is known to have relatively low power to detect total (c) and direct (c’) effects (Fritz & MacKinnon, 2007; A. F. Hayes, 2009).

The Sobel test estimates the magnitude of the indirect effect by using the product of the a and b coefficients (a.b). This product is then divided by an estimate of the standard error of a.b to yield a z statistic. The statistical significance of the z value is evaluated in the usual manner. The z statistic is limited by its inapplicability to cases where the sampling distribution of the indirect effect is non-normal, which is common.

Bootstrapping is a method to calculate a confidence interval for the indirect effect which takes into account non-normality of the sampling distribution of the indirect effect.

By resampling 5000 estimates of the indirect effect using the Hayes (2015) macro in SPSS, 95% confidence intervals for the indirect effect can be constructed. If the upper and lower confidence limits do not encompass 0, then the researcher can reject the null hypothesis that the indirect effect is equal to zero in the population.

Hypothesis 2.2: In treatment seeking AD participants, alcohol dependence severity will mediate the relationship between PTSD diagnosis and physical aggression.

The same methods as used for Hypothesis 2.1 were used, with the exception that physical aggression (rather than total aggression) will serve as the dependent variable.

\

CHAPTER 4: RESULTS

Demographic data are presented in Table 3. The breakdown of race within each of the three groups was: Controls (29.3% Black, 59.4% White, 11.1% Other), Non-treatment seeking ADs (76.7% Black, 16.7% White, 6.7% Other), and Inpatient ADs (39.1% Black, 52.7% White, 8.1% Other). The gender breakdown within each group was as follows: Controls (59.41% male, 40.59% female), Non-treatment seeking ADs (80.00% male, 20.00% female), and Inpatient ADs (69.42% male, 30.58% female). The average age for each group was: Controls (31.22), Non-treatment seeking ADs (42.21), and Inpatient ADs (42.98).

Chi-squared tests indicated that the three participant groups (Controls, non-treatment seeking ADs, inpatient ADs) differed in gender and race. A 1-way ANOVA indicated a significant age difference between the three groups. Therefore, these three demographic variables (age, gender, and race group) served as control variables for each ANCOVA result described below.

SPECIFIC AIM 1

Specific Aim 1 examined if AD and AD severity is associated with aggression.

Hypothesis 1.1 tested whether participants with AD self-reported greater levels of total aggression than Controls. In the omnibus ANOVA and ANCOVA, Buss-Perry total aggression scores were significantly different across groups (Table 3 & Figure 2).

Planned contrasts revealed that there was a significant effect for Group, $F(1, 680) = 69.675, p = .000, \eta_p^2 = 0.093$, where Non-treatment-seeking ADs reported higher total aggression scores than Controls. Inpatient ADs also reported higher total aggression scores than Controls, $F(1, 1033) = 219.881, p = .000, \eta_p^2 = 0.176$. When comparing Non-

treatment-seeking ADs to Inpatient ADs as an exploratory analysis, total aggression was higher in Inpatient ADs in comparison to Non-treatment seeking ADs, $F(1, 708) = 5.848$, $\eta_p^2 = 0.008$, $p = .016$.

Hypothesis 1.2 tested whether participants with AD self-report greater levels of aggression on the subscales of aggression (physical, verbal, hostility, and anger). Table 3 reports data from the omnibus ANOVA and ANCOVAs, revealing a significant difference between the three groups for each of the BPAQ subscales.

There were significant differences between Non-treatment-seeking ADs and Controls on the four Buss-Perry subscales: Physical Aggression, $F(1, 680) = 64.105$, $\eta_p^2 = 0.086$, $p < .001$ (Figure 3); Verbal Aggression, $F(1, 680) = 17.436$, $\eta_p^2 = 0.025$, $p < .001$ (Figure 4); Anger, $F(1, 680) = 56.654$, $\eta_p^2 = 0.077$, $p < .001$ (Figure 5); Hostility, $F(1, 680) = 45.463$, $\eta_p^2 = 0.063$, $p < .001$ (Figure 6).

Inpatient ADs were higher on each BPAQ subscale than Controls: Physical Aggression, $F(1, 1033) = 122.602$, $\eta_p^2 = 0.106$, $p < .001$ (Figure 3); Verbal Aggression, $F(1, 1033) = 44.778$, $\eta_p^2 = 0.042$, $p < .001$ (Figure 4); Anger, $F(1, 1033) = 183.190$, $\eta_p^2 = 0.151$, $p < .001$ (Figure 5); Hostility, $F(1, 1033) = 241.830$, $\eta_p^2 = 0.190$, $p < .001$ (Figure 6).

Each subscale was then compared between the AD groups (non-treatment seeking and inpatients) as exploratory analyses. Physical Aggression, $F(1, 708) = 0.0001$, $p = .972$ and Verbal Aggression, $F(1, 708) = 1.187$, $p = .276$, were not significantly different between the two AD groups. However, Anger, $F(1, 708) = 5.833$, $\eta_p^2 = 0.008$, $p = .016$, and Hostility, $F(1, 708) = 19.880$, $\eta_p^2 = 0.027$, $p < .001$, were significantly higher in the Inpatient AD group.

Hypothesis 1.3 tested whether ADS was associated with greater aggression in AD inpatients. Results reported in Table 5 show that higher ADS score is positively associated with both total aggression and physical aggression in inpatient ADs. As noted earlier, data from the non-treatment-seeking AD group and Controls were not analyzed due to the lack of ADS data in the non-treatment seeking AD and Controls.

SPECIFIC AIM 2

Specific Aim 2 examined whether Alcohol Dependence severity mediates the relationship between PTSD and aggression within the inpatient AD group.

Hypothesis 2.1: In treatment-seeking AD participants, alcohol dependence severity will mediate the relationship between PTSD diagnosis and total aggression.

For Total aggression (Hypothesis 2.1; Figure 7), the results were as follows. PTSD predicted total aggression (significant c path) (Tables 4. 5). PTSD also significantly predicted ADS (significant a path). ADS significantly predicted total aggression when controlling for PTSD (significant b path) (Table 5). PTSD continued to predict total aggression when controlling for ADS (significant c' path) (Table 5).

In sum, the a, b, c, and c' paths were all significant (Figure 7; see Table 5 for coefficients). The data suggest that ADS partially mediates the association between PTSD and total aggression.

The significance of the indirect effect (a.b) was also tested using the Sobel test. The Sobel test indicated a significant indirect effect for the total aggression: *Sobel Statistic* = 2.0586, *SE* = 0.514, *p* = 0.034. The bootstrapped 95% confidence interval for Total Aggression was [0.1650, 2.2533], also indicating a significant indirect path.

Hypothesis 2.2: In treatment-seeking AD participants, alcohol dependence severity will mediate the relationship between PTSD diagnosis and physical aggression.

For Physical aggression (Hypothesis 2.2, right side of Table 5), the results were as follows. PTSD predicted physical aggression (significant c path). PTSD also significantly predicted ADS (significant a path). ADS significantly predicted physical aggression when controlling for PTSD (significant b path). PTSD continued to predict physical aggression when controlling for ADS (significant c' path).

As above, the a, b, c, and c' paths were again all significant; the data suggested ADS partially mediates the association between PTSD and physical aggression.

The Sobel test for the indirect effect for Physical Aggression fell below the level of significance: *Sobel Statistic* = 1.761, *SE* = 0.130, *p* = .078. However, the confidence interval for indirect effect for the Physical Aggression model was significant (bootstrapped 95% CIs, 0.0375 to 0.5554), indicating a significant indirect effect.

CHAPTER 4: DISCUSSION

The main results of this study were as follows. First, alcohol dependence was associated with self-reported aggression. Individuals with AD reported higher level of self-reported aggression than those without AD. Moreover, within inpatients with AD, severity of alcohol dependence assessed with ADS scores was associated with self-reported aggression. Second, within inpatients with AD, severity of alcohol dependence partially mediated the association between PTSD and reported aggression. The results from each specific aim will be discussed in further detail below.

When evaluating Specific Aim 1, both Non-treatment-seeking and Inpatient AD groups had significantly higher Buss-Perry total scores than Controls. The results also showed that inpatient and non-treatment-seeking ADs were significantly higher on each component of aggression: physical aggression, verbal aggression, anger, and hostility. Furthermore, in the regression analysis, increased alcohol dependence symptoms as measured by the ADS were positively associated with increased Buss-Perry aggression scores in the inpatient AD group.

This study is the first study using a U.S. sample to find that AD is associated with self-reported aggression. This study also showed that non-treatment seeking AD participants reported more aggression than a control group without AD. Previous studies have only compared inpatient ADs to healthy controls (Table 1).

This study is the first to report that aggression is elevated in non-treatment seeking ADs, in addition to inpatient ADs. It is also worth pointing out that the effect of AD on aggression was still present even though the Controls in this study had a relatively high drinking level (on average over 3 drinks per day; see Table 3). Although no Control

participants were positive for AD on the SCID, the exact number of participants with some number of AD symptoms was not calculated for this study. Our results also indicated that as dependence severity increased in Inpatient ADs, aggression levels rose (Table 5). Thus, the association between AD/AD severity and aggression appears robust across multiple analyses.

The data revealed that the largest effect sizes for the association between AD and aggression were for anger and hostility, which is consistent with the results of a previous study (Gerevich, Bácskai & Czobor, 2007). This may be due to the greater sensitivity of anger and hostility, meaning that AD may affect these constructs more easily. It may also be because anger and hostility are more easily experienced than the observable behaviors of physical and verbal aggression.

The data do not reveal the direction of the relationships between AD/ADS and aggression due to the cross-sectional nature of the data. Alcohol dependence could cause aggression, or aggression could cause greater alcohol dependence. In addition, a third variable may underlie the association. For example, some models suggest there is a common genetic basis of externalizing behavior that includes both problematic alcohol consumption and aggression (Krueger et al., 2007). That is, more impulsive individuals may drink more and be prone to aggressive behavior.

Data from laboratory studies reviewed earlier - in which alcohol administration is manipulated as an independent variable - provide evidence that acute alcohol administration can cause increases in aggression as assessed by laboratory tasks, although most of this research has involved healthy social drinkers. More research is needed to identify these complex relationships. Specifically, more research is needed measuring

laboratory-measured aggression in participants with AD before and after administration of alcohol, which to this author's knowledge has not been investigated.

If AD does cause greater aggression, the data do not reveal why this occurs. A simple explanation could be that individuals with higher ADS scores experience a greater number or more severe episodes of intoxication; these episodes then would increase the risk of aggression. Unfortunately, the BPAQ does not inquire to when and where aggression occurs.

An alternative explanation is that aggression may be increased in AD by withdrawal or by affective changes due to chronic alcohol use. For example, brain regions compromised by alcohol dependence may disrupt behavioral control and executive functioning which results in increased aggression (Giancola & Corman, 2007). In addition, frequent symptoms of alcohol withdrawal may induce affective changes that contribute to increased irritability and aggression. In addition, alcohol dependence may lead to changes in participants' environments. For example, participants with AD may more frequently visit bars which offer more opportunity for violent (aggressive) encounters.

Data from laboratory tasks may be useful to examine associations between AD/ADS and aggression in greater detail. As noted earlier, currently there are sparse experimental data regarding laboratory measures of aggression within AD/AUD populations as compared to control subjects. For example, it is not known whether intoxicating doses of alcohol (e.g., 0.80 mg/dl) induce aggression in AD similar to what has been found for social drinkers (Giancola, 2002). In addition, it is not known whether severity of AD symptoms predicts aggression during laboratory paradigms such as the

TAP. Also relevant to this study is how laboratory aggression may differ between AD participants with PTSD and AD participants without PTSD. There also appear to be no experimental studies examining laboratory measures of aggression in PTSD.

In Specific Aim 2, it was hypothesized that within inpatient ADs, the association between PTSD and aggression would be mediated by severity of AD. There was support for this hypothesis: ADS partially mediated the relationship between PTSD and BPAQ total aggression scores. That is, there was evidence for both an indirect effect of PTSD on aggression as well as a direct effect (independent of alcohol use). Confidence in this finding was bolstered by the fact that it was observed in three different analysis types (causal steps, Sobel test, and bootstrapping method). For physical aggression, a significant effect was observed in two of the three methods.

The presence of the indirect effect begs the question of why PTSD is associated with (or causes) increased alcohol dependence. Some research suggests that individuals with PTSD self-medicate with alcohol (Leeies, Pagura, Sareen, & Bolton. 2010). For example, PTSD has been shown to precede alcohol dependence symptoms (Mcfarlane, 1998), consistent with our hypothesis in Specific Aim 2. It is also possible that some of the participants with PTSD may attempt to regulate problematic emotions such as anger and irritability through the anxiolytic effects of alcohol. An alternative possibility is that persons pre-disposed to experiencing traumatic events, and eventually suffering from PTSD, may be also susceptible to alcohol use problems. Given the cross-sectional nature of the present study, it is possible that PTSD may increase aggression independently of alcohol; this increase in aggression may in turn lead to alcohol misuse.

The results also indicated that within Inpatient ADs, PTSD had a direct effect on self-reported aggression that was independent of severity of alcohol dependence. This suggests that PTSD leads to aggression through mechanisms other than alcohol use, although this was only tested in Inpatient ADs. PTSD is associated with negative emotionality and may bring out changes in emotion regulation. Flashbacks and increased anxiety contribute to irritability, fear, and anger. Further, avoidance in PTSD may deplete emotional buffers such as social support; this depletion may ultimately result in antisocial behavior such as aggression. However, based on the previous data, hyperarousal symptoms are most predictive of aggression in PTSD (Watkins et al., 2017; Eabi et al., 2016). Given the relative lack of research for the specific mechanisms, more research is needed to determine the causal relationship between symptoms and subsequent aggression.

LIMITATIONS

The study had a number of limitations. First, the data were cross-sectional, which limits our ability to make statements on the causal relationships between PTSD, AD, and aggression. In particular, many researchers have noted the limitations of mediation analyses conducted on cross-sectional data, and cautioned that researchers should use longitudinal designs for testing mediation. As has been noted, the results of mediation analysis are only valid if the causal paths specified by the mediation models are correct. If the causal pathways specified by the model are not correct, then the path estimates are likely biased. For example, in the current study, if aggression causes changes in alcohol dependence (as well as vice versa), then the reported path estimates are not valid.

Moreover, some authors have argued that mediation analysis on cross-sectional data can produce biased path estimates even when the causal model is correctly specified.

For example, Maxwell & Cole (2007) suggest that use of cross-sectional data can lead to biased estimates of mediation in longitudinal data. More pertinent here, if significant indirect effect in a cross-sectional study were observed, this would not necessarily imply that a significant indirect effect would be observed in a longitudinal study (Maxwell & Cole, 2007). Therefore, results from the mediation analyses should be treated with caution pending replication in longitudinal datasets.

Second, the healthy control group used in the current study may not reflect the general population without AD. For example, the average drinks per day (see Table 3) were relatively high in our control group. The control group consisted of a large group of college students which may not have the typical drinking patterns of other control groups. There may also have been socioeconomic differences between the three groups which could not be controlled for that may have explained some of the differences found in aggression.

Third, the source, chronicity, and severity of PTSD was not assessed in this study. Hypothetically, greater severity and exposure to trauma may be related to increased aggression just as increased alcohol dependence is associated with greater aggression. The type of trauma may be important in regards to increased aggression (Sansone, Leung, & Wiederman, 2012). It is unknown whether combat-related, sexual abuse, or childhood abuse may have the most detrimental effects on aggression outcomes. This limitation also impairs our ability to identify which type of population (e.g., veterans, civilians) these results are most likely to generalize to. The research was completed at a major federal research hospital which may point to more civilian trauma histories, although this assumption cannot be verified.

Fourth, because individuals with PTSD will differ from those without PTSD in exposure to trauma, it is not clear whether the associations involving PTSD reflect PTSD or mere exposure to trauma. For example, being exposed to traumatic combat events could plausibly increase alcohol consumption and aggression even in the absence of PTSD. It is unclear if traumatic exposure alone leads to increased aggression. However, based on our data and other studies, PTSD diagnosis, is typically related to negative outcomes such as increased aggression.

Fifth, this study relied on a self-report measure of aggression and did not use a laboratory measure of aggression. Self-report measures may be susceptible to under-reporting, self-serving biases, and lack of agreement between different raters (Warnecke et al., 1997).

Last, DSM-IV diagnosis were used and may not reflect new diagnostic changes implemented through DSM-5 for AUD and PTSD. The mediation model may also reflect moderate to severe AUD but this was not able to be determined through the present study. However, DSM-IV diagnosis requires at least four symptoms to be met for diagnosis. In DSM-5, moderate AUD requires at least four symptoms while severe AUD requires at least six symptoms. The number of each symptom criteria being met could not be ascertained with the dataset used in this study.

STRENGTHS

The study also had strengths. First, a large sample size was used. The large sample sizes bolster confidence in our findings due to the increased statistical power of our analyses.

Second, the study also used several well-validated measures of aggression, psychiatric diagnosis, and alcohol dependence severity. In addition, the measure of

aggression (BPAQ) was the same scale used in several previous studies in this area, allowing for direct comparison of findings across studies (Table 1).

Third, the study used two groups of AD, which increases the generalizability of the findings from Specific Aim 1. In addition, the results for the comparison of each AD group to controls was similar, strengthening our hypothesis that aggression is elevated in AD across outpatient and inpatient contexts.

CONCLUSION

In this large cross-sectional study, participants with AD in both inpatient and non-treatment settings self-reported higher levels of aggression than healthy controls. This is the first study to report an association between AD and aggression in a U.S. sample. Within the inpatient subsample, the severity of AD was associated with higher aggression, and the severity of AD partially mediated this relationship between PTSD and aggression.

Some clinical implications may be derived from this study. Regarding assessment, the study suggests both PTSD and AD are independent risk factors for aggression, which may cause additional medical, social, and legal consequences for this population. Clinicians may also find it useful to use data on alcohol dependence severity to gauge risk for aggressive behavior as this study found as AD severity increased, aggression increased. Regarding therapy, treatment programs for dually diagnosed PTSD and AD may choose to incorporate anger management components, legal assistance, and additional relaxation strategies into their programs. For non-treatment-seeking ADs, information on the potentially harmful consequences of aggression may be used to enhance motivation for treatment during brief interventions.

FUTURE DIRECTIONS

As noted earlier, more experimental data using measures of laboratory aggression are needed. Experimental paradigms such as the TAP may be used to test the pharmacological dosages required for aggressive behavior to be elicited in AD. Persons with co-occurring AD and PTSD may be particularly sensitive to provocation. Second, other mechanisms linking PTSD and aggression should be further examined. Third, further research could test whether the association between severity of dependence and aggression is stronger in individuals with PTSD than without PTSD (i.e., a test of moderation). Finally, more data are required on the associations linking AD, aggression and distal violence outcomes.

Table 1. Literature Review: Aggression in Alcohol Dependence

Study	Aggression Measure	Normal/Control Group*	Alcohol Dependence*	Cohen's <i>d</i> *	Covariates	Notes
Mann et al., 1995	Freiburg Personality Inventory (FPI-R)	n>2000 5.0 (SD=2.0)	n=258 inpatients 4.94 (SD=1.71)	0.03 overall aggression	Gender and age	AD sample classified as “well adjusted”; covariates used to transform aggression raw score to “stanine” score.
Gerevich, Bácskai & Czobor, 2007	Buss-Perry (Hungarian)	n=1199	n=330 inpatients	0.66 PA 0.69 VA 1.05 A 1.21 H	Age, gender, and educational level (effect size not reported)	Buss-Perry total and raw scores not reported; effect size not reported for analysis with covariates although authors stated significant persisted
Bácskai, Czobor, & Gerevich, 2011	Buss-Perry (Hungarian version)	n=212 57.0 (13.0) 15.77 (0.47) 12.6 (0.23) 13.82 (0.35) 15.3 (0.36)	n=101 inpatients 81.7 (17.4) 23.04 (0.79) 15.47 (0.41) 21.77 (0.58) 22.56 (0.60)	1.61 Total Aggression 11.18 PA 8.63 VA 16.60 A 14.67 H	Age, gender, and educational level	Standard deviations may be incorrectly reported for subscales
Bozkurt et al., 2013	Buss-Perry Turkish version	n=63 30.56 (13.56) 6.6 (4.5) 7.24 (3.54) 8.18 (5.11) 8.54 (5.62)	n=94 inpatients 44.54 (20.72) 10.29 (6.56) 8.35 (4.10) 11.38 (6.57) 14.52 (6.98)	0.80 Total Aggression 0.66 PA 0.29 VA 0.54 A 0.94 H	None stated	N/A

Note. PA=Physical Aggression, VA=Verbal Aggression, A=Anger, H=Hostility; * Mean (standard deviation) and effect sizes reported vertically for Buss-Perry total score and PA, VA, A, H subscales. Hungarian and Turkish versions are adapted and not identical in scoring to English version.

Table 2. Assessments by Screening Protocol

Protocol	Non-treatment seeking (ADs and Controls)	Treatment Seeking (Inpatient ADs)
Duration	1-2 days	1-7 days
Computerized Assessments	Buss-Perry Questionnaire, Timeline Follow-Back, Demographics	Alcohol Dependence Scale*, Buss-Perry Questionnaire, Timeline Follow-back, Demographics
Interview Assessments	Structured Clinical Interview for Axis I Disorders	Structured Clinical Interview for Axis I Disorders
Treatment	None	Withdrawal medications, vitamin supplementation, psychotherapy
Other assessments not included in this thesis	Withdrawal, suicide assessment, NEO Personality Inventory, Intelligence Testing	

Note: *Alcohol Dependence Scale was collected on a small number of Non-treatment patients

Table 3: Summary Statistics for 3 Groups

Variable ↓	All		Controls	Non-Tx ADs	Inpatient ADs		H	F-Value ANOVA/ t/χ^2	df	p- value	Effect Size*	F-value ANCOVA	p-value ANCOVA
	N=1218		n=505	n=180	n=533								
Age	37.99 (11.83)		31.22 (9.86)	42.21 (11.99)	42.98 (10.25)			184.245	2, 1215	<0.001	0.233	n/a	n/a
Gender (%)								28.251	2	<0.001	0.152	n/a	n/a
Male	66.83		59.41	80.00	69.42								
Female	33.17		40.59	20.00	30.58								
Race (%)								127.543	4	<0.001	0.229	n/a	n/a
Black/AA	40.6		29.3	76.7	39.1								
White	50.2		59.6	16.7	52.7								
Other*	9.1		11.1	6.7	8.1								
PTSD (%)	10.76		0.99	5.55	21.76			122.532	2	<0.001	0.107	72.246	<0.001
Drinks per day	8.96 (7.68)		3.39 (2.21)	8.62 (5.46)	14.11 (7.95)			420.001	1, 1191	<0.001	0.374	354.337	<0.001
ADS	18.974 (8.90)		2.00 (2.36)	12.40 (7.26)	20.78 (7.83)			128.852	2, 616	<0.001	0.319	143.333	<0.001
Buss-Perry													
Total	65.26 (20.66)		55.97 (15.01)	70.32 (20.31)	72.36 (21.99)		1.1	102.562	2, 1215	<0.001	0.152	108.922	<0.001
PA	18.52 (7.66)		15.73 (5.67)	21.38 (7.77)	20.19 (8.41)		1.2	64.709	2, 1215	<0.001	0.100	67.534	<0.001
VA	13.54 (4.10)		12.81 (3.63)	13.97 (3.79)	14.09 (4.50)		1.2	14.240	2, 1215	<0.001	0.038	23.903	<0.001
H	18.93 (7.10)		15.57 (5.55)	19.67 (7.10)	21.86 (7.23)		1.2	123.646	2, 1215	<0.001	0.164	118.568	<0.001
A	14.27 (5.71)		11.86 (4.01)	15.31 (5.68)	16.21 (6.22)		1.2	90.681	2, 1215	<0.001	0.129	89.872	<0.001

Note. Data are Mean (SD) unless otherwise noted.; *H* = Hypothesis; *Partial eta square for ANOVAs; Cramers V for gender, depressive, & PTSD; Other Race Group included: Multiracial, Native Hawaiian or Other Pacific Islander, Unknown Race Unanswered, American Indian/Alaska Native Asian. PA = Physical Aggression, VA = Verbal Aggression, H = Hostility, A= Anger; ADS = Alcohol Dependence Scale: *N* as indicated in the table except for drinks per day with Controls =482, Non-Tx = 179, and ADs= 1194 and ADS with Controls = 38, Non-Tx =48, and ADs = 619

Table 4. Inpatient Alcohol Dependent Characteristics

Group→	All AD Inpatients		Inpatients with PTSD	Inpatients without PTSD
Variable↓	N=553		n=116	n=417
Age	42.98 (10.25)		40.92 (10.06)	43.55 (10.24)
Gender (%)				
Male	69.4		49.1	75.1
Female	30.6		50.9	24.9
Race (%)				
Black/AA	39.1		39.7	53.7
White	52.7		49.1	39.1
Other	8.1		11.2	7.2
ADS	20.78 (7.83)		22.80 (7.76)	20.21 (7.76)
PTSD (%)	21.8		100.0	0.0
Drinks/day	14.11 (7.95)		14.18 (7.62)	14.09 (8.05)
Buss-Perry				
Total	72.36 (21.99)		82.42 (23.66)	69.56 (20.68)
PA	20.19 (8.41)		22.66 (9.74)	19.50 (7.88)
VA	14.09 (4.50)		15.76 (4.75)	13.63 (4.33)
H	21.86 (7.23)		25.07 (6.99)	20.97 (7.05)
A	16.21 (6.22)		18.83 (6.59)	15.46 (5.91)

Note. Data are Mean (SD) unless otherwise noted.; AA = African American; Other Race Group included: Multiracial, Native Hawaiian or Other Pacific Islander, Unknown Race Unanswered, American Indian/Alaska Native Asian. PA = Physical Aggression, VA = Verbal Aggression, H = Hostility, A= Anger; ADS = Alcohol Dependence Scale

Table 5. Regression results for Mediation Models

IV↓	<i>H</i>	Path	<i>Total Aggression</i>							<i>H</i>	<i>Physical Aggression</i>					
			<i>df</i>	<i>B</i>	<i>Beta</i>	<i>SE</i>	<i>t</i>	<i>P</i>			<i>df</i>	<i>B</i>	<i>Beta</i>	<i>SE</i>	<i>t</i>	<i>p</i>
ADS	1.3	-	5, 527	0.634	0.226	0.117	5.430	<.001		1.3	5, 527	0.140	0.130	0.044	3.161	.002
ADS controlling for PTSD	2.1	b	6, 526	0.574	0.204	0.114	5.021	<.001		2.2	6, 526	0.124	0.116	.0440	2.828	.005
PTSD	2.1	c	5, 527	12.543	0.236	2.192	5.722	<.001		2.2	6, 527	3.229	0.129	0.831	3.887	<.001
PTSD controlling for ADS	2.1	c'	5, 527	11.486	0.216	2.154	5.333	<.001		2.2	6, 526	3.000	0.147	0.829	3.617	<.001

Note. All results presented controlled for age, gender, and Race; *H* = Hypothesis; a path for ADS regressed on PTSD (controlling for age, gender, & race): *B* =1.843, *SE*=0.817, *t*=2.256, *p*=.024.

	No PTSD	PTSD	
No AUD/SUD	828	32	860
AUD/SUD	132	8	140
	960	40	1000

Based on Petrakis, Gonzalez, Rosenheck, M.D., & Krystal (2002) and Petrakis et al (2011)

Figure 1. Diagram of the comorbidity between AUD/SUD and PTSD. Data are estimated counts (out of 1000) with and without PTSD and AUD/SUD

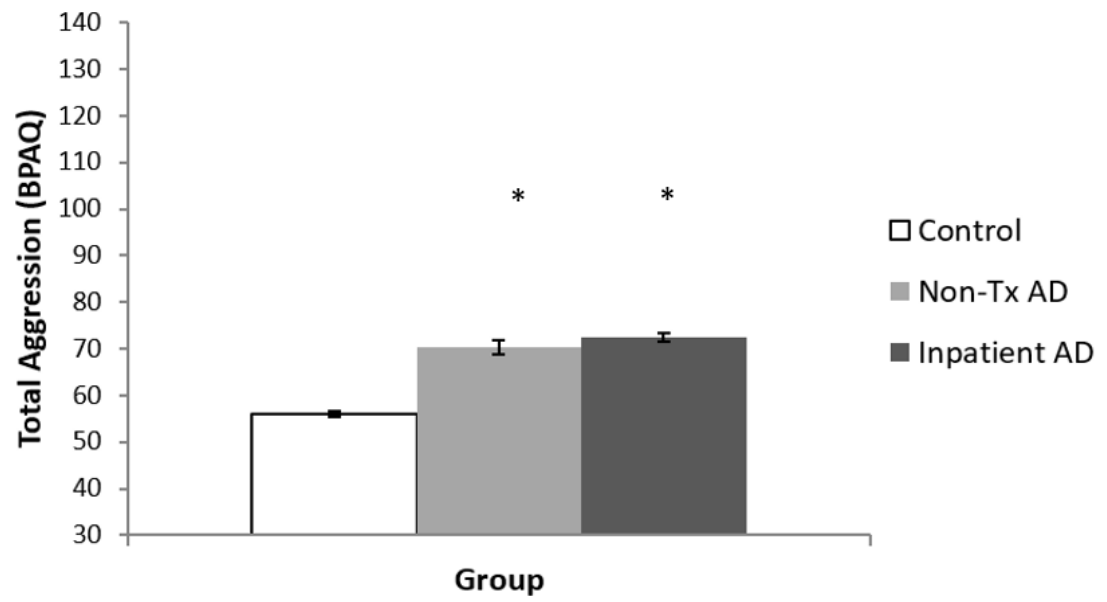


Figure 2. Specific Aim 1, Hypothesis 1.1 Results: Total Aggression; * p value < .01 vs. Control Group; ANCOVA

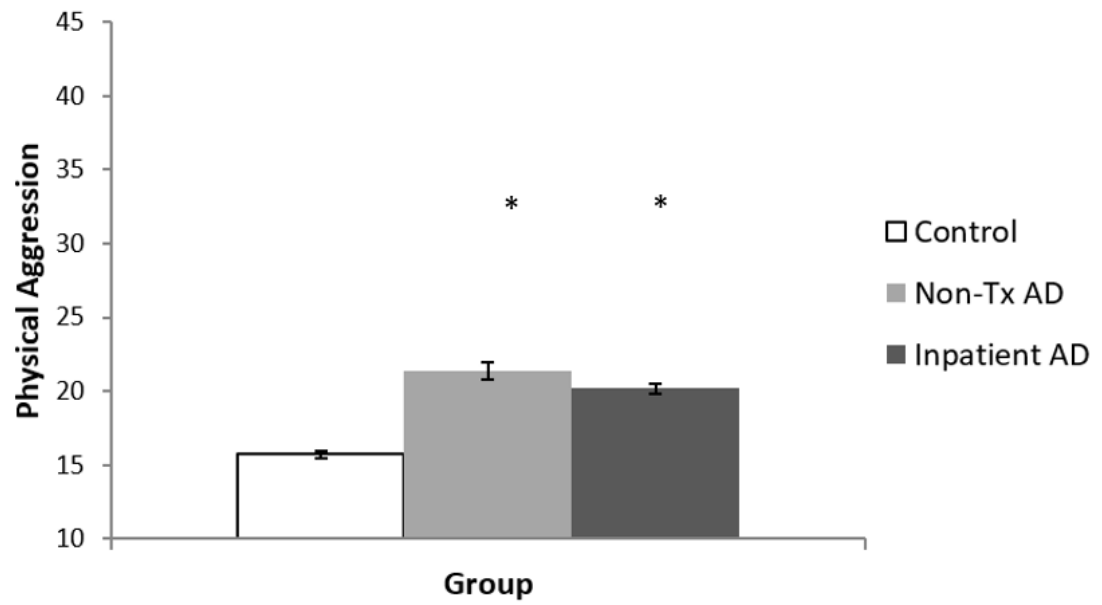


Figure 3. Specific Aim 1, Hypothesis 1.2 Results: Physical Aggression; * p value < .01 vs. Control Group; ANCOVA

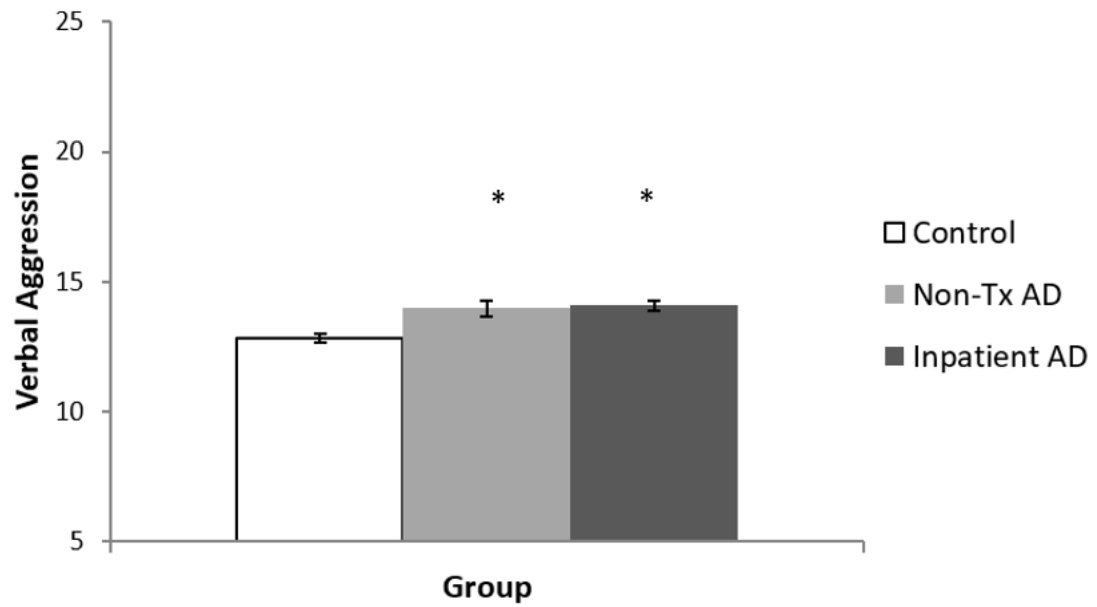


Figure 4. Specific Aim 1, Hypothesis 1.2 Results: Verbal Aggression; * p value < .01 vs. Control Group; ANCOVA

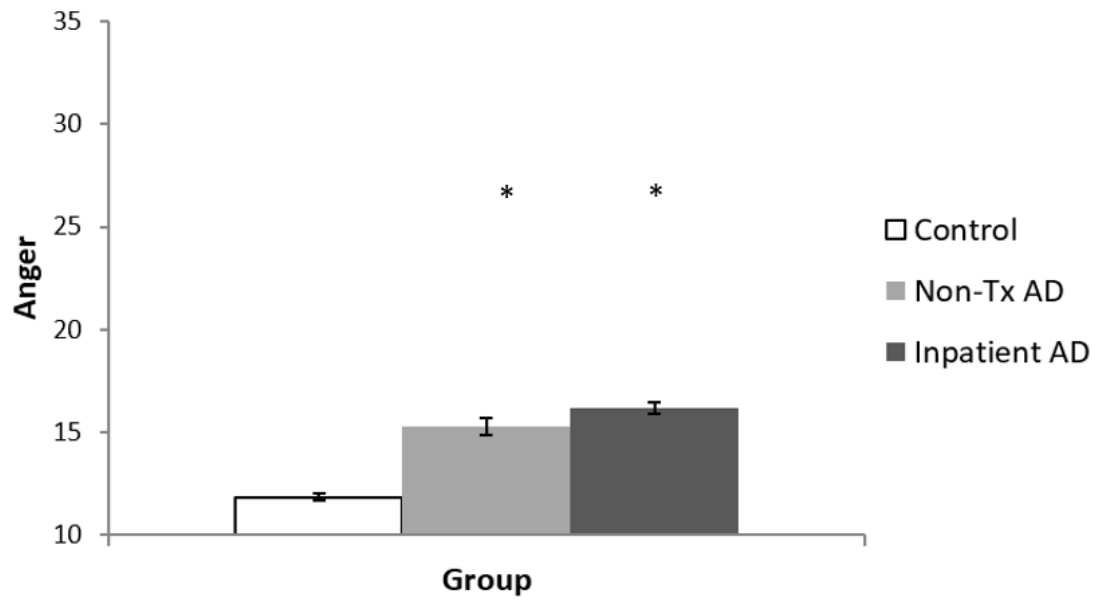


Figure 5. Specific Aim 1, Hypothesis 1.2 Results: Anger; * p value < .01 vs. Control Group; ANCOVA

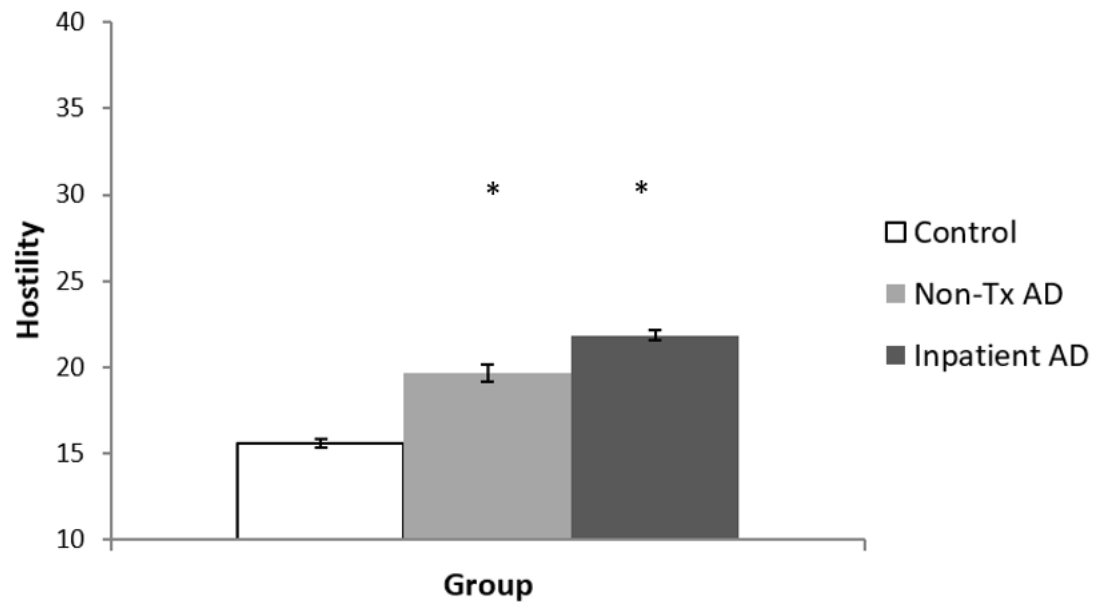


Figure 6. Specific Aim 1, Hypothesis 1.2 Results: Hostility * p value < .01 vs. Control Group; ANCOVA

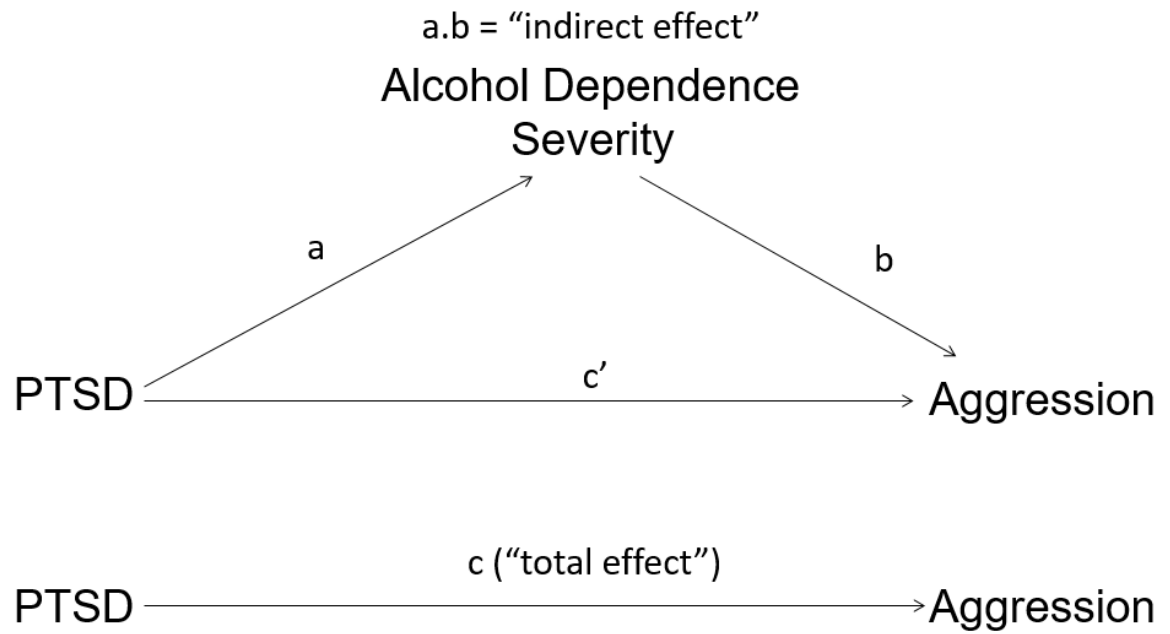


Figure 7. Mediation Model using Baron and Kenny's (1986) terminology; c = total effect; a.b = indirect path, c' =direct effect (unmediated path)

REFERENCES

- Abbey, A. (2011). Alcohol's role in sexual violence perpetration: Theoretical explanations, existing evidence and future directions. *Drug and Alcohol Review*, 30(5), 481-489. doi: 10.1111/j.1465-3362.2011.00296.x.
- Aebi, M., Mohler-Kuo, M., Barra, S., Schnyder, U., Maier, T., & Landolt, M. (2017). Posttraumatic stress and youth violence perpetration: A population-based cross-sectional study. *European Psychiatry*, 40, 88-95. doi:10.1016/j.eurpsy.2016.08.007
- Ali, B., Ryan, J. S., Beck, K. H., & Daughters, S. B. (2013). Trait Aggression and Problematic Alcohol Use Among College Students: The Moderating Effect of Distress Tolerance. *Alcohol Clin Exp Res Alcoholism: Clinical and Experimental Research*, 37(12), 2138-2144. doi:10.1111/acer.12198.
- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, D.C.
- American Psychiatric Association (2013) *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, D.C.
- Bácskai, E., Czobor, P., & Gerevich, J. (2008). Heavy Drinking as a Differential Predictor of Physical Aggression in Clinical and General Populations. *Progress in Neuropsychopharmacology and Biological Psychiatry*, 32(3), 668-72. Epub 2007 Nov 23.
- Bácskai, E., Czobor, P., & Gerevich, J. (2011). Gender differences in trait aggression in young adults with drug and alcohol dependence compared to the general population. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 35(5), 1333-1340. doi: 10.1016/j.pnpbp.2011.04.005. Epub 2011 Apr 22.
- Bala, S., Marcos, M., Gattu, A., Catalano, D., & Szabo, G. (2014). Acute Binge Drinking Increases Serum Endotoxin and Bacterial DNA Levels in Healthy Individuals. *PLoS ONE*, 9(5). doi: 10.1371/journal.pone.0096864. eCollection 2014.
- Barrett, E.L., Mills, K.L., Teesson, M. (2013). Mental Health Correlates of Anger in the General Population: Findings from the 2007 National Survey of Mental Health and Wellbeing. *Australian & New Zealand Journal of Psychiatry*, 47(5):470-6. doi: 10.1177/0004867413476752.
- Berenz, E. C., Roberson-Nay, R., Latendresse, S. J., Mezuk, B., Gardner, C. O., Amstadter, A. B., & York, T. P. (2016). Posttraumatic Stress Disorder and Alcohol Dependence: Epidemiology and Order of Onset. *Psychological Trauma: Theory, Research, Practice, and Policy*. doi:10.1037/tra0000185

- Buchholz, K. R., Bohnert, K. M., Sripada, R. K., Rauch, S. A., Epstein-Ngo, Q. M., & Chermack, S. T. (2017). Associations between PTSD and intimate partner and non-partner aggression among substance using veterans in specialty mental health. *Addictive Behaviors*, 64, 194-199. doi:10.1016/j.addbeh.2016.08.039
- Blanco C, Xu Y, Brady K, Perez-Fuentes G, Okuda M, Wang S. (2013). Comorbidity of posttraumatic stress disorder with alcohol dependence among US adults: results from National Epidemiological Survey on Alcohol and Related Conditions. *Drug Alcohol Depend.* 132:630-8
- Bilban, M., & Škibin, L. (2005). Presence of alcohol in suicide victims. *Forensic Science International*, 147(Supplement), S9-12.
- Bozkurt, M., Evren, C., Yilmaz, A., Can, Y., & Cetingok, S. (2013). Aggression and Impulsivity in Different Groups of Alcohol and Heroin Dependent Inpatient Men. *Bulletin of Clinical Psychopharmacology (BCP)*, 23(4), 335-44. doi: 10.5455/bcp.20130127021314
- Blonigen, D., Durbin, C., Hicks, B., Johnson, W., McGue, M., & Iacono, W. (2015). Alcohol Use Initiation is Associated with Changes in Personality Trait Trajectories from Early Adolescence to Young Adulthood. *Alcoholism: Clinical and Experimental Research*, 39(11), 2163-2170. doi: 10.1111/acer.12878. Epub 2015 Sep 30.
- Bloomfield, K., Stockwell, T., Gmel, G., & Rehn, N.(2003). International Comparisons of Alcohol Consumption. *Alcohol Research: Current Reviews*.
- Buss, A.H., & Perry, M. (1992). The Aggression Questionnaire. *Journal of Personality and Social Psychology*, 63, 452-459.
- Chermack, S., & Taylor, S. (1995). Alcohol and human physical aggression: Pharmacological versus expectancy effects. *J. Stud. Alcohol Journal of Studies on Alcohol*, 56(4), 449-456.
- Cohen, J. (1977). *Statistical power analysis for the behavioral sciences*. San Diego, CA: Academic Press.
- Coid J., Yang, M., Roberts, A., Ullrich, S., Moran, P., Bebbington, P., Brugha, T., Jenkins, R., Farrell, M., Lewis, G., & Singleton, N. (2006). Violence and Psychiatric Morbidity in a National Household Population--a Report from the British Household Survey. *American Journal Epidemiology*, 164(12):1199-208. Epub 2006 Oct 10.
- Corrigan, P.W. & Watson A.C. (2005). Findings from the National Comorbidity Survey on the frequency of violent behavior in individuals with psychiatric disorders *Psychiatry Research*, 136(2-3), 153-62.

- Crews, F., Sarkar, D., Qin, L., Zou, J., Boyadjieva, N., & Vetreno, R. (2015). Neuroimmune Function and the Consequences of Alcohol Exposure. *Alcohol Research: Current Reviews*, 37(2), 331-51.
- Diamond, P. M. (2006). The Short-Form Buss-Perry Aggression Questionnaire (BPAQ-SF): A Validation Study With Federal Offenders. *Assessment*, 13(3), 227-240. doi:10.1177/1073191106287666
- Elbogen, E.B., Johnson, S.C., Wagner, H.R., Sullivan C., Taft C.T., & Beckham J.C. (2014). Violent Behaviour and Post-traumatic Stress Disorder in US Iraq and Afghanistan Veterans. *British Journal of Psychiatry*, 204, 368-75. doi: 10.1192/bjp.bp.113.134627. Epub 2014 Feb 27.
- Elkins, I., King, S., McGue, M., & Iacono, W. (2006). Personality Traits and the Development of Nicotine, Alcohol, and Illicit Drug Disorders: Prospective Links From Adolescence to Young Adulthood. *Journal of Abnormal Psychology*, 115(1), 26-39.
- Falsstewart, W., & Kennedy, C. (2005). Addressing intimate partner violence in substance-abuse treatment. *Journal of Substance Abuse Treatment*, 29(1), 5-17.
- Fritz, M. S., & MacKinnon, D.P. (2007). Required sample size to detect the mediated effect. *Psychological Science*, 18(3), 233-239.
- Gao, B., & Bataller, R. (2011). Alcoholic Liver Disease: Pathogenesis and New Therapeutic Targets. *Gastroenterology*, 141(5), 1572-1585. doi: 10.1053/j.gastro.2011.09.002. Epub 2011 Sep 12.
- García-Forero, C., Gallardo-Pujol, D., Maydeu-Olivares, A., & Andrés-Pueyo, A. (2009). Disentangling impulsiveness, aggressiveness and impulsive aggression: An empirical approach using self-report measures. *Psychiatry Research*, 168(1), 40-49. doi: 10.1016/j.psychres.2008.04.002. Epub 2009 May 22.
- Gerevich, J., Bácskai, E., & Czobor, P. (2007). Aggression Levels in Treatment Seeking Inpatients With Alcohol-Related Problems Compared to Levels in the General Population in Hungary. *The Journal of Nervous and Mental Disease*, 195(8), 669-672.
- Giancola, P. R. (2002). Alcohol-related aggression in men and women: The influence of dispositional aggressivity. *Journal of Studies on Alcohol*, 63(6), 696-708. doi:10.15288/jsa.2002.63.696.
- Giancola, P.R. & Corman, M.D. (2007). Alcohol and aggression: a test of the attention-allocation model. *Psychological Science*, 18(7), 649-55.
- Giancola, P. R., Josephs, R. A., Dewall, C. N., & Gunn, R. L. (2009). Applying the

- Attention-Allocation Model to the Explanation of Alcohol-Related Aggression: Implications for Prevention. *Substance Use & Misuse*, 44(9-10), 1263-1279. doi:10.1080/10826080902960049
- Gillikin, C., Habib, L., Evces, M., Bradley, B., Ressler, K. J., & Sanders, J. (2016). Trauma exposure and PTSD symptoms associate with violence in inner city civilians. *Journal of Psychiatric Research*, 83, 1-7. doi:10.1016/j.jpsychires.2016.07.027
- Gobin, R.L., Green, K.E., Iverson, K.M. (2015). Alcohol Misuse Among Female Veterans: Exploring Associations With Interpersonal Violence and Mental Health. *Substance Use and Misuse*, 50(14), 1765-77. doi: 10.3109/10826084.2015.1037398. Epub 2015 Dec 7.
- Grant, B., Goldstein, R., Saha, T., Chou, S., Jung, J., Zhang, H., . . . Hasin, D. (2015). Epidemiology of DSM-5 Alcohol Use Disorder. *JAMA Psychiatry*, 72(8), 757-66. doi: 10.1001/jamapsychiatry.2015.0584.
- Hasin, D., Stinson, F., Ogburn, E., & Grant, B. (2007). Prevalence, Correlates, Disability, and Comorbidity of DSM-IV Alcohol Abuse and Dependence in the United States. *Archives of General Psychiatry*, 64(7), 830-42.
- Hayes, A. F. (2009) Beyond Baron and Kenny: Statistical mediation analysis in the new millennium. *Communication Monographs*, 76(4),408-420.
- Hayes, A. F. (2015). An Index and Test of Linear Moderated Mediation. *Multivariate Behavioral Research*, 50 (1), 1-22. doi: 10.1080/00273171.2014.962683.
- Huang, B., White, H., Kosterman, R., Catalano, R., & Hawkins, J. (2001). Developmental Associations Between Alcohol and Interpersonal Aggression During Adolescence. *Journal of Research in Crime and Delinquency*, 38(1), 64-83. doi: 10.1007/s10508-007-9309-6. Epub 2008 Feb 20.
- Kaysen, D., Atkins, D. C., Simpson, T. L., Stappenbeck, C. A., Blayney, J. A., Lee, C. M., & Larimer, M. E. (2014). Proximal relationships between PTSD symptoms and drinking among female college students: Results from a daily monitoring study. *Psychology of Addictive Behaviors*, 28(1), 62-73. doi:10.1037/a0033588
- Kose, S., Steinberg, J. L., Moeller, F. G., Gowin, J. L., Zuniga, E., Kamdar, Z. N., . . . Lane, S. D. (2015). Neural correlates of impulsive aggressive behavior in subjects with a history of alcohol dependence. *Behavioral Neuroscience*, 129(2), 183-196. doi: 10.1037/bne0000038.
- Kessler, R.C., Sonnega, A., Bromet, E., Hughes, M., Nelson, C.B. (1995). Posttraumatic stress disorder in the National Comorbidity Survey. *Arch. Gen. Psychiatry* 52, 1048-60

- Koob, G.F. & LeMoal, M. (1997). Drug abuse: hedonic homeostatic dysregulation. *Science*, 278(5335), 52-8.
- Krueger, R. F., Markon, K. E., Patrick, C. J., Benning, S. D., & Kramer, M. D. (2007). Linking antisocial behavior, substance use, and personality: An integrative quantitative model of the adult externalizing spectrum. *Journal of Abnormal Psychology*, 116(4), 645-666.
- Kwako, L., Spagnolo, P., Schwandt, M., Thorsell, A., George, D., Momenan, R., . . . Heilig, M. (2015a). The Corticotropin Releasing Hormone-1 (CRH1) Receptor Antagonist Pexacerfont in Alcohol Dependence: A Randomized Controlled Experimental Medicine Study. *Neuropsychopharmacology*, 40(5), 1053-1063. doi: 10.1038/npp.2014.306.
- Kwako, L. E., George, D. T., Schwandt, M. L., Spagnolo, P. A., Momenan, R., Hommer, D. W., . . . Heilig, M. (2014b). The neurokinin-1 receptor antagonist aprepitant in co-morbid alcohol dependence and posttraumatic stress disorder: A human experimental study. *Psychopharmacology*, 232(1), 295-304. doi: 10.1007/s00213-014-3665-4.
- Lamotte, A. D., Taft, C. T., Weatherill, R. P., Casement, M. D., Creech, S. K., Milberg, W. P., . . . McGlinchey, R. E. (2017). Sleep problems and physical pain as moderators of the relationship between PTSD symptoms and aggression in returning veterans. *Psychological Trauma: Theory, Research, Practice, and Policy*, 9(1), 113-116. doi:10.1037/tra0000178
- Lau, M., Pihl, R., & Peterson, J. (1995). Provocation, Acute alcohol intoxication, Cognitive performance, and Aggression. *Journal of Abnormal Psychology*, 104(1), 150-155.
- Lee, M., Schwandt, M., Bollinger, J., Dias, A., Oot, E., Goldman, D., . . . Leggio, L. (2015). Effect of Functionally Significant Deiodinase Single Nucleotide Polymorphisms on Drinking Behavior in Alcohol Dependence: An Exploratory Investigation. *Alcoholism: Clinical and Experimental Research*, 39(9), 1665-1670. doi: 10.1111/acer.12814. Epub 2015 Jul 24.
- Leeies M, Pagura J, Sareen J, Bolton JM. 2010. The use of alcohol and drugs to self-medicate symptoms of posttraumatic stress disorder. *Depress. Anxiety* 27:731-6
- Lobbetael, J., Leurgans, M., & Arntz, A. (2011). Inter-rater reliability of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I) and Axis II Disorders (SCID II). *Clinical Psychology & Psychotherapy*, 18(1), 75-79. doi: 10.1002/cpp.693.
- Maldonado-Molina, M., Reingle, J., & Jennings, W. (2010). Does Alcohol Use Predict Violent Behaviors? The Relationship Between Alcohol Use and Violence in a

- Nationally Representative Longitudinal Sample. *Youth Violence and Juvenile Justice*, 9(2), 99-111.
- Mann, K., Ackermann, K., Jung, M., Morlock, P., & Mundle, G. (1998). Aggressiveness, Onset Of Dependence, And Treatment Outcome In Socially Well-Adapted Alcoholics. *Alcohol and Alcoholism*, 33(1), 16-19.
- Mcfarlane, A.C. (1998). Epidemiological Evidence about the Relationship between PTSD and Alcohol Abuse: The Nature of the Association. *Addictive Behaviors*, 23(6), 813–825. doi:10.1016/S0306-4603(98)00098-7.
- Miller, T., Levy, D., Cohen, M., & Cox, K. (2006). Costs of Alcohol and Drug-Involved Crime. *Prevention Science*, 7(4), 333-342.
- Miller, C. A., Parrott, D. J., & Giancola, P. R. (2009). Agreeableness and alcohol-related aggression: The mediating effect of trait aggressivity. *Experimental and Clinical Psychopharmacology*, 17(6), 445-455. doi: 10.1037/a0017727.
- National Institute on Alcohol Abuse and Alcoholism. (1997). Alcohol, Violence, and Aggression. *Alcohol Alert*, 38.
- Newberry, M., Williams, N., & Caulfield L. (2013). Female Alcohol Consumption, Motivations for Aggression and Aggressive Incidents in Licensed Premises. *Addictive Behaviors*, 38(3), 1844-51. doi: 10.1016/j.addbeh.2012.08.009.
- Nordløyken, A., Pape, H., & Heir, T. (2016). Alcohol consumption in the aftermath of a natural disaster: a longitudinal study. *Public Health*, 132, 33-39. doi:10.1016/j.puhe.2015.11.007
- Patton, J., Stanford M., and Barratt E. (1995) Factor structure of the Barratt impulsiveness scale. *Journal of Clinical Psychology*, 51, 768-774.
- Parrott, D. J., & Giancola, P. R. (2006). The Effect of Past-year Heavy Drinking on Alcohol-related Aggression. *J. Stud. Alcohol Journal of Studies on Alcohol*, 67(1), 122-130. doi:10.15288/jsa.2006.67.122.
- Parrott, D. J. & Giancola, P. R. (2011) Alcohol Dependence and Physical Aggression: the Mediating Effect of Dispositional Impulsivity. *Journal of Drug Addiction, Education, and Eradication*, 7(4), 315-332.
- Petrakis, I.L., Gonzalez, G., Rosenheck, R., & Krystal, J.H.. (2002). Comorbidity of Alcoholism and Psychiatric Disorders An Overview *Alcohol Research: Current Reviews*, 26(2), 81-89
- Petrakis, I. L., Rosenheck, R., & Desai, R. (2011). Substance Use Comorbidity

- among Veterans with Posttraumatic Stress Disorder and Other Psychiatric Illness. *The American Journal on Addictions*, 20(3), 185-189. doi:10.1111/j.1521-0391.2011.00126.x
- Possemato, K., Maisto, S. A., Wade, M., Barrie, K., Mckenzie, S., Lantinga, L. J., & Ouimette, P. (2015). Ecological momentary assessment of PTSD symptoms and alcohol use in combat veterans. *Psychology of Addictive Behaviors*, 29(4), 894-905. doi:10.1037/adb0000129
- Preacher, K., & Leonardelli, G. (2003). Calculation for the Sobel test: An Interactive Calculation Tool for Mediation tests. Retrieved August 31, 2016 from <http://quantpsy.org/sobel/sobel.htm>
- Sacks, J., Gonzales, K., Bouchery, E., Tomedi, L., & Brewer, R. (2015). 2010 National and State Costs of Excessive Alcohol Consumption. *American Journal of Preventive Medicine*, 49(5), E73-E79. doi: 10.1016/j.amepre.2015.05.031. Epub 2015 Oct 1.
- Sansone, R.A., Leung, J.S., & Wiederman, M.W. (2012). Five Forms of Childhood Trauma: Relationships With Aggressive Behavior in Adulthood. *Primary Care Companion for CNS Disorders*, 14(5). doi: 10.4088/PCC.12m01353
- Schwandt, M., Heilig, M., Hommer, D., George, D., & Ramchandani, V. (2013). Childhood Trauma Exposure and Alcohol Dependence Severity in Adulthood: Mediation by Emotional Abuse Severity and Neuroticism. *Alcoholism: Clinical and Experimental Research*, 37(6), 984-992. doi: 10.1111/acer.12053. Epub 2012 Dec 27.
- Sells, J.R., Waters, A.J, Schwandt, M.L., Kwako, L.E., Heilig, M., George, D.T., Ramchandani, V.A. (2016). Characterization of comorbid PTSD in treatment-seeking alcohol dependent inpatients: Severity and personality trait differences. *Drug and Alcohol Dependence*, 163, 242-6. doi: 10.1016/j.drugalcdep.2016.03.016.
- Seo, D., Patrick, C.J., & Kennealy, P.J. (2008). Role of Serotonin and Dopamine System Interactions in the Neurobiology of Impulsive Aggression and its Comorbidity with other Clinical Disorders. *Aggression and Violent Behavior*, 13(5), 383-395.
- Skara, S., Pokhrel, P., Weiner, M., Sun, P., Dent, C., & Sussman, S. (2008). Physical and Relational Aggression as Predictors of Drug Use: Gender Differences among High School Students. *Addictive Behaviors*, 33(12), 1507-1515. doi: 10.1016/j.addbeh.2008.05.014. Epub 2008 Jun 17.
- Sobell, L.C. & Sobell, M.B. (1992). *Timeline Follow-back: A Technique for Assessing Self-reported Ethanol Consumption*. In J. Allen & R. Z. Litten (Eds.), *Measuring Alcohol Consumption: Psychosocial and Biological Methods* (pp. 41-72). Totowa, NJ: Humana Press.

- Spagnolo, P., Ramchandani, V., Schwandt, M., Zhang, L., Blaine, S., Usala, J., . . . Heilig, M. (2014). Effects of Naltrexone on Neural and Subjective Response to Alcohol in Treatment-Seeking Alcohol-Dependent Patients. *Alcoholism: Clinical and Experimental Research*, 38(12), 3024-3032. doi: 10.1111/acer.12581.
- Substance Abuse and Mental Health Services Administration (2012). *National Survey on Drug Use and Health (NSDUH)*.
- Taylor, S. (1967). Aggressive behavior and physiological arousal as a function of provocation and the tendency to inhibit aggression. *Journal of Personality*, 35, 297-310.
- Thomson, A., Guerrini, I., & Marshall, E. (2012). The Evolution and Treatment of Korsakoff's Syndrome: out of sight, out of mind?. *Neuropsychology Review*, 22(2), 81-92. doi: 10.1007/s11065-012-9196-z.
- Tremblaya, P. F. & Ewartb, L.A. (2005). The Buss and Perry Aggression Questionnaire and its Relations to Values, the Big Five, Provoking Hypothetical Situations, Alcohol Consumption Patterns, and Alcohol Expectancies. *Personality and Individual Differences*, 38(2), 337–346. doi: 10.1016/j.paid.2004.04.012.
- Read, J. P., Colder, C. R., Merrill, J. E., Ouimette, P., White, J., & Swartout, A. (2012). Trauma and posttraumatic stress symptoms predict alcohol and other drug consequence trajectories in the first year of college. *Journal of Consulting and Clinical Psychology*, 80(3), 426-439. doi:10.1037/a0028210'
- Read, J.P., Wardell, J.D., & Colder, C.R.. (2013). Reciprocal associations between PTSD symptoms and alcohol involvement in college: a three-year trait-state-error analysis. *Journal of Abnormal Psychology*, 122(4),984-97. doi: 10.1037/a0034918.
- Reulbach, U., Biermann, T., Bleich, S., Hillemacher, T., Kornhuber, J., & Sperling, W. (2006). Alcoholism And Homicide With Respect To The Classification Systems Of Lesch And Cloninger. *Alcohol and Alcoholism*, 42(2), 103-107. doi: 10.1093/alcalc/agl098.
- Van Voorhees, E.E., Dennis, P.A., Neal, L.C., Hicks, T.A., Calhoun, P.S., Beckham, J.C., & Elbogen, E.B. (2016) Posttraumatic Stress Disorder, Hostile Cognitions, and Aggression in Iraq/Afghanistan Era Veterans. *Psychiatry*. 79(1):70-84. doi: 10.1080/00332747.2015.1123593.
- Watkins, L. E., Sippel, L. M., Pietrzak, R. H., Hoff, R., & Harpaz-Rotem, I. (2017). Co-occurring aggression and suicide attempt among veterans entering residential treatment for PTSD: The role of PTSD symptom clusters and alcohol misuse. *Journal of Psychiatric Research*, 87, 8-14. doi:10.1016/j.jpsychires.2016.12.009

- Warnecke, R.B., Johnson, T.P., Chavez, N., Sudman, S., O'Rourke, D.P., Lacey, L., & Horm, J. (1997). Improving question wording in surveys of culturally diverse populations. *Annals of Epidemiology*, 7, 334-342
- White, H., Brick, J., & Hansell, S. (1993). A Longitudinal Investigation of Alcohol Use and Aggression in Adolescence. *Journal of Studies on Alcohol, Supplement*, 11, 62-77.
- White, H., & Hansell, S. (1998). Acute and Long-Term Effects of Drug Use on Aggression from Adolescence into Adulthood. *Journal of Drug Issues*, 28(4), 837-858.
- Wieczorek, W., Welte, J., & Abel, E. (1990). Alcohol, drugs and murder: A study of convicted homicide offenders. *Journal of Criminal Justice*, 18(3), 217-227.
- World Health Organization (2006). *Interpersonal Violence and Alcohol*. WHO Policy Briefing.
- World Health Organization (2014). *Global status report on alcohol and health 2014*. Retrieved July 27, 2017, from http://www.who.int/substance_abuse/publications/global_alcohol_report/en/
- World Health Organization (2015) *Alcohol Fact Sheet*. Retrieved January 12, 2016, from <http://www.who.int/mediacentre/factsheets/fs349/en/>.
- World Health Organization (n.d.) *Intimate Partner Violence and Alcohol*. Retrieved January 12, 2016, from http://www.who.int/violence_injury_prevention/violence/world_report/factsheets/fs_intimate.pdf
- Xue, Y., Zimmerman, M., & Cunningham, R. (2009). Relationship Between Alcohol Use and Violent Behavior Among Urban African American Youths From Adolescence to Emerging Adulthood: A Longitudinal Study. *American Journal of Public Health*, 99(11), 2041-2048. doi: 10.2105/AJPH.2008.147827. Epub 2009 Sep 17.
- Young, R., Sweeting, H., & West, P. (2008). A Longitudinal Study of Alcohol Use and Antisocial Behaviour in Young People. *Alcohol and Alcoholism*, 43(2), 204-214.