ALCOHOL DEPENDENCE AND PTSD: DIFFERENCES IN CLINICAL PRESENTATION AND RESPONSE TO COGNITIVE-BEHAVIORAL SUBSTANCE USE THERAPY BY ORDER OF ONSET

by

SUDIE E. BACK

(Under the Direction of Joan L. Jackson)

ABSTRACT

Alcohol dependence (AD) and posttraumatic stress disorder (PTSD) frequently co-occur. However, little is known about the importance of their temporal order of onset. In this study, differences in clinical presentation and response to cognitive-behavioral substance use therapy by order of onset were examined among 94 (51 men, 43 women) treatment-seeking individuals with AD and comorbid PTSD. Participants were interviewed, completed a battery of assessments, and received 12 weeks of individual, manualized psychotherapy. The findings revealed that women were more likely than men to have primary PTSD (i.e., the onset of PTSD preceded the onset of AD). At treatment entry, women with primary AD and men with primary PTSD presented as more distressed and/or depressed, as compared to their counterparts. Individuals with primary PTSD reported a more extensive trauma history than individuals with primary AD. Examination of treatment response revealed that the majority of individuals in the study demonstrated significant improvements in PTSD and AD symptomatology. A relationship between increased alcohol intake and higher PTSD symptom levels was observed. In general, the primary PTSD group appeared to derive greater overall benefit from this form of therapy (e.g., greater improvement in physical health, alcohol use, social functioning), as compared to the primary AD group. Finally, women with primary

AD appeared particularly vulnerable to continued psychiatric distress and depression at the end of treatment. These findings increase awareness of the importance of considering the order of onset, the heterogeneity among this dual diagnosis, and may ultimately lead to improvements in treatment design.

INDEX WORDS: Alcohol dependence, PTSD, posttraumatic stress disorder, cognitive-behavioral therapy, order of onset, comorbidity, dual diagnosis

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DEDICATION

To my mentors, Drs. Hilary Lips, Bonnie Dansky, Kathleen Brady, and Joan Jackson And to my husband, Stephen Caskie

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CHAPTER 1 INTRODUCTION

Alcohol dependence and posttraumatic stress disorder (PTSD) frequently cooccur. This comorbidity is associated with a more severe clinical presentation, poorer prognosis, and poorer treatment outcome when compared to individuals with either alcohol dependence or PTSD alone. Despite this, little is known about how to best treat individuals with alcohol dependence and PTSD. Historically, treatment and research centers for substance abuse and trauma/PTSD have been mutually exclusive organizations (Brown & Ouimette, 1999). Until recently, many substance use treatment centers did not even assess for trauma history or PTSD (Bollerud, 1990; Hien, Nunes, Levin, & Fraser, 2000; Najavits, Weiss, & Shaw, 1997). Clinical lore held that patients with this dual diagnosis should first receive treatment for their addiction and then receive treatment for their trauma and PTSD symptoms (Najavits, 2003). Today, the majority of clinicians and researchers encourage the implementation of integrated, comprehensive treatments for individuals with alcohol dependence and PTSD whereby both disorders are targeted concurrently in therapy. However, beyond this point of agreement, there is little guidance for how to best treat both disorders.

Patients with comorbid alcohol dependence and PTSD represent a heterogeneous group. Attempts to identify subgroups of differential responders to treatment would be useful. Some authors have suggested that therapy for individuals with alcohol dependence and PTSD might be improved by matching the treatment focus with the order of onset (Deykin & Buka, 1997). Thus, individuals presenting with *primary alcohol dependence* (i.e., the alcohol dependence developed prior to the PTSD) might benefit

most from treatment focused on the addiction, whereas individuals presenting with *primary PTSD* (i.e., the PTSD developed before the alcohol dependence) might benefit most from trauma-focused treatment. This idea has not yet been empirically tested.

The current study is designed to help shed light on this theoretically and clinically meaningful question. The goal of the current study is to help determine the clinical utility of classifying patients with comorbid alcohol dependence and PTSD by order of onset. Specifically, this study will examine differences in clinical presentation and response to cognitive-behavioral substance use therapy by temporal order of onset. Such information may help identify subgroups in need of particular preventative efforts, and allow clinicians to better structure therapeutic efforts, ultimately leading to improvements in the treatment of individuals with comorbid alcohol dependence and PTSD.

The following review of the literature will provide an overview of 1) epidemiologic data on the co-occurrence of alcohol dependence and PTSD, 2) characteristics associated with PTSD/Substance Use Disorder (SUD) comorbidity, 3) etiology of PTSD/SUD comorbidity, 4) data on the order of onset of PTSD and SUDs, 5) research on the order of onset among individuals with SUDs and other comorbid Axis I disorders, and 6) issues regarding sequential and concurrent treatment. Next, the goals and implications of the current study will be reviewed, followed by the hypothesis, method, and plan for statistical analyses. Demographic characteristics of the sample will be provided in a table following this review, as well.

Regarding the epidemiology of PTSD/SUD comorbidity, the extant literature contains findings that are most often obtained by examining 1) the prevalence of PTSD among individuals with SUDs and 2) the prevalence of SUDs among individuals with PTSD. Thus, the following two sections on epidemiology are structured in a manner that reflects this approach.

PTSD Among Individuals with Alcohol Use Disorders

Alcohol dependence is one of the most common psychiatric disorders, second only to major depression (Kessler et al., 1994). Data from the National Comorbidity Study (NCS; Kessler et al., 1994; Kessler et al., 1997) and the NIMH Epidemiologic Catchment Area program (ECA; Regier et al., 1990) reveal that approximately 14% of the general population has a lifetime history of alcohol dependence. Furthermore, alcohol dependence is the most common substance use disorder, occurring about twice as often as other drug use disorders (Kessler et al., 1994; Regier et al., 1990).

Alcohol dependence is characterized in the Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994) by a cluster of cognitive, behavioral and physiological symptoms that indicate impaired control over alcohol consumption. Individuals with alcohol dependence may experience *tolerance* (i.e., need for greater amounts of the substance to achieve intoxication, or a diminished effect with the same amount of the substance); *withdrawal* (i.e., physiological and/or cognitive changes that occur when blood alcohol concentrations decrease rapidly (e.g., within 4-12 hours) after the cessation of alcohol intake; or the use of the substance to avoid experiencing or to relieve withdrawal symptoms); or display a pattern of *compulsive use* (e.g., intake greater amounts than were intended; unsuccessful attempts to quit or cut down; spent a great deal of time obtaining, using, or recovering from the effects of alcohol; continued use despite knowledge of the problems caused or exacerbated by alcohol use).

Of individuals with a history of alcohol dependence, the majority of men (78.3%) and women (86.0%) meet criteria for at least one other psychiatric disorder (Kessler et al., 1997). Common among individuals with alcohol dependence is PTSD. PTSD, a psychiatric disorder which may develop following exposure to extreme stress, is characterized in the DSM-IV by three symptom clusters: 1) *reexperiencing* the stressor (e.g., intrusive recollections, dreams), 2) persistent *avoidance* of stimuli associated with

the stressor (e.g., efforts to avoid thoughts, feelings, activities, people who serve as reminders) and affective *numbing* (e.g., detachment from others, reduced ability to feel emotions), and 3) *hyperarousal* symptoms (e.g., sleep disturbance, startle response, hypervigilance). PTSD is a chronic condition, with more than one-third of people with PTSD failing to remit after many years (Kessler et al., 1997).

The association between alcohol use disorders and PTSD has been well established (Epstein, Saunders, Kilpatrick, & Resnick, 1998; Fullilove et at., 1993; Keane & Kaloupek, 1997, McFarlane, 1998; Najavits, Weiss, & Shaw, 1997; Stewart, 1996; Stewart, Conrod, Pihl, & Dongier, 1999). In the general population, approximately 5.0% of men and 10.4% of women meet lifetime criteria for PTSD (Kessler et al., 1995). The rates of PTSD among men and women with alcohol dependence are at least twice as high as those in the general population. The findings from Kessler et al.'s (1997) epidemiologic work reveal that approximately 10.3% of men and 26.2% of women with alcohol dependence in the general population meet criteria for lifetime PTSD (Kessler et al., 1997).

Studies involving clinical samples also report a high incidence of exposure to trauma and PTSD. Among 297 chemically-dependent adolescents, 24.3% of adolescent males and 45.3% of adolescent females met lifetime criteria for PTSD (Deykin & Buka, 1997). In another study of 100 individuals presenting for outpatient substance abuse treatment, 38% of women and 17% of men met criteria for PTSD (Brady, Grice, Dustan, & Randall, 1993). These findings demonstrate a high prevalence of PTSD among alcohol-dependent individuals.

Alcohol Use Disorders Among Individuals with PTSD

The majority of individuals with PTSD meet criteria for at least one other psychiatric disorder. Kessler et al. (1995) found that 88.3% of men and 79.0% of women with lifetime PTSD had a history of at least one other disorder. Individuals with PTSD are at an increased risk for developing an alcohol use disorder. Among individuals with

PTSD in the general population, approximately 51.9% of men and 27.9% of women meet lifetime criteria for alcohol abuse or dependence. The lifetime prevalence rate of alcohol dependence in the general population is estimated at 20.1% for men and 8.2% for women (Kessler et al., 1994). Data from the St. Louis Epidemiologic Catchment Area study (ECA; Helzer et al., 1988) found that individuals with PTSD were 1.6 times more likely than individuals without PTSD to meet criteria for a current or lifetime alcohol use disorder.

The association between PTSD and alcohol use disorders is found across a number of trauma types (Najavits, Weiss, & Shaw, 1997). Stewart (1996) reviewed studies related to natural disasters, assault, and combat and found evidence suggesting that exposure to each of these may lead to the development of alcohol use disorders. Stewart noted that some types of trauma (i.e., heavy combat, sexual assault) and characteristics of the trauma (e.g., severity, duration, frequency) are associated with an increased likelihood of the development of PTSD. It is not clear at this time whether differences in rates of alcohol use disorders vary as a function of the nature of the traumatic event (Stewart, 1996).

Data from the National Vietnam Veterans Readjustment Study (NVVRS; Kulka et al., 1990) found that 74% of male and 29% of female veterans with PTSD in their nonclinical sample also met lifetime criteria for alcohol abuse. Kilpatrick, Resnick, Saunders, & Best (1998) examined data from a large national sample of women and found that individuals with crime-related PTSD were 3.2 times more likely than individuals who had experienced a crime but did not develop PTSD to report serious alcohol problems. Individuals with PTSD were 13.7 times more likely than individuals who had not experienced a crime to report serious alcohol problems. The findings suggest that exposure to criminal victimization may increase the risk of developing alcohol problems, and that exposure to criminal victimization that is followed by the development of PTSD may increase the risk of alcohol problems even more. This finding

is supported in the literature by other investigations (Epstein, Saunders, Kilpatrick, & Resnick, 1998). The majority of studies examining exposure to trauma, development of PTSD, and alcohol use disorders report that the development of PTSD, rather than mere exposure to trauma (i.e., without the subsequent development of PTSD), is more closely linked to alcohol use problems and disorders (McFarlane, 1998; Stewart, 1996). Characteristics Associated with PTSD/SUD Comorbidity

The presence of comorbid PTSD among individuals with SUDs is associated with a more severe presentation, poorer prognosis and treatment outcome, and higher relapse rates (Back, Dansky, Coffey, Saladin, Sonne, & Brady, 2000; Brown, Stout, & Mueller, 1999; Compton, Cottler, Phelps, Abdallah, & Spitznagel, 2000; Hien, et al., 2000; Kranzler, Del Boca, & Rounsaville, 1996; Najavits, Weiss, & Shaw, 1997; Triffleman, Carroll, & Kellogg, 1999). Patients with comorbid PTSD and SUDs, as compared to SUDs only, evidence higher rates of Axis I and II disorders, medical problems, psychological symptoms, and interpersonal problems; poorer treatment adherence, compliance with aftercare, and motivation for treatment (Hien et al., 2000; Kofoed, Friedman, & Peck, 1993; Najavits et al., 1998). Ouimette, Finney, and Moos (1999) found that SUD-PTSD patients had poorer substance use and psychosocial outcomes at 1 and 2-years post substance use treatment than did SUD-only patients. Among a sample of 1,480 male veterans, Ouimette et al. (1999) found that SUD-PTSD patients drank significantly more alcohol at intake, 1-year and 2-years posttreatment; and evidenced significantly more problems from substance use (e.g., health, legal, occupational) at intake, 1-year, and 2-years posttreatment. In addition, SUD-PTSD patients demonstrated less improvement on indices of psychosocial functioning (e.g., Brief Symptom Inventory, friend resources, occupational functioning) than did SUD-only patients.

Brown, Stout, and Mueller (1999) examined the use of inpatient addiction treatment over a 6-month period and found that SUD-PTSD patients incur \$3,262 more in hospital overnight treatment costs, as compared to SUD-only patients. In addition, SUD patients with PTSD exhibit poorer treatment outcome than SUD patients with other comorbid psychiatric disorders (Ouimette, et al., 1999). Thus, the presence of comorbid PTSD specifically is associated with poor treatment prognosis (Ouimette, et al., 1999).

Finally, patients with comorbid SUDs and PTSD may also be at greater risk for subsequent victimization due to, for example, deficits in judgement and other cognitive impairment associated with substance use (Kilpatrick, Resnick, Saunders, & Best, 1998). In a study of 91 patients with cocaine dependence with or without PTSD, Back et al. (2000) found that cocaine-dependent patients with PTSD reported higher rates of sexual and physical revictimization as compared to cocaine-dependent patients without PTSD.

Because of the high co-occurrence of alcohol dependence and PTSD and the poor prognosis of these individuals, further investigation of specific characteristics of this dual diagnosis is warranted. Examining variations in the presentation of this comorbidity by order of onset is important for theoretical and clinical reasons. In their chapter on the DSM-IV and assessment, Acierno, Hersen, and van Hasselt (1997) suggest that a symptom assessment that is more thorough than what the DSM-IV offers and one that explores intradiagnostic distinctions within a category would allow clinicians to be better able to select optimal interventions by allowing them to "match their treatments and treatment modalities to each patient's presenting psychopathology" (Acierno, Hersen, & van Hasselt, 1997, p. 583). The idea is that there may be intradiagnostic groups within heterogeneous labels that might help identify those individuals who might benefit more from a particular form of intervention. Acierno and his colleagues (1997) further note that two individuals may be diagnosed with the same disorder (or dual disorders), but their behavior may be maintained by disparate elements and that because of this, these two individuals will necessitate different forms of treatment in order to achieve lasting improvement in their conditions. "The path by which psychopathology developed regularly provides essential direction to the course a treatment should take" (Acierno, Hersen, & van Hassel, 1997, p. 585).

Thus, identifying differences by order of onset may help inform etiologic theories on the pathogenesis of comorbid alcohol dependence and PTSD, and increase treatment utility by allowing for the identification of differential treatment responders. As stated by Nishith and colleagues, "the order of onset of substance use disorders and psychiatric disorders may provide valuable information as to the motives underlying substance abuse" (Nishith, Mueser, Srsic, & Beck, 1997, p. 766). Thus far, research has focused mainly on demonstrating that an association between the two disorders exists, but little is known about how differing pathways might affect presentation and response to treatment. In clinical practice, patients with alcohol dependence and PTSD generally receive similar forms of psychosocial treatment, regardless of which disorder is primary (i.e., developed first and contributed to the development or maintenance of the comorbid disorder). Differing developmental antecedents may influence clinical decisions about which treatment strategies are optimal for a given individual (Brady, Dansky, Sonne, & Saladin, 1998).

Etiology of PTSD/SUD Comorbidity

Several theories have been proposed to account for the co-occurrence of PTSD and SUDs. Two common theoretical models, the self-medication hypothesis and the high-risk exposure hypothesis, will be briefly reviewed. In addition, issues related to the influence of a third variable that might help explain the co-occurrence of PTSD and SUDs will be discussed.

<u>Self-medication hypothesis.</u> According to the self-medication hypothesis, individuals use substances to control or reduce (i.e., self medicate) negative and unpleasant affective states (e.g., depression, guilt) (Khantzian, 1985). In addition, individuals with PTSD may use alcohol to quell intrusive cognitive symptoms or hypervigilance, or reduce behavioral avoidance (cf., Stewart, 1996). A key feature of PTSD is avoidance of stimuli that remind the individual of the traumatic event. In an attempt to reduce behavioral avoidance and be able to cope with exposure to these stimuli, individuals may self medicate (Stewart, 1996). For example, among women with sexual abuse histories, Skorina and Kovach (1986) found evidence suggesting that some women use alcohol in order to reduce behavioral avoidance of sexually-related activities, which might serve as trauma reminders. Comorbid presentation of alcohol dependence and PTSD that develops via self medication is considered "*primary PTSD*" because the development of PTSD precedes the onset of alcohol dependence, and the PTSD is viewed as primary in terms of the manifestation of this comorbid condition.

According to Brown and Wolfe (1994) "the self-medication hypothesis can be considered a modification of the more general tension-reduction hypothesis" (p. 52). The Tension Reduction Theory (TRT; as cited in Stewart, 1996) is a two-stage etiologic model of substance use. The TRT proposes that 1) alcohol use leads to tension reduction, then 2) this tension reduction is negatively reinforcing so it increases the likelihood that alcohol will be consumed as a means of reducing tension in the future. Individuals with PTSD may be at a heightened risk for learning to reduce tension via alcohol use.

<u>High-risk exposure hypothesis.</u> The high-risk exposure hypothesis posits that the use of substances places individuals at risk for PTSD by increasing the likelihood of exposure to Criterion A events due to heavy substance use or circumstances of use (e.g., people, places) (Chilcoat & Breslau, 1998; McFarlane, 1998). For example, an individual might be assaulted while in an unsafe area attempting to procure illegal substances, or a serious car accident might occur as a result of the driver being intoxicated. Comorbid presentation of alcohol dependence and PTSD that develops via high-risk exposure is considered "*primary alcohol dependence*" because the onset of the alcohol dependence diagnosis precedes the onset of the PTSD diagnosis and the alcohol problems are viewed as primary in terms of the development of this comorbid condition.

<u>Third variables.</u> It is also possible that neither the self-medication nor the highrisk hypothesis fully account for comorbidity of alcohol use disorders and PTSD. Other third variables (e.g., family dysfunction, family history of SUDs, neurochemical system dysregulation) may help account for this association (Kofoed, Friedman, Peck, 1993; Stewart, 1996). Research investigating the influence of such third variables (Dembo, Williams, Wothke, Schmeidler, & Brown, 1992) demonstrates that trauma exposure contributes unique variance to the prediction of alcohol use disorders, above and beyond what these other third variables account for in the studies. In addition, anxiety sensitivity (i.e., fear of anxiety symptoms) may be related to the development and maintenance of both alcohol use dependence and PTSD (Stewart, 1996).

Order of Onset

While causality cannot be determined by examining temporal relationship alone, differences in the order of onset of dual diagnoses may be important in assessing etiologic link (Compton et al., 2000; Stewart & Conrod, 2003). The majority of studies examining the order of onset among individuals with PTSD and alcohol use disorders reveal the PTSD is most often the primary disorder (i.e., PTSD temporally precedes the onset of the alcohol use disorder) (Jacobsen, Southwick, & Kosten, 2001; Stewart & Conrod, 2003). Using data from the NCS, Kessler et al. (1997) estimated that when PTSD is accompanied by a comorbid disorder, PTSD is primary from 29.3% to 51.3% of the time in men and from 40.8% and 57.6% of the time in women. When PTSD is comorbid with any alcohol or substance use disorder, PTSD is primary in approximately 65.3% of men and 84.3% of women (Kessler et al., 1997). The findings from these studies generally support the self-medication hypothesis.

Data from a national probability household sample of adult women in the U.S. (Epstein et al., 1998) revealed that 65% reported the onset of first PTSD symptom prior to the onset of their first alcohol abuse symptoms, 30% reported the first alcohol abuse symptom prior to the first PTSD symptom, and 4% reported the same age of onset for both disorders. In a study of women with PTSD and SUDs, Najavits, Weiss, and Shaw (1999) reported that 60.7% of the women experienced the onset of PTSD prior to the onset of their substance use disorder.

While the majority of findings in the extant literature support the notion that PTSD generally precedes substance use disorders, Cottler and her colleagues (Cottler, Compton, Mager, Spitznagel, & Janca, 1992) reported that in participants of the St. Louis ECA study, alcohol and drug use more often predated PTSD symptoms. The authors argued that substance abusers might be at greater risk of exposure to Criterion A events (i.e., the high-risk hypothesis; Chilcoat & Breslau, 1998). Differences in methodology used by Cottler et al. (e.g., subthreshold criteria for substance and PTSD diagnoses), which might help explain the disparate findings, have been noted in the literature (Epstein et al., 1998; Stewart, 1996). With the exception of the findings of Cottler et al. the majority of investigations provide indirect support for the self-medication hypothesis (Khantzian, 1985) which necessitates that PTSD temporally precede substance use. <u>Research on Order on Onset among Patients with SUDs and Other Comorbid Disorders</u>

Several studies on the order of onset have been conducted that involve individuals with SUDs and comorbid psychiatric disorders other than PTSD. This work has demonstrated baseline and end of treatment differences among groups based on the temporal order of the onset of their dual diagnoses. The findings from these studies highlight the importance of considering the order of onset and of conducting similar research using individuals with SUDs and PTSD.

Using Schuckit's terminology, Nishith et al. (1997) conducted a study to examine whether parolees with primary versus secondary SUDs would respond differentially to cognitive therapy for SUDs. Eighty-eight men who had been incarcerated for alcohol and drug-related crimes participated in mandatory, weekly, outpatient cognitive therapy targeting their substance use and relapse prevention issues. Approximately 59% (n = 52) completed treatment (i.e., attended more than six sessions). Among completers, the average age of onset of alcohol use disorders was 21.19 years old, of drug use disorders was 21.67 years old, and of comorbid Axis I psychiatric disorders was 26.88 years old. Thus, most patients in this sample developed a SUD prior to the onset of another psychiatric disorder. Approximately 77% (n = 40) were considered to have a primary SUD and the remaining 23% (n = 12) were considered to have a secondary SUD. Baseline comparisons revealed that parolees with secondary SUDs had significantly higher scores on the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Beck Hopelessness Scale (BHS). No significant differences in substance use were observed at baseline. Pre-post comparisons revealed that both groups demonstrated significant decrease in BDI, BAI, and BHS scores over treatment. With regard to substance use, patients with a secondary SUD evidenced significant decrease in substance use ratings from pre- to posttreatment. No significant pre-post difference in substance use ratings was observed for patients with a primary SUD. Nishith et al. concluded that cognitive therapy for SUDs, as delivered in their study, may be more effective for patients with secondary as compared to primary SUDs. It should be noted, however, that the patients in Nishith et al.'s (1997) study were men with criminal histories who were mandated to treatment. As such, they may represent a unique group of patients and the findings may not generalize well to other groups. Moreover, it is important to note that Nishith et al. did not distinguish between types of Axis I disorders. Further research is needed to help determine the clinical utility of order of onset in response to therapeutic interventions, and whether certain dual diagnosis subgroups (e.g., PTSD and SUDs) are useful as predictors of differential treatment response.

Schuckit (1985) examined a group of 577 male Vietnam veterans who were seeking treatment for alcohol to determine the clinical, prognostic significance of distinguishing between individuals with 1) primary alcohol use disorders, 2) primary drug abusers, 3) primary antisocial personality disorder (ASP), and 4) primary affective disorder. These four groups represented the four largest primary diagnostic groups in their sample. Schuckit suggested that "it is important to attempt to distinguish primary and secondary disorders to indicate those psychiatric syndromes that might require more vigorous long-term treatment" (p. 1048). The findings highlight the heterogeneity of individuals with alcohol use disorders and revealed marked differences between the four groups.

Schuckit (1985) found that primary alcoholics demonstrated a later age of onset and a significantly higher rate of lifetime alcohol-related problems as compared to secondary alcoholics (i.e., groups 2-4). Higher rates of mental health problems at baseline and 1-year follow-up were also found among patients with secondary SUDs (Schuckit, 1985). For example, mental health problems (e.g., number of visits to mental health professional, number of lifetime major depressive episodes, number of past suicide attempts) were more severe at intake for individuals with a primary affective disorder as compared to primary alcoholics. Compared to men with primary drug use or primary ASP, men who were in the primary alcohol group demonstrated significantly higher income and residential stability, and fewer legal problems at 12-months follow-up. Follow-up data further revealed that the primary affective group was at greater risk for depression, but had higher rates of abstinence and lower rates of substance misuse as compared to the other three groups. Individuals with primary ASP demonstrated a poor prognosis for alcohol, drug, and social problems at follow-up as compared to the other groups. Individuals with primary drug use disorders were likely to continue drug use and evidence social impairment as compared to the other groups. Overall, the findings from Schuckit (1985) demonstrate the potential clinical utility of establishing the temporal order of onset among individuals with alcohol use disorders and other comorbid disorders.

Research on Order of Onset among Patients with PTSD and SUDs

While no study to our knowledge has examined differences in clinical presentation or response to treatment by order of onset among individuals with alcohol dependence and PTSD, one study has examined baseline differences among individuals with *cocaine* dependence and PTSD by order of onset. Brady et al. (1998) examined baseline differences in 38, treatment-seeking, outpatients with comorbid cocaine

dependence and PTSD. Brady classified patients into two groups: primary PTSD and primary cocaine. Patients who reported that the onset of PTSD occurred prior to the onset of cocaine dependence were included in the *primary PTSD* group. Patients who reported that the onset of cocaine dependence occurred prior to the onset of PTSD were included in the *primary cocaine* group. The findings revealed that 17/38 were classified as primary PTSD and 16/38 as primary cocaine patients. Patients in the primary PTSD group were more likely to be women, exhibit higher rates of Axis II diagnoses, meet criteria for another drug abuse diagnosis (i.e., benzodiazepines and opiates), and report a history of sexual assault. Patients in the primary cocaine group were more likely to report a history of physical assault and exposure to trauma as a result of the procurement and use of illicit substances. The primary PTSD group scored higher on all measures of PTSD symptomatology (i.e., Impact of Events Scale, SCL-90 PTSD subscale, Modified PTSD Symptom Scale), although the differences were not statistically significant. Brady et al. reported that the lack of significance may be due to the small sample size. Examination of differences between groups on a number of drug use parameters (e.g., number of years used, dollar amount spent in past month, baseline ASI drug composite score) failed to reveal any significant differences. Given the almost equal distribution of primary cocaine and primary PTSD diagnoses in the sample, Brady et al. (1998) suggested a need to conceptualize PTSD and SUD comorbidity with respect to temporal order of onset. The question still remains as to whether these differences (or lack of differences) at baseline between the two groups affects treatment response.

Similar to the findings of Brady et al. (1998), Sonne et al. (in press), in an examination of a subset of the participants described in the methodology section of this proposal, found that women were more likely than men to have primary PTSD and to report exposure to sexually-related traumatic events as compared to men. Further examination of baseline gender differences revealed that there were no significant

differences at baseline on demographic information (i.e., age, race, years of education, marital status), ASI composite scores, the CAPS, IES, MISS, or HamD scores. Treatment Issues: Sequential vs. Concurrent Therapy

Traditionally, treatment and research centers for substance abuse and trauma/PTSD have been mutually exclusive organizations (Brown & Ouimette, 1999). Until recently, many SUD treatment centers did not even assess for trauma history or PTSD (Bollerud, 1990; Hien et al, 2000; Najavits, Weiss, & Shaw, 1997). There exists a long-standing controversy as to whether patients with comorbid SUDs and PTSD should receive sequential or concurrent (i.e., integrated) or parallel (i.e., receives treatment in two different settings) psychotherapy (cf., Brown & Wolfe, 1994; Weiss & Najavits, 1998). Little empirical data exist to guide treatment decisions.

Sequential therapy involves treating one disorder first and then the other. In clinical practice, this generally involves treating the substance use problem first, and then approaching the trauma work. Different treatment providers are often employed in sequential treatment, with an addictions specialist treating the substance use disorder, followed by a specialist in trauma treating the PTSD. Clinical lore posits that individuals who are currently using substances are unable to appropriately and adequately handle the trauma work necessary to resolve PTSD.

Concurrent therapy (i.e., integrated treatment) involves treating the substance use disorder and the PTSD simultaneously. Generally, one treatment provider conducts the therapy, delivering both components concurrently. Parallel treatment, in which two different service providers deliver the treatment, is also an option (Weiss & Najavits, 1998). It is believed by some that delaying the treatment of PTSD increases the risk for relapse because the patient whose PTSD symptoms are not adequately addressed in therapy will promptly return to substances to manage these symptoms (Brown & Wolfe, 1994).

Although examination of temporal order of onset does not establish a causal link between alcohol dependence and PTSD, examination of patients' perceptions of the functional interplay between their PTSD symptoms and alcohol use has provided some support for a causal relationship. Rachman (1991) suggested that in order to help determine whether a relationship between comorbid disorders is functional or merely statistical, attention should be paid to the patients' beliefs about the connectedness of the two disorders. A recent study conducted by Brown, Stout, and Gannon-Rowley (1998) demonstrated that when asked, the majority of patients with PTSD and a SUD perceived the two disorders to be functionally related (e.g., the use of substances affects their PTSD symptoms, and their PTSD symptoms affect their use of substances) and preferred that they be treated concurrently. In a research review of SUD and PTSD comorbidity among women, Najavits et al. (1997) noted that PTSD symptoms present as triggers for substance use among many women with this dual diagnosis. In another study of 25 patients with a SUD and another comorbid Axis I disorder, Gomez et al. (2000) found that 60% felt that one disorder led to the other and 64% believed that their substance use was a result of their comorbid Axis I disorder. Given that substance use and PTSD symptoms are believed by many researchers and patients to be functionally linked, the treatment of PTSD plays an important role for this dually-diagnosed population.

Recent data suggest that providing PTSD treatment to SUD-PTSD patients may improve substance use outcome. Ouimette, Moos, and Finney (1998) examined predictors of remission from substance use among 125 male veterans with comorbid SUDs and PTSD who received psychotherapy (i.e., cognitive behavioral, 12-step, and eclectic) for substance abuse/dependence. Approximately half (51.2%) of the sample met criteria for an alcohol use disorder. The remaining portion of the sample were either drug dependent (20.8%) or dependent on both alcohol and drugs (28.0%). Ouimette and colleagues examined whether receiving treatment for PTSD during the 2 year follow-up period was associated with remission from substances. The findings revealed that remitted patients received significantly more PTSD visits during the first year follow-up period than nonremitted patients. In addition, PTSD-focused treatment during the second year and the total number of PTSD sessions over the 2-year follow-up period were the most significant predictors of remission. Ouimette et al. concluded that PTSD-focused treatment is, therefore, an essential component of treatment for individuals with a SUD and comorbid PTSD.

Most clinicians and researchers now encourage the development and implementation of integrated, comprehensive treatments for individuals with SUDs and PTSD (Back, Dansky, Carroll, Foa, & Brady, 2001; Brady, Dansky, Back, Foa, & Carroll, 2001; Bollerud, 1990; Gomez et al., 2000; Kofoed, Friedman, & Peck, 1993; Najavits, 2003; Najavits, Weiss, & Shaw, 1997, 1999; Najavits, Weiss, Shaw, & Muenz, 1998; Stewart, 1996). As stated by Kofoed et al. (1993), presentations of comorbid SUDs and PTSD "must be treated simultaneously because the complex self-sustaining interrelationship between intra-psychic, behavioral and biological aspects of PTSD and concurrent alcoholism or drug abuse demands a comprehensive treatment approach" (p. 164). It is recommended that all patients with a SUD be screened for trauma exposure and PTSD, and that SUD-PTSD patients be provided with concurrent treatment that addresses the addiction and trauma/PTSD issues (Ouimette, Moos, & Finney, 1998; Najavits et al., 1998). However, beyond this point of agreement, there is little guidance for how to best treat both disorders. For example, divergent opinions exist about which problem should be dealt with first or if both problems should be the focus of treatment from the outset (McFarlane, 1998).

Regardless of the order of onset, some authors view the alcohol or substance use as secondary to the PTSD and believe that if the PTSD is resolved, the substance use will also resolve without necessarily being targeted in therapy. Stewart (1996, p. 103) notes several problems associated with this viewpoint (e.g., independent of etiology, once alcohol use has developed to alcohol dependence, it has "taken on a life of its own."). It has also been reported in case examples that if the PTSD is treated without treating the SUD, substance use can intensify as PTSD symptoms intensify due to the initiation of trauma work (Stewart et al., 1999). Other authors believe that if the addiction is targeted and resolved, then the PTSD will resolve on its own. According to Stewart (1996), however, if the PTSD symptoms are not treated in therapy, these symptoms may intensify following cessation of substance use, which may subsequently lead to the patient using substances again to provide temporary symptom relief (cf. Kofoed, Friedman, & Peck, 1993). In her review of the literature, Najavits (1997) also notes that "PTSD symptoms are widely reported to become worse with initial abstinence, perhaps because the use of substances no longer masks PTSD symptoms" (p. 276). Thus, SUD patients with comorbid PTSD may be at heightened risk for relapse if their PTSD symptoms are not addressed and treated in therapy. Najavits also notes in her review that the worsening of PTSD symptoms with abstinence from substance use has been described anecdotally, but not studied systematically (cf., Brown & Wolfe, 1994; cf., Hien et al., 2000). Little empirical research has addressed these important questions. Furthermore, it is not clear whether there exist certain subgroups of SUD-PTSD patients (e.g., those with primary vs. secondary SUDs) who are at greater risk for relapse and poorer treatment outcome. Goals and Implications of the Study

The main goal of the current study is to help determine the clinical utility of classifying patients with comorbid alcohol dependence and PTSD by order of onset. This study will examine differences in 1) clinical presentation at baseline and 2) response to cognitive-behavioral substance use therapy among individuals with either primary alcohol dependence or primary PTSD.

The information provided by this study may help to 1) identify subgroups in need of particular preventative efforts, 2) provide information that can be used by clinicians to better structure therapeutic efforts, and 3) ultimately lead to improvements in the treatment of individuals with comorbid alcohol dependence and PTSD. The current study will help determine the extent to which temporal order of onset affects treatment response to cognitive-behavioral substance use therapy. If the two subgroups demonstrate a differential response to therapy, then this information may be used to help guide treatment focus and match patients to more optimal interventions. In addition, the findings will allow us to determine whether differences in order of onset represent meaningful subtypes, and thereby assist in the refinement of the classification of alcohol dependent individuals with comorbid PTSD.

Hypotheses

- H1: Previous research suggests that individuals with secondary SUDs demonstrate more severe mental health problems at baseline when compared to individuals with primary SUDs. Based on this prior research, it was hypothesized that participants with primary PTSD/secondary SUDs would present with a more severe clinical profile at baseline.
- H2: According to the self-medication hypothesis, individuals use substances in order to self-medicate or control painful affective states. This theory is particularly relevant to individuals with primary PTSD. Based on this theory, it was predicted that participants with primary PTSD would demonstrate less PTSD symptom improvement in response to cognitive-behavioral substance use therapy, as compared to participants with primary alcohol dependence.
- H3: Stewart (1996) suggested that if the PTSD symptoms are not treated in SUD-PTSD patients, these symptoms may intensify following cessation of substance use, which may subsequently lead to the patient using substances again to provide temporary symptom relief. This theory is particularly relevant to individuals with primary PTSD. Thus, it washypothesized that participants with primary PTSD, as compared to primary alcohol dependence, would demonstrate a shorter latency to relapse and a greater percentage of days drinking.

H4: Deykin and Buka (1997) proposed that matching patients to treatment focus based on the temporal order of onset might be beneficial. Based on this treatmentmatching hypothesis, it was predicted that participants with primary alcohol dependence would exhibit greater overall response to cognitive-behavioral substance abuse treatment, as compared to participants with primary PTSD.

CHAPTER 2 METHOD

Participants

Participants in the current study are 94 (51 men, 43 women) treatment-seeking individuals who participated in a 12-week outpatient study that included psychotherapy and pharmacotherapy (sertraline or placebo) to treat comorbid alcohol dependence and PTSD. Participants were primarily recruited from the following facilities: 1) the Center for Drug and Alcohol Programs at the Medical University of South Carolina and 2) the Department of Alcohol and Other Drug Abuse Services, a state-funded substance abuse treatment center in Charleston, South Carolina. Media advertisement (e.g., newspaper) and clinical referral were also used to recruit participants. Ads recruited for individuals who used alcohol and had problems resulting from their use, and individuals who had been through a very stressful event (e.g., rape, assault, car accident) and were having a hard time putting it out of their mind. Participants were financially compensated \$30 for completing the baseline and treatment termination assessments (\$60 total).

The purpose of the original study for which the participants were recruited was to evaluate the efficacy of sertraline in decreasing both alcohol consumption and PTSD symptoms in treatment-seeking individuals with current alcohol dependence and comorbid civilian PTSD. It was hypothesized that individuals receiving sertraline would evidence greater improvement on alcohol use indices and PTSD symptom measurements at the end of treatment, in comparison to individuals receiving placebo. Although the data regarding the age of onset of alcohol dependence and PTSD were carefully obtained during the study, the original study was not intended to address the issue of order of onset, which is what the current study proposes to investigate. At this time, no manuscripts have been published using these participants.

Table 1 presents the subject characteristics for the sample. Participants met DSM-IV diagnostic criteria for alcohol dependence and current PTSD, were 18 years or older, and were medically stable. Individuals with current psychotic, bipolar, dissociative identity, or eating disorders or individuals with suicidal ideation were excluded from the study. This was done primarily because their conditions suggested that they would require other medications or treatments in addition to the protocol interventions, or because treatment with placebo would be considered unethical. Finally, pregnant or breast feeding women, individuals requiring ongoing concomitant therapy with a psychotropic drug, and individuals with other current comorbid substance *dependence* disorders (excluding caffeine and nicotine) in the past 60 days were excluded.

Materials

Assessment of substance use disorders. The Structured Clinical Interview for the DSM-IV, patient version (SCID; First et al., 1995) was administered by trained clinicians and used for diagnosis of alcohol and other substance use disorders. The SCID is a semistructured diagnostic interview designed to diagnose most adult Axis I disorders (e.g., mood, psychotic, anxiety, somatoform, substance use, and eating disorders). The SCID contains a section that assesses alcohol abuse and dependence and a section that assesses non-alcohol use disorders, including sedatives, hypnotics and anxiolytics; cannabis; stimulants; opioids; cocaine; hallucinogens/PCP; and other substances (e.g., steroids, glue, inhalants, nitrous oxide). The original SCID (Spitzer & Williams, 1984) was the first comprehensive semistructured interview based on the DSM-III criteria. The SCID has been revised to reflect modifications for each version of the DSM.

Williams et al. (1992) reported on the multisite, 2-week test-rest reliability of 592 patients (n = 390) and nonpatients (n = 202). Kappas above .60 were observed for most

major disorders (Williams et al., 1992). Across all disorders, an overall kappa of .61 for current and .68 for lifetime disorders was observed among the patients. For alcohol abuse or dependence within the patient sample, the kappa across all sites was .75 for current and .73 for lifetime (Williams et al., 1992). At the Substance Abuse Treatment Unit, which specialized in the treatment of SUDs, the kappa was .83 for current and .73 for lifetime alcohol abuse or dependence (Williams et al., 1992).

The Addiction Severity Index (ASI; McLellan et al., 1992), "one of the most widely used assessment instruments in the substance abuse field" (Alterman, Brown, Zaballero, & McKay, 1994, p. 201), was used to evaluate alcohol use history (e.g., number of years used) and severity. The ASI is a semi-structured interview that obtains demographic information and assesses functioning in seven areas: medical, employment, drug use, alcohol use, family/social, legal, and psychiatric. It has been translated into nine different languages (McLellan et al., 1992). The ASI was designed to cover a broad range of areas of functioning that could potentially be affected by substance abuse treatment, thus making it appropriate as an outcome measure (McLellan et al., 1992). Multi-item composite scores representing the level of severity for each problem area can be calculated and range from 0 (no problem) to 1.0 (extreme problem) (McLellan, Luborsky, Woody, & O'Brien, 1980; Weisner, McLellan, & Hunkeler, 2000). Adequate internal consistency for the seven composite scores has been demonstrated (e.g., Cronbach's alpha of .77 medical, .63 employment, .87 alcohol, .62 drug, .66 legal, .72 family/social, and .87 psychiatric with a mean alpha of .73; Alterman et al., 1994). The ASI has been found to have good inter-rater reliability (.90 medical, .74 employment, .98 alcohol, .92 drugs, 1.00 legal, .96 family/social, .94 psychiatric; Alterman et al., 1994) and test-retest reliability (.83 to .99) over a 2 or 3-day interval (McLellan et al., 1980; McLellan et al., 1992).

Breathalyzer tests (AlcoSensor III, Intoximeters, Inc., St. Louis, MO) were administered weekly prior to each therapy session to 1) ensure that patients were sober upon presenting for therapy and 2) provide a means of substantiating self-reports of alcohol use. Breathalyzer tests are noninvasive, inexpensive, and easily administered means of determining breath alcohol concentration and are, therefore, a useful means of verifying clients' self-reported alcohol consumption. Breathalyzer tests, however, only allow for detection of recent (i.e., past 24 hours) alcohol use (Foy, Rychtarik, & Prue, 1988). Thus, it is important to assess alcohol use through additional means, such as selfreport.

The Timeline Follow-Back (TLFB; Sobell & Sobell, 1992) was used to assess baseline alcohol consumption (i.e., the 60 days prior to study entry) and was administered weekly during treatment. The TLFB is a calender-based instrument on which the clinician records the number of standard drink units (SDUs) that are reportedly consumed by the individual each day for a given period of time (e.g., 30 days). One SDU is equivalent to 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of liquor (Sobell & Sobell, 1992). Variables that can be generated from the TLFB include, for example, percent of days drinking, percent of heavy drinking days, and average number of drinks per drinking day. The psychometric properties of the TLFB have been shown to be adequate. Sobell and Sobell (1992) report that the TLFB technique is "the best psychometrically evaluated and field tested drinking-assessment in the literature to date" (p. 60). For outpatient alcoholics, test-retest reliability ranges from .79 to .92 for 30 days of drinking and from .85 to .91 for 90 days of drinking (Sobell & Sobell, 1992). The correlations between subjects' and collaterals' reports of the subject's drinking have been high (e.g., .79 to .92 for average number of days abstinent) (Sobell & Sobell, 1992). Convergent validity has been demonstrated by comparing the TLFB with two established measures of alcohol severity, the Alcohol Dependence Scale (ADS) and the Short Michigan Alcohol Screening Test (SMAST), and two biochemical assessments, the gamma-glutamyl-transpeptidase (-GGT) and serum glutamicoxaloacetic-transaminase (SGOT). Higher scores on the ADS and SMAST were shown to correlated significantly

(.51 to .53) with the number of heavy drinking days (e.g., ≥ 10 or ≥ 12 drinks). Higher scores on the ADS also correlated significantly (.52) with the average number of drinks per drinking day as assessed by the TLFB. Low consumption days correlated significantly and negatively (-.26 to -.39) with the ADS and SMAST. That is, the higher the number of low consumption days, the lower the ADS and SMAST scores. Sobell and Sobell (1992) report that these findings demonstrate a direct relationship between the level of alcohol severity as assessed by the ADS and SMAST and reported drinking as assessed by the TLFB.

Regarding the biochemical measurements, Sobell and Sobell (1992) found that 5 of 6 TLFB drinking variables (i.e., frequency of days drinking in the past 30 or 60 days, amount of alcohol consumed in the past 30 or 60 days, average number of drinks per drinking day in the past 30 or 60 days) were significantly correlated with the -GGT and SGOT.

Assessment of victimization and PTSD. Crime-related (e.g., sexual and physical assault), non-crime related (e.g., natural disaster, serious accident), and combat-related traumatic events were assessed using the *National Women's Study (NWS) PTSD Module* (Kilpatrick, Resnick, Saunders, & Best, 1989). The NWS was derived from the Diagnostic Interview Schedule (DIS) used in the National Vietnam Veterans Readjustment Study (NVVRS). The NWS is a structured clinical interview that contains 20 items and is designed for use by lay interviewers. Participants first answer whether or not they have experienced a particular event and, if so, how old they were the first time and the last time. The NWS has been shown to have good reliability and validity (Resnick, Kilpatrick, Dansky, Saunders, & Best, 1993; Norris & Riad, 1997).

PTSD symptom frequency and intensity and PTSD diagnosis were evaluated using the *Clinician Administered PTSD Scale*, a structured interview (CAPS; Blake et al., 1995). The CAPS was developed at the National Center for PTSD and is designed for use by clinicians and nonclinicians (Blake et al., 1995). In addition to assessing diagnostic PTSD symptoms, the CAPS also assesses eight associated features of PTSD (guilt over committed or omitted acts, survivor guilt, homocidality, disillusionment with authority, hopelessness, memory impairment, sadness and depression, and feelings of being overwhelmed). The CAPS also rates social and occupational functioning, as well as global severity. The CAPS has been shown to have excellent psychometric properties. Test-retest reliability over a 2-3 day interval ranged from .90 to .98, internal consistency was .94, and the kappa coefficient was .78 (Blake et al., 1995; cf. Weiss, 1997).

The Civilian Mississippi Scale for PTSD (MISS; Keane, Caddell, & Taylor, 1988) was also used to evaluate current PTSD symptoms. The Civilian MISS represents a modified version of the Mississippi Scale for Combat-Related PTSD (Keane, Caddell, & Taylor, 1988). The combat version inquires about symptoms "since the military" whereas the civilian version inquires about symptoms "in the past." The MISS has 39 items that assess reexperiencing, withdrawal and numbing, arousal, and self-persecution (e.g., guilt and suicidality). Items are rated on a 5-point Likert scale and scores range from 39 to 195. A total score is calculated by adding each item. High internal consistency (.86) has been demonstrated (Norris & Riad, 1997). One study involving 53 psychiatric inpatients demonstrated that the MISS was able to distinguish between patients with and without trauma histories who had similar levels of general distress, as evidenced by comparable scores on the SCL-90 (Hovens & van der Ploeg, 1993). Thus, the differences detected by the MISS were not merely generalized distress, but were specific to traumatic experiences (Norris & Riad, 1997). However, other studies have reported that the MISS correlates more highly with the Beck Depression Inventory (.71) and the Spielberger Trait Anxiety Scale (.70) than with the Impact of Events Scale (.36) and the Revised Purdue PTSD Scale (.52) (Lauterbach, Vrana, King, & King, 1997; cf., Norris & Riad, 1997). Although the MISS is widely used, there is some uncertainty about its convergent and discriminant validity (Norris & Raid, 1997; Vreven, Gudanowski, King, & King, 1995).

Finally, the *Impact of Events Scale* (IES; Horowitz, Wilner, & Alvarez, 1979), a 15-item, self-report measure was used to assess PTSD intrusive and avoidant symptoms experienced during the past week. Items are rated on a Likert scale (0 = not at all to 5 = often) and scores range from 0 to 75. Horowitz et al. (1979) reported a split-half reliability of .86 for the total scale. Cronbach's alpha of .79 for intrusive symptoms and .82 for avoidance symptoms have been reported indicating high internal consistency (Horowitz et al., 1979). Test-retest reliability over a one-week period was reported to be .87 for the total score, .89 for the intrusion subscale and .79 for the avoidance subscale (Horowitz et al., 1979). The IES has also been shown to discriminate individuals from a nonclinical community sample that have experienced stressful events as compared to outpatients who are seeking treatment for stress-related events (e.g., violence, accidents, illness) (Horowitz et al., 1979). A recent review of the IES (Joseph, 2000) noted that the IES is one of the most widely used measures of PTSD symptoms. Joseph's (2000) review concluded that the psychometric properties of the IES are satisfactory and that the IES is a good measure of intrusive and avoidant PTSD symptoms, although not PTSD, per se.

The *Hamilton Rating Scale for Depression* (HamD; Hamilton, 1960), a 21-item structured interview, was used to measure the current severity of depression. The HamD is the most commonly used clinician rating scale for depression (O'Hara & Rehm, 1983). Items on the HamD are rated on either a 3-point or 5-point scale and the highest score possible is 52. The cutoff scores are as follows: 25 or above indicates severe depression, greater than 17 indicates mild depression, and less than 6 indicates virtually no depression (Endicott, Cohen, Nee, Fleiss, & Sarantakos, 1981). Scores rarely exceed 35 (Carroll, Fielding, & Blashki, 1973).

Endicott et al. (1981) reported high intercorrelations between the HamD and the depression syndrome (.84) and endogenous features (.80) sections of the Schedule for Affective Disorders and Schizophrenia—Change Version (SADS-C). Endicott et al. (1981) also reported that the HamD was negatively correlated (-.69) with the Global

Assessment Scale of the SADS-C. Carroll et al. (1973) found that the HamD clearly discriminated between three groups of patients: inpatients (29.5 7.8), day patients (23.7 4.2), and general practice (14.7 5.8) patients. In addition, O'Hara and Rehm (1983) found that the intraclass correlations for the HamD was .91 when rated by four expert raters and .76 when rated by three novice raters (i.e., undergraduate students). The mean of the HamD (averaged across the four expert raters) was 14.50 7.42 and was not statistically different from the mean of HamD as assessed by the novice raters (13.72 6.82). In the current study, trained clinicians administered the HamD.

Assessment of order of onset. During the SCID interview, the age in years at which participants first met criteria for alcohol dependence was determined by trained clinicians. During the CAPS interview, the age at which participants met criteria for PTSD was determined. To examine differences in clinical presentation and treatment response by order of onset, primary PTSD and primary alcohol dependence groups were generated. Individuals who reported that the age of onset of PTSD temporally preceded the age of onset of alcohol dependence were compiled to form the "*primary PTSD* group." Individuals who reported that the age of onset of alcohol dependence temporally preceded the age of onset of PTSD were compiled to form the "*primary alcohol* group." Individuals who reported that the age of onset for alcohol dependence and PTSD were the same or simultaneous (i.e., onset is reported to be the same age for each disorder) were excluded from the analyses.

<u>Assessment of comorbidity.</u> Axis I psychiatric diagnoses (other than PTSD, which was assessed using the CAPS) were made according to the SCID. To differentiate transient substance-induced symptoms from enduring psychiatric symptoms participants were interviewed after 7 days of abstinence from alcohol as verified by self-report and breathalyzer tests (three breathalyzer tests scheduled evenly across the 7-day period).

<u>Assessment of other forms of therapy.</u> The Therapy Contract Record (TCR) was developed by the researchers at MUSC and administered weekly to assess if and how

often participants attended Alcoholics or Narcotics Anonymous groups, other support groups for substance use, or church or other forms of supportive assistance. Variables that can be generated from the TCR include, for example, the weekly number of contacts, total number of contacts during the course of therapy, and type of contacts utilized.

Procedure

Participants signed an IRB-approved consent form and were then interviewed and administered a battery of self-rating scales after at least 7 days of abstinence from alcohol and drugs as evidenced by self-report, a breathalyzer test, and a urine drug screen. This was done to preclude misdiagnosis of psychiatric disorders because of symptoms related to alcohol withdrawal. Trained clinicians conducted the interviews. Diagnoses and baseline assessments were made before any treatment was implemented.

<u>Psychotherapy.</u> Individuals received 12 sessions of standardized, manual-guided cognitive-behavioral therapy for alcohol dependence. The therapy protocol was identical to the Cognitive Behavioral Coping Skills Therapy that was used in Project MATCH (Project MATCH Research Group, 1997) and included seven core sessions: introduction to coping skills training, coping with cravings and urges to drink, managing thoughts about alcohol and drinking, problem solving, drink refusal skills, planning for emergencies and coping with a lapse, and seemingly irrelevant decisions. After the core sessions were completed, various elective sessions were offered including, for example, sessions targeting awareness of anger, anger management, assertiveness, starting conversations, nonverbal communication, enhancing social support networks, jobseeking skills, and couples involvement. Patients enrolled in the study did not receive psychotherapy targeting their trauma or PTSD symptoms, nor were they participating in any treatments for PTSD during the time of this study. Furthermore, therapists were instructed not to discuss any trauma-related material, issues or PTSD symptoms during therapy. All sessions were audiotaped.
<u>Medication component.</u> Patients were randomized to receive either sertraline (fixed dose of 150 mg) or placebo during the study. The resulted in 28 men and 21 women (total of 49) having received sertraline and 23 men and 22 women (total of 45) having received placebo, for a total sample of 94 participants. The study was a doubleblind study, such that neither the participants nor the clinicians knew which participants were receiving sertraline and which were receiving placebo. Sertraline hydrocloride (i.e., Zoloft), a serotonin selective reuptake inhibitor (SSRI) antidepressant, is the first medication to be FDA approved for the treatment of PTSD.

Prior to the recent pharmacological trials for PTSD, few controlled studies (i.e., 5 in 1992) of medication treatment for PTSD had been conducted, and all of these studies were limited to men. SSRIs have more recently been investigated because they are well tolerated and have a good side effect profile (Brady et. al., 2000). In animal studies, sertraline has been shown to "effectively attenuate the behavioral syndrome that occurs...after exposure to uncontrollable stress" (Brady et al., 2000, p. 1838). Two openlabel studies employing small samples demonstrated efficacy for sertraline in female rape victims (n = 7; Rothbaum, Ninan, & Thomas, 1996) and individuals with comorbid alcohol dependence and PTSD (n = 9; Brady, Sonne, & Roberts, 1995). Following this, a larger (n = 187) double-blind, placebo-controlled trial of sertraline treatment for PTSD was conducted at outpatient clinics at 8 academic medical centers and 6 clinical research centers in the US (Brady et al., 2000). Approximately 26% of the sample had a history of alcohol dependence or abuse and 14% had a history of drug dependence or abuse. Comparisons of baseline to end point change demonstrated that improvement on 3 of 4 primary measures (i.e., CAPS, Clinical Global Impressions—Severity, and Clinical Global Impressions—Improvement) was significantly greater for the sertraline as compared to the placebo group. The fourth primary measure, the IES, demonstrated a trend toward significance. The findings also suggested that sertraline was particularly effective in decreasing avoidance/numbing and arousal, but not reexperiencing/intrusion

PTSD symptoms. In addition, the sertraline group demonstrated greater improvement on the HamD, and measures of social and occupational functioning (Brady et al., 2000).

Serotonin [5-hydroxytryptamine (5-HT)] dysregulation has been implicated in both PTSD (van der Kolk, 1997) and alcohol dependence (Kranzler & Anton, 1994). Thus, the use of SSRIs to treat individuals with PTSD and alcohol dependence is particularly important. SSRIs have demonstrated modest efficacy in decreasing alcohol consumption among alcohol-dependent individuals involved in small-scale studies. For example, in a small, uncontrolled, open-label study, Bogenschutz & Nurnberg (1996) demonstrated decreases in frequency of drinking and craving, and consequences of drinking among seven men and two women with alcohol use disorders who received sertraline for 1 year. One SSRI, fluoxetine, however, has been shown to have negative results in several studies (Pettinati et al., 2000b).

Pettinati and her colleagues (Pettinati, Olson, & Becker 2000a, Pettinati, Volpicelli, Kranzler, Luck, Rukstalis, & Cnaan, 2000b) note that the amount of 5-HT dysregulation among alcohol-dependent individuals varies across patients. As such, the ability of SSRIs to improve alcohol-related symptoms may vary. In a study of 100 outpatients (52 men, 48 women), Pettinati et al. (2000b) grouped participants into two categories (Type A , n = 55; Type B, n = 45) based on Cloninger's system using a *k*-mean clustering procedure. Type B is associated with earlier onset, family history, more childhood risk factors, sociopathy, psychopathology, alcohol-related problems and polydrug use (Pettinati et al., 2000b). In contrast, Type A is associated with a less severe and "complicated" profile. The results of the study suggested an interaction between medication group and alcohol subtype, such that sertraline was associated with greater improvement in alcohol-use indices (e.g., number of drinking days, continued abstinence) for Type A alcoholics.

Two other randomized trials of SSRIs have investigated the utility of distinguishing between alcohol subgroups. One study by Irwin, Schuckit, and Smith (as

cited in Pettinati et al., 2000b) found no benefit and the second study by Kranzler, Burleson, Brown, and Babor (as cited in Pettinati et al, 2000b) found that Type B alcoholics actually worsened on fluoxetine as compared to placebo. Further research is needed to confirm and help clarify the utility of sertraline, and other SSRIs, in the treatment of alcohol use disorders (Pettinati et al., 2000b).

Plan for Statistical Analyses

Hypothesis 1 predicted that participants with primary PTSD/secondary SUDs would present with a more severe clinical profile at baseline. In tests of this hypothesis, the independent variables will be order of onset status (primary PTSD or primary alcohol dependence) and gender (men or women). The continuous dependent variables will be the ASI composite scores (medical, employment, drug use, alcohol use, family/social, legal, psychiatric) and the HamD score. A series of 2 X 2 analyses of variance (ANOVA) tests will be conducted on these variables. Chi-square tests will be used to test differences in the presence of comorbid Axis I diagnoses. Differences between groups in trauma history (e.g., number of traumas, type of traumas) will also be explored.

Hypothesis 2 predicted that participants with primary PTSD would demonstrate less PTSD symptom improvement in response to cognitive-behavioral substance use therapy, as compared to participants with primary alcohol dependence. Repeated measures ANOVA will be used to test Hypothesis 2. The independent variables will be order of onset status (primary PTSD or primary alcohol dependence) and gender (men or women). The dependent variables will be the IES, MISS, and CAPS total scores. Clinical response to treatment, as defined by 30% or greater decrease on the CAPS total score will also be assessed. The decrease of 30% reduction has been previously used by researchers in this area (Brady et al., 2000; Rothbaum, Ninan, & Thomas, 1996). Chisquare tests will be used to measure the percent of treatment responders by order of onset status, gender, and medication group. Hypothesis 3 posited that participants with primary PTSD, as compared to primary alcohol dependence, would demonstrate a shorter latency to relapse and a greater percentage of days drinking. In the test of this hypothesis, differences in latency (i.e., number of days) to first use and to first heavy drinking day (i.e., ≥ 6 drinks for men and \geq 4 drinks for women; Project MATCH, 1997) will be examined by order of onset status, gender, and medication group using cox regression. A 2 X 2 X 2 ANOVA will be conducted to examine differences between groups in the percent of days drinking. The independent variables will be order of onset status (primary PTSD or primary alcohol dependence) and gender (men or women). The continuous dependent variable will be the percent of days during treatment that the participant reported consuming alcohol.

Hypothesis 4 was based on a treatment-matching hypothesis and predicted that participants with primary alcohol dependence would exhibit greater overall response to cognitive-behavioral substance abuse treatment, as compared to participants with primary PTSD.

To test this hypothesis, the independent variables will be the order of onset status (primary PTSD or primary alcohol dependence) and gender (men or women). The continuous dependent variables will be the ASI composite scores (medical, employment, drug use, alcohol use, family/social, legal, psychiatric) and the HamD score. Repeated measures ANOVA will be used with these variables. Chi-square tests will be used to examine difference in retention (completed treatment or did not complete treatment). Differences in the average number of sessions completed and attendance at groups outside of the study (e.g., church, AA or NA) will also be explored.

<u>Power.</u> Given the lack of direct studies in the extant literature, a medium effect size was selected for estimating power. First, power was estimated for a 2 X 2 X 2 ANOVA using a computerized power program. Given 3 factors with 2 levels per factor, alpha of .05 and a sample size of 94, power is .96 if the effect is large (\geq .40) and .81 if

the effect is medium (\geq .30). For a small effect, less power exists. Anything less than a small effect of .25 reduces the power below .70.

Next, estimates of power for chi-square tests were generated using the phi coefficient (). According to Cohen (1988), a medium effect produces a of .30. Using the formula $_{antic}^2 = ()^2(N)$, 8.46 is the expected outcome of the proposed study, with = .30, and N = 94 (Keppel, Saufley, & Tokunaga, 1992). Using df = 1, power = .85. Thus, for a medium effect or greater, the current study has sufficient power to detect differences when they exist.

Demographic Characteristics of Total Sample $(N - 94)$	Demographic Characteristics of Total Sample $(N =$
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Characteristic		
Age, M (SD)	36.62 (8.46)	
Education, years M (SD)	12.70 (2.29)	
Gender		
% Men	54.3	
% Women	45.7	
Marital Status		
% Married	22.3	
% Single, never married	29.8	
% Separated	18.1	
% Divorced	24.5	
% Widowed	3.2	
Race		
% Caucasian	85.1	
% African American	11.7	
% Hispanic	1.1	
% American Indian or Asian	2.1	

CHAPTER 3 RESULTS

Thirty-three individuals (35.1%) met criteria for primary alcohol dependence (23 men, 10 women) and fifty-three individuals (56.4%) met criteria for primary PTSD (22 men, 31 women). Seven individuals were included in the simultaneous onset group and were, therefore, excluded from the analyses. Order of onset data were missing for one individual. Thus, the following analyses were conducted on a total of 86 individuals (45 men, 41 women). Table 2 presents the demographic characteristics of the participants used in the analyses.

There were no significant marital status or racial differences between the primary PTSD and primary alcohol groups. Women were more likely to have primary PTSD than primary alcohol dependence (75.6% vs. 24.4%), $^{2}(1) = 6.61$, p = .01. There was a trend for the primary alcohol group to be older (M = 39.30) than the primary PTSD group (M = 35.75), although this finding was not statistically significant (p = .06).

Differences in Clinical Presentation

A series of 2 (Order of Onset: primary PTSD or primary alcohol dependence) X 2 (Gender: men or women) analyses of variance (ANOVA) were performed on baseline measures. Whenever interactions were significant, tests of simple effects were computed. To address potential violations of the sphericity assumption, Huynh-Feldt was used for ANOVA tests and Levene's Test of Equality of Error Variances was used for t-tests to correct the degrees of freedom.

<u>ASI.</u> Table 3 presents the means and standard deviations for the baseline ASI composite scores. A significant Order X Gender interaction was observed for the ASI

Psychiatric score, F(1,82) = 5.29, p = .02. This finding is illustrated in Figure 1. Follow up tests indicated that among women, those with primary alcohol dependence scored significantly higher on the ASI Psychiatric as compared to women with primary PTSD, F(1,39) = 5.46, p = .03. Among the primary PTSD group, there was a trend toward significance for men to score higher than women on the ASI Psychiatric, F(1,51) = 3.36, p = .07.

For the ASI *Alcohol* score, there was a trend toward a main effect of Gender, with men scoring higher than women (M = .60 vs. M = .52), F(1,81) = 3.08 p = .08. For the ASI *Family/Social* score, there was a trend toward significance on the main effect of Order, with primary PTSD individuals scoring higher than primary alcohol dependent individuals (M = .40 vs. M = .30), F(1,82) = 3.05, p = .09. No other significant main effects or interactions were found for the ASI baseline composite scores.

<u>HamD</u>. A significant Order X Gender interaction was observed for baseline HamD scores, F(1,82) = 5.11, p = .03. This finding is illustrated in Figure 2. Tests of simple effects indicated that among men, individuals with primary PTSD were more depressed than those with primary alcohol dependence (M = 20.1 vs. M = 16.0), F(1, 42)= 4.09 p = .05. Among women, individuals in the primary alcohol group scored higher than individuals in the primary PTSD group (M = 20.3 vs. M = 17.2), but this finding did not reach statistical significance (p > .05).

<u>SCID diagnoses.</u> Differences in the number of comorbid Axis I diagnoses were examined. No significant main effects or interactions were observed. The average number of Axis I diagnoses among participants (including PTSD and alcohol dependence diagnoses) was 3.59 (*SD* = 1.25).

<u>Trauma history.</u> Table 4 presents the average number of traumas endorsed by participants. Examination of differences in overall trauma history revealed a main effect of Order, indicating that individuals with primary PTSD endorsed significantly more lifetime traumatic events on the NWS as compared to individuals with primary alcohol

dependence (M = 9.55 vs. M = 7.88), F(1,82) = 4.25, p = .04. Main effects of Gender were found for several trauma types. In comparison to women, men reported significantly greater exposure to combat (M = .16 vs. M = .00), F(1,82) = 6.15, p = .02; witnessing someone seriously injured or violently killed (M = 1.51 vs. M = 1.02), F(1,82) = 5.26, p =.02; and serious accidents (M = 2.47 vs. M = 1.15), F(1,82) = 16.33, p = .00. In comparison to men, women reported significantly more exposure to traumas of a sexual nature (M = 2.88 vs. M = 1.11), F(1,82) = 21.48, p = .00, and to being attacked without a weapon but with the intent to seriously injure (M = 1.71 vs. M = 1.09), F(1,82) = 4.99, p = .03.

A main effect of Order was also observed for sexual traumas, indicating that individuals in the primary PTSD group reported a greater number of sexual traumas than did individuals in the primary alcohol group (M = 2.38 vs. M = 1.27), F(1,82) = 4.43, p = 04.

<u>Alcohol consumption.</u> Differences in consumption of alcohol during the 90 days prior to treatment entry were examined. Independent variables were Order and Gender. Dependent variables were 1) the percent of days drinking (PDD) and 2) the average number of drinks per drinking day (ADD). A main effect of Gender was observed for ADD, indicating that men consumed a greater number of drinks per drinking day during the 90 days prior to treatment as compared to women (M = 10.3 vs. M = 6.3), F(1, 81) =8.67, p = .00. No other main effects or interactions were observed for ADD. For individuals with primary alcohol dependence, the pretreatment ADD was 9.10 (SD =5.98). For individuals with primary PTSD, the pretreatment ADD was 7.94 (SD = 5.94). This difference was not statistically significant.

No main effects or interactions were observed for pretreatment PDD. For individuals with primary alcohol dependence, the average pretreatment PDD was 69.4% (SD = 27.2%), and for individuals with primary PTSD the average PDD was 63.7% (SD

= 29.2%). The average pretreatment PDD for men was 69.4% (SD = 26.3%) and for women it was 61.9% (SD = 30.4%).

PTSD Symptom Improvement During Treatment

Repeated measures analysis of variance (ANOVA) was used to examine improvement in PTSD symptoms over the course of therapy. The between-subjects factors were Order of Onset (primary PTSD or primary alcohol dependence) and Gender (men or women). The within-subject factor was Time (baseline, week 4, week 8, and week 12). Eta squared (η^2) is included as an estimate of effect size. Eta squared represents the proportion of total variability attributable to a factor, where 0 to .06 is defined as a small effect size, .06 to .15 is a medium effect size, and .15 or greater is a large effect size (Cohen, 1988).

Table 5 presents the means and standard deviations for the IES, MISS, and CAPS total scores over the course of therapy. These are also displayed in Figure 3. For each of these PTSD measures, a significant main effect of Time was revealed, indicating that the participants, as a whole, improved over the course of therapy: IES, F(3,120) = 9.28, p = .00, $\eta^2 = .42$; MISS, Huynh-Feldt, F(2.38, 92.90) = 23.25, p = .00, $\eta^2 = .37$; CAPS, F(3,135) = 34.61, p = .00, $\eta^2 = .44$. No significant main effects of Order or Gender, or interaction effects were observed for these 3 instruments.

Clinical response to treatment, as defined by a 30% or more reduction in the CAPS total score, was examined by Order, Gender, and Medication group. Approximately 55.6% of the primary alcohol group and 69.0% of the primary PTSD group were treatment responders (i.e., evidenced a 30% reduction from baseline to end of treatment). This difference was not statistically significant. Regarding gender, 60.0% of men and 67.6% of women were treatment responders, and this difference was not statistically significant. Finally, 63.9% of individuals taking sertraline and 63.6% of individuals taking the placebo were treatment responders, and this difference was not statistically significant. Even though a large number of individuals did experience a significant decrease in PTSD symptoms over the course of therapy, approximately 36% of the sample did not. Comparisons between individuals who were and were not treatment responders revealed that treatment responders consumed significantly less alcohol during therapy. The ADD during therapy was significantly less for treatment responders as compared to treatment nonresponders (M = 1.23 vs. M = 2.75, F(1, 61) = 6.09, p = .02), as was the average number of total drinks consumed each week (M = 8.33 vs. M = 17.64, F(1,61) = 5.29, p = .03). No significant differences in the average PDD during therapy were observed between treatment responders and treatment nonresponders (0.19 vs. 0.29, p > .05). <u>Alcohol Consumption During Treatment</u>

Latency to alcohol consumption. Cox regression survival analysis was used to examine latency to 1) first use of alcohol and 2) first heavy drinking day (i.e., ≥ 6 drinks for men and ≥ 4 drinks for women; Project MATCH, 1997). The independent variables were Order, Gender, and Medication Group. No significant main effects or interactions were revealed (p > .05), indicating that the survival probabilities were not significantly different across groups. On average, latency to the first use of alcohol was 9.19 days (SD = 16.83) and latency to first heavy drinking day was 10.9 days (SD = 15.89).

<u>Percent of days drinking.</u> Figure 4 displays the percent of days drinking (PDD) at pretreatment (i.e., 90 days before treatment entry) and over the course of therapy. The average percent of days drinking during therapy for the entire sample was 23%. There was a main effect of Time for PDD, indicating that individuals in both the primary alcohol and primary PTSD groups improved over time, Huynh-Feldt, F(6.56,426.29) = 24.27, p = .00, $\eta^2 = .27$. No other significant main effects or interactions were observed.

<u>Additional indices of alcohol use</u>. Figure 4 also illustrates the average drinks per drinking day (ADD) at pretreatment and during therapy. A main effect of Time was observed for ADD, Huynh-Feldt, F(4.90, 318.63) = 18.73, p = .00, $\eta^2 = .22$.

Figure 5 displays the average PDD and ADD during treatment. Although there is a pattern for men with primary alcohol dependence to drink more often and to consume greater amounts of alcohol, this finding did not reach statistical significance. <u>Overall Response to Cognitive-Behavioral Therapy for Substance Abuse</u>

<u>ASI.</u> Repeated measures ANOVA was used to examine improvement in ASI composite scores over the course of therapy. The between-subjects factors were Order and Gender. The within-subject factor was Time (baseline, week 12). Table 6 presents the means and standard deviations for the ASI composite scores at baseline and week 12.

For the Medical composite score, there was a significant Time X Order interaction, $\Lambda = .88$, F(1,49) = 6.54, p = .01, $\eta^2 = .12$. This finding is illustrated in Figure 6. Tests of simple effects indicated that individuals in the primary PTSD group demonstrated significant improvement over time, $\Lambda = .80$, F(1,31) = 7.60, p = .01, $\eta^2 =$.20. Individuals in the primary alcohol dependence group did not improve over time (p >.05).

For the *Alcohol* composite score, there was a significant Time X Order interaction, $\Lambda = .86$, F(1,50) = 8.16, p = .01, $\eta^2 = .14$ (see Figure 6). Follow up tests indicated that individuals in both groups demonstrated significant improvement from baseline to the end of treatment: primary alcohol, t(21) = 3.27, p = .01; primary PTSD, t(31) = 8.76, p = .00. Although there was no main effect of Order on baseline Alcohol composite scores, there was a trend for the primary PTSD group to score lower (M = .22, SD = .16) than the primary alcohol group (M = .31, SD = .19) at the end of treatment, suggesting greater improvement among individuals in the primary PTSD group, F(1,53)= 3.63, p = .06.

For the *Family/Social* score, a significant Time X Order interaction effect was observed, $\Lambda = .81$, F(1,50) = 11.78, p = .00, $\eta^2 = .19$ (see Figure 6). Tests of simple effects indicated that individuals in the primary PTSD group significantly improved over the course of therapy, t(31) = 4.54, p = .00, but individuals in the primary alcohol group

did not, p > .05. A significant Order X Gender interaction was also observed for the *Family/Social* score, F(1,50) = 5.54, p = .02, $\eta^2 = .10$ (see Figure 7). Follow up tests indicated that, among the primary PTSD group, men improved significantly more over the course of therapy as compared to women, $\Lambda = .83$, F(1,30) = 6.31, p = .02, $\eta^2 = .17$. Among individuals in the primary alcohol group, however, there were no gender differences (see Figure 7).

For the *Psychiatric* score, a significant three-way Time X Order X Gender interaction was observed, $\Lambda = .89$, F(1,51) = 6.38, p = .02, $\eta^2 = .11$. Among individuals in the primary PTSD group, a significant two-way Time X Gender interaction was observed, indicating that men demonstrated greater improvement over the course of therapy as compared to women, $\Lambda = .84$, F(1,31) = 6.04, p = .02, $\eta^2 = .16$ (see Figure 8). Among individuals in the primary alcohol group only, a significant main effect of Time was observed, indicating that participants in the primary alcohol group as a whole improved over the course of therapy, $\Lambda = .45$, F(1,20) = 24.89, p = .00, $\eta^2 = .55$ (see Figure 8). No other significant main effects or interactions were observed.

A trend toward a main effect of Order was observed for the *Employment* subscale, indicating that individuals in the primary alcohol group scored higher than individuals in the primary PTSD group, F(1,47) = 3.44, p = .07, $\eta^2 = .07$.

Significant main effects of Time were observed for the D*rug Use* subscale, $\Lambda = .89$, F(1,41) = 5.31, p = .03, and the Legal subscale, $\Lambda = .89$, F(1,50) = 6.30, p = .02. This indicates that participants, as a whole, improved on these subscales over the course of therapy.

<u>HamD.</u> A significant Order X Gender interaction was observed, F(1,45) = 4.56, p = .04, $\eta^2 = .09$. Follow up tests indicated that, among individuals in the primary PTSD group, there was a main effect of Time, indicating that depressive symptoms decreased over the course of therapy for all participants with primary PTSD, $\Lambda = .33$, Huynh-Feldt

 $F(2.84, 79.39) = 17.31, p = .00, \eta^2 = .67$ (see Figure 9). No other significant main effects or interactions were observed.

Among individuals in the primary alcohol group, there was also a main effect of Time, $\Lambda = .49$, Huynh-Feldt, F(2.33, 39.64) = 10.73, p = .00, $\eta^2 = .39$ (see Figure 9). In addition, a trend toward a main effect of Gender was observed among individuals in the primary alcohol group, indicating that women scored higher than men on the HamD, F(1,17) = 4.14, p = .06, $\eta^2 = .20$.

<u>Retention.</u> Overall, 65.1% (n = 56) of the sample completed treatment, as defined a priori by attending 7 of the 12 sessions. Approximately 67.9% (n = 36) of the primary PTSD and 60.6% (n = 20) of the primary alcohol group completed treatment, and this difference was not statistically significant. Approximately 78.0% (n = 32) of women and 53.3% (n = 24) of men completed treatment, and this difference was statistically significant, $\chi^2(1) = 5.77$, p = .02.

<u>Number of sessions.</u> The average number of therapy sessions attended during the course of treatment was examined. Independent variables were Order and Gender. A main effect of Gender was observed, indicating that women attended a greater number of sessions (M = 8.73, SD = 3.82) than men (M = 6.98, SD = 4.13), F(1,82) = 6.57, p = .01, $\eta^2 = .07$.

Other group attendance. The average number of outside groups (e.g., Alcoholics Anonymous, church groups) that participants attended each week was examined using repeated measures ANOVA. The between-subjects factors were Order and Gender. The within-subject factor was Time (baseline, week 4, week 8, and week 12). A main effect of Gender was observed, indicating that men attended significantly more groups each week (M = 2.60, SD = 3.50) as compared to women (M = .78, SD = .79), F(1,39) = 5.56, p = .02, $\eta^2 = .13$. After excluding one outlier who attended approximately 15 groups (mainly Alcoholics Anonymous) per week, the results were still significant for a main

<u>Demographic Characteristics of Participants Used in the Analyses (n = 86)</u>

Characteristic	
Age, M (SD)	37.12 (8.64)
Education, years M (SD)	12.75 (2.29)
Gender	
% Men	52.3
% Women	47.7
Marital Status	
% Married	23.3
% Single, never married	31.4
% Separated	15.1
% Divorced	25.6
% Widowed	3.5
Race	
% Caucasian	83.7
% African American	12.8
% Hispanic	1.2
% American Indian or Asian	2.3

	Order of Onset			
	Primary PTSD		Primary	Alcohol
	Men	Women	Men	Women
	M(SD)	M(SD)	M(SD)	M(SD)
Baseline Measure				
Addiction Severity Index				
Medical	0.35 (0.38)	0.38 (0.36)	0.25 (0.38)	0.30 (0.32)
Employment	0.45 (0.33)	0.39 (0.28)	0.55 (0.35)	0.49 (0.32)
Alcohol Use	0.60 (0.23)	0.53 (0.18)	0.59 (0.21)	0.49 (0.25)
Drug Use	0.06 (0.08)	0.04 (0.06)	0.04 (0.09)	0.01 (0.02)
Family/Social	0.44 (0.27)	0.36 (0.23)	0.29 (0.21)	0.32 (0.25)
Legal	0.14 (0.21)	0.11 (0.18)	0.10 (0.18)	0.03 (0.09)
Psychiatric	0.52 (0.18)	0.43 (0.19)	0.48 (0.17)	0.58 (0.11)

Means and Standard Deviations of Baseline Addiction Severity Index Scores

Trauma History a	and Total	Number of	Traumas	Endorsed
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	Order of Onset			
	Primary PTSD		Primary	Alcohol
	Men Women		Men	Women
	M(SD)	M(SD)	M(SD)	M (SD)
Type of Trauma				
Natural Disaster	1.45 (1.22)	1.16 (0.90)	0.87 (0.69)	0.90 (0.74)
Combat	0.09 (0.29)	0.00 (0.00)	0.22 (0.42)	0.00 (0.00)
Aggravated Assault ^a	2.50 (1.65)	1.41 (1.57)	1.52 (1.27)	1.40 (1.34)
Attacked ^b	1.36 (0.95)	1.65 (1.47)	0.83 (1.15)	1.90 (1.60)
Parental Assault	1.00 (0.98)	1.32 (1.54)	0.83 (0.98)	0.60 (0.70)
Serious Injury	0.77 (1.11)	0.52 (0.77)	0.26 (0.62)	0.80 (1.03)
Fear Killed/Injured ^c	0.86 (0.99)	0.74 (0.95)	0.52 (0.90)	0.30 (0.48)
Witness ^d	1.45 (0.91)	1.22 (1.43)	1.56 (1.59)	0.40 (0.52)
Homicide ^c	1.05 (1.21)	0.90 (1.01)	0.78 (1.09)	0.70 (0.82)
Other Event	1.50 (1.54)	1.10 (1.14)	1.00 (0.90)	1.30 (0.82)
Sexual Traumas	1.36 (1.50)	3.09 (1.45)	0.87 (1.06)	2.20 (1.75)
Serious Accidents	2.27 (1.49)	1.23 (1.17)	2.65 (1.97)	0.90 (0.74)
Total No. Of Traumas	9.27 (2.43)	9.74 (3.04)	7.52 (2.68)	8.70 (3.65)

^aBeing physically attacked with a weapon.

^bBeing attacked without a weapon but with the intent to seriously injure.

^cExperiencing other situations in which the person feared they might be killed or seriously injured.

^dWitnessing someone seriously injured or violently killed.

^eHomicide or sudden death or a family member or close friend.

Means and Standard Deviations of PTSD Measures at Baseline, Week 4, Week 8 and Week 12

	Order of Onset			
	Primary PTSD		Primary	Alcohol
	Men	Women	Men	Women
	M(SD)	M(SD)	M(SD)	M (SD)
PTSD Measures				
IES Total				
Baseline	34.11 (16.06)	43.41 (15.99)	48.00 (15.40)	41.14 (19.89)
Week 4	27.54 (20.63)	35.95 (14.46)	39.19 (19.61)	41.42 (10.18)
Week 8	26.44 (16.83)	34.12 (15.71)	30.90 (21.48)	36.00 (26.50)
Week 12	22.89 (17.18)	29.94 (18.33)	33.38 (22.07)	29.29 (21.19)
MISS Total				
Baseline	123.67 (22.15)	111.69 (23.74)	111.01 (25.56)	115.19 (15.49)
Week 4	106.65 (27.41)	103.21 (22.80)	100.47 (27.82)	100.14 (10.96)
Week 8	100.74 (19.94)	97.31 (21.34)	100.30 (29.04)	99.14 (30.23)
Week 12	95.22 (22.99)	95.00 (19.69)	94.60 (23.56)	99.71 (14.11)
CAPS Total				
Baseline	51.89 (17.89)	57.47 (18.64)	57.36 (20.19)	68.25 (20.32)
Week 4	38.53 (26.33)	38.86 (20.32)	43.64 (24.21)	51.00 (17.03)
Week 8	25.89 (14.52)	33.86 (17.95)	38.55 (26.44)	49.87 (25.58)
Week 12	27.53 (19.25)	31.04 (21.03)	30.27 (20.61)	44.13 (24.15)

<u>Note</u>. IES = Impact of Events Scale, MISS = Mississippi Scale for PTSD, CAPS = Clinician Administered PTSD Scale.

Order of Onset				
Primary PTSD		Primary	/ Alcohol	
Men	Women	Men	Women	
M(SD)	M(SD)	M(SD)	M (SD)	
0.44 (0.42)	0.43 (0.35)	0.27 (0.39)	0.34 (0.34)	
0.22 (0.32)	0.31 (0.33)	0.25 (0.33)	0.50 (0.23)	
0.39 (0.30)	0.43 (0.30)	0.55 (0.35)	0.51 (0.36)	
0.31 (0.26)	0.31 (0.26)	0.54 (0.37)	0.51 (0.37)	
0.58 (.21)	0.54 (0.17)	0.55 (0.22)	0.41 (0.22)	
0.14 (.14)	0.25 (0.16)	0.29 (0.20)	0.33 (0.17)	
0.05 (0.07)	0.05 (0.07)	0.04 (0.09)	0.01 (0.02)	
0.02 (0.03)	0.02 (0.03)	0.00 (0.00)	0.01 (0.01)	
0.59 (0.22)	0.34 (0.23)	0.22 (0.18)	0.34 (0.27)	
0.21 (0.22)	0.20 (0.22)	0.21 (0.16)	0.32 (0.23)	
0.20 (0.26)	0.01 (0.16)	0.13 (0.20)	0.04 (0.11)	
0.04 (0.06)	0.05 (0.15)	0.05 (0.12)	0.00 (0.00)	
0.63 (0.09)	0.40 (0.19)	0.42 (0.18)	0.60 (0.09)	
0.24 (0.22)	0.25 (0.25)	0.27 (0.25)	0.34 (0.18)	
	Primar Men M (SD) 0.44 (0.42) 0.22 (0.32) 0.39 (0.30) 0.31 (0.26) 0.58 (.21) 0.14 (.14) 0.05 (0.07) 0.02 (0.03) 0.59 (0.22) 0.21 (0.22) 0.20 (0.26) 0.04 (0.06) 0.63 (0.09) 0.24 (0.22)	Order of Primary PTSD Men Women M (SD) M (SD) 0.44 (0.42) 0.43 (0.35) 0.22 (0.32) 0.31 (0.33) 0.39 (0.30) 0.43 (0.30) 0.39 (0.30) 0.43 (0.30) 0.39 (0.30) 0.43 (0.30) 0.39 (0.30) 0.43 (0.30) 0.31 (0.26) 0.31 (0.26) 0.58 (.21) 0.54 (0.17) 0.14 (.14) 0.25 (0.16) 0.05 (0.07) 0.05 (0.07) 0.02 (0.03) 0.02 (0.03) 0.59 (0.22) 0.34 (0.23) 0.20 (0.26) 0.01 (0.16) 0.04 (0.06) 0.05 (0.15) 0.63 (0.09) 0.40 (0.19) 0.24 (0.22) 0.25 (0.25)	Order of Onset Primary PTSD Primary Men Women Men M (SD) M (SD) M (SD) 0.44 (0.42) 0.43 (0.35) 0.27 (0.39) 0.22 (0.32) 0.31 (0.33) 0.25 (0.33) 0.39 (0.30) 0.43 (0.30) 0.55 (0.35) 0.31 (0.26) 0.31 (0.26) 0.55 (0.37) 0.58 (.21) 0.54 (0.17) 0.55 (0.22) 0.14 (.14) 0.25 (0.16) 0.29 (0.20) 0.05 (0.07) 0.05 (0.07) 0.04 (0.09) 0.02 (0.03) 0.02 (0.03) 0.02 (0.03) 0.59 (0.22) 0.34 (0.23) 0.22 (0.18) 0.21 (0.22) 0.20 (0.22) 0.21 (0.16) 0.20 (0.26) 0.01 (0.16) 0.13 (0.20) 0.63 (0.09) 0.40 (0.19) 0.42 (0.18) 0.24 (0.22) 0.25 (0.25) 0.27 (0.25)	

Means and Standard Deviations of the ASI Composite Scores at Baseline and Week 12

Note. ASI = Addiction Severity Index.



<u>Figure 1</u>. Baseline ASI Psychiatric Subscale Score.



<u>Figure 2.</u> Baseline Hamilton Depression Score.

effect of Gender, with men attending more groups (M = 1.83, SD = 1.47) than women (M = .78, SD = .79), F(1,38) = 8.14, p = .01, $\eta^2 = .18$.









<u>Figure 4.</u> Percent of Days Drinking and Average Drinks per Drinking Day Over the Course of Therapy.



Figure 5. Average Percent of Drinking Days (PDD) and Average Drinks Per Drinking Day (DDD) During Treatment.



<u>Figure 6.</u> ASI Medical, Alcohol, and Family/Social Subscale Scores Over the Course of Treatment.

ASI Family/Social Subscale







Figure 7. ASI Family/Social Subscale Scores Over the Course of Treatment by Order and Gender



<u>Figure 8.</u> ASI Psychiatric Subscale Scores Over the Course of Treatment by Order and Gender

Hamilton Depression Scale





Figure 9. Hamilton Depression Scores Over the Course of Treatment by Order and Gender

TIME

Men Women

Week 12

5

0 Baseline

CHAPTER 4

DISCUSSION

The primary goal of this study was to investigate the clinical utility of considering the relative order of onset of PTSD and alcohol dependence in individuals with both disorders. This is the first study to our knowledge that has examined differential presentation and treatment response among individuals with alcohol dependence and PTSD by order of onset. The findings revealed theoretically and clinically meaningful differences at baseline and at the end of treatment.

Clinical Presentation

Consistent with prior research (Jacobsen, Southwick, & Kosten, 2001; Stewart, Pihl, Conrod, & Dongier, 1998), the diagnosis of PTSD most often precedes the diagnosis of alcohol dependence. In the current sample, 56.4% reported primary PTSD. Findings from other studies, including both community and treatment-seeking samples, estimate that PTSD is primary in approximately 65% to 84% of cases among SUD-PTSD individuals (Epstein et al., 1998; Kessler et al., 1997; Najavits, Weiss, & Shaw, 1999). The rates found in these other studies may be higher because some samples included individuals with drug dependence, which typically begins at a later age than alcohol dependence, and some samples were comprised of only women. Similar to the findings of the current study, higher rates of primary PTSD are more often found among women as compared to men (Brady et al. 1998; Kessler et al., 1997; Najavits, Weiss, & Shaw, 1999).

Examination of pretreatment clinical symptom presentation revealed several interesting findings. Based on previous research (Nishith et al., 1997; Schuckit, 1985), it

was predicted that individuals with primary PTSD would present with a more severe clinical profile, as compared to individuals with primary alcohol dependence. Some support for this hypothesis was found. Men with primary PTSD demonstrated higher levels of distress and depression, as evidenced by their scores on the ASI Psychiatric subscale and the Hamilton Depression Scale, when compared to their counterparts. However, women with primary alcohol dependence demonstrated higher levels of distress and depression when compared to their counterparts. Several factors involving social, psychological, and biological elements may help explain these findings. From a sociocultural view, men with primary PTSD and women with primary alcohol dependence represent the more aberrant, socially deviant groups. That is, statistically one would expect that women would first develop PTSD and then alcohol dependence. In contrast, one would expect that men would first develop alcohol dependence and then PTSD. Thus, the potential stigma associated with these particular developmental paths of psychopathology may be even more intense, and result therefore in higher levels of distress and depression than would be expected for individuals who fall within the expected trajectories of developing these dual disorders (cf. Sinha & Rounsaville, 2002). Research has shown that women seeking treatment for alcohol problems encounter greater opposition to treatment from their family, friends, and partners as compared to men (Canterbury, 2002). Sociocultural factors such as these could affect, in particular, the sympomatology observed among women with primary alcohol dependence. Further research is needed to systematically examine the sociocultural experiences of men and women with primary and secondary alcohol dependence and PTSD, and their associated influence on psychological health.

Biological differences among men and women may also help explain these findings. For example, research demonstrates that when compared to men, women 1) have lower levels of alcohol dehydrogenase, which means that they metabolize alcohol at a much slower rate, 2) achieve higher blood alcohol levels after drinking comparable amounts of alcohol due to a lower total body water content, which means that they become intoxicated after consuming smaller amounts of alcohol, and 3) have smaller sized livers, which may further affect the metabolism of alcohol, (Blume, 1998; Canterbury, 2002; Lex, 2000; Randall, Roberts, Del Boca, Carroll, Connors, & Mattson, 1999). These differences in biology and the way that alcohol affects the physiology of women are likely related to the phenomenon of "telescoping." Telescoping is a term used to describe the fact that women with alcohol dependence evidence a shorter time from first use of alcohol to the development of alcohol-related problems, have significantly higher morbidity rates, and have a greater sensitivity to the toxic effects of alcohol on the myocardium, brain tissue, and liver than do men with alcohol dependence (Canterbury, 2002; Randall et al., 1999). Thus, it could be that women who develop alcohol dependence early on suffer from even greater social stigma, than do men who develop alcohol dependence early on in their lives. This could result in greater depression and overall distress among these women.

Further support was provided for the hypothesis that individuals with primary PTSD would present with a more severe clinical profile. Individuals with primary PTSD reported a more extensive trauma history as compared to individuals with primary alcohol dependence. While individuals in both groups reported exposure to multiple lifetime traumatic events, the overall number was significantly higher for the primary PTSD group. In addition, there was a trend toward significance for the primary PTSD group to score higher than the primary alcohol group on the ASI Family/Social scale.

Only one other study to our knowledge has been published on differences in clinical presentation among individuals with an SUD and PTSD. Brady et al. (1998) examined differences among individuals with cocaine dependence and PTSD. Consistent with Brady et al.'s findings, there were no significant differences in baseline substance use severity by order of onset. Other studies examining individuals with a SUD and comorbid anxiety (not specific to PTSD) or affective disorder have also failed to find significant differences in baseline substance use severity by primary or secondary disorder (Nishith et al., 1997). It is also possible, however, that the similarity in symptomatology among individuals with differing order of onset is related to recruitment. The participants in the current study and the other studies mentioned represent clinical samples of individuals who were required to meet diagnostic criteria for substance dependence according to the SCID. It is possible that in community samples differences in PTSD and/or substance use severity by order of onset might be observed. Response to Treatment

Examination of PTSD symptom improvement over the course of therapy revealed that the majority of participants significantly improved over time. Recall that the treatment employed in this study was CBT for substance abuse. PTSD was not directly targeted or addressed in therapy. Given this, the PTSD improvement observed during treatment was unexpected. It had been predicted that participants with primary PTSD would demonstrate less PTSD symptom improvement in response to CBT for substance use, as compared to participants with primary alcohol dependence, but this hypothesis was not supported. Instead, the findings suggest that as levels of alcohol consumption decrease, so do levels of PTSD symptoms. For those individuals in the study who did not experience a significant reduction in PTSD symptoms, their alcohol use during treatment was more severe. The alcohol may, therefore, be at least partially responsible for exacerbating and/or maintaining their PTSD symptoms. Consumption of alcohol could do so by serving as an avoidance mechanism, increasing affective numbing, decreasing interest or pleasure in activities, and by increasing hyperarousal symptoms of irritability, sleep disturbance, and difficulty concentrating (cf. Stewart et al., 1998). Attempts to differentiate symptoms caused by PTSD, by alcohol, or by a combination of both are very difficult. It is also possible that the causes of symptoms may change over time. For example, trauma survivors may at first experience PTSD symptoms as a result of the

trauma, but then their use of alcohol may also contribute to the maintenance of these symptoms and possibly the development of PTSD over time. Future research is needed to help increase understanding of how these dual disorders interact over time.

Although the finding of global PTSD improvement among participants in the study was not predicted, it is similar to the finding of Dansky, Brady, and Saladin (1998). Dansky et al. examined changes in PTSD symptoms among 34 individuals with cocaine dependence and PTSD who were enrolled in a 12-week pharmacological trial. Like the current study, their study did not include any treatment for PTSD. At the end of treatment, approximately 60% of the participants who met criteria for PTSD at treatment entry no longer met criteria. Thus, approximately 60% of participants in their study experienced significant improvement over the course of therapy, even though their PTSD symptoms were not directly targeted in therapy. This finding is similar to the current finding that approximately 64% of the sample were PTSD treatment responders (i.e., they experienced a decrease of 30% of more on their CAPS total score). No other study to our knowledge has been published on PTSD symptom improvement among alcoholdependent individuals who are receiving treatment for their addiction. Other researchers have noted that symptoms of anxiety often abate among individuals with comorbid anxiety disorders (e.g., generalized anxiety disorder, simple phobia) and addiction as their levels of substance use abate (Thevos et al., 1991).

Interestingly, there was no observation of PTSD symptoms increasing over time. Some authors have reported that PTSD symptoms increase following initial abstinence from alcohol, and that this serves to increase the risk of relapse as a result of individuals returning to substance use to manage their elevated symptoms (cf. Stewart, 1999). This hypothesis has been noted in the literature and some anecdotal research has provided support for this, but this has not been systematically investigated. In the current study, PTSD symptoms did not increase, but rather decreased as alcohol use decreased. There may be particular subgroups of individuals within the SUD-PTSD category that are at greater risk for relapsing because of elevations in their PTSD symptoms following initial abstinence. In the current study, it was observed that individuals who did not experience a significant reduction in PTSD symptoms consumed more alcohol during treatment. However, it is unclear whether the consumption of alcohol served to maintain their level of PTSD symptoms, or whether their PTSD symptoms served to maintain their level of alcohol consumption, or some combination thereof. Regarding order of onset, this study found no significant differences between groups in PTSD improvement or in the latency of time to first drink or first heavy drinking day.

Examination of alcohol use during the course of therapy revealed that both the primary PTSD and primary alcohol groups demonstrated significant improvement in the percent of days drinking (PDD) and the average drinks per drinking day (ADD). Thus, as a whole, participants drank less often and consumed less alcohol during therapy. Consistent with prior research, men consumed greater amounts of alcohol at pretreatment (Lex, 2000). A nonsignificant pattern was observed for men with primary alcohol dependence to have higher levels of PDD and ADD over the course of treatment than other participants in the study. Although this finding did not reach statistical significance, the pattern observed in the current study could indicate a particular need for more intensive efforts targeting alcohol use among men with primary alcohol dependence. More research, however, is needed to help clarify this potential need. Overall, the findings from this study are consistent with prior research showing that CBT for substance use is effective in reducing alcohol consumption among individuals with alcohol dependence (Galanter & Kleber, 1999; Miller et al., 1995).

In addition to alcohol use indices, other indices of improvement (e.g., medical health, quality of family and social relationships, level of psychiatric distress, employment) were examined. In general, the primary PTSD group appeared to derive greater benefit from therapy as compared to the primary alcohol group when considering these other indices. Guided by the few studies that have examined order of onset among other dual diagnosis groups (e.g., substance use and comorbid depression or antisocial personality disorder), it was hypothesized that individuals with primary alcohol dependence would respond more favorably to this therapy, which focused on substance use problems. However, this hypothesis was not supported. Individuals with primary alcohol dependence may be more treatment resistant, may require other forms of treatment, or may require longer periods of treatment in order to demonstrate progress with regard to improvement in peripheral areas. In addition, it may be that some of the "nonspecifics" of therapy (e.g., empathy, active listening) are more therapeutic for individuals with primary PTSD. Further research is needed to increase understanding of how and why order of onset relates to differential treatment response.

Regarding overall levels of emotional distress, women with primary alcohol dependence appeared to be particularly vulnerable as evidenced by their high scores on the ASI Psychiatric subscale and the Hamilton depression scale throughout the course of therapy. Given this, it is reasonable to suggest that women with primary alcohol dependence may be at greater risk for relapse or other psychological difficulties following treatment. This subgroup may be in need of particular preventative interventions or aftercare treatment to guard against these potential risks. Even though their PTSD symptoms and alcohol use consumption decreased during treatment, residual depression and psychiatric distress that remain untreated among these individuals may lead to a return to substances following treatment. Research demonstrates that the link between depression and relapse to alcohol appears to be especially pertinent for women (Brady & Randall, 1999; Gilman & Abraham, 2001). Women have been found to be more likely than men to use substances in response to dysphoric states, affective triggers, and external stressors (Brady & Randall, 1999). Again, this highlights the potential vulnerability of these individuals, in particular, to return to alcohol in order to cope with residual or treatment resistant negative affect.
Women did attend a significantly greater number of sessions during therapy than men. Previous psychotherapy treatment studies have reported that individuals with greater distress, particularly anxiety and depression, often remain in treatment longer (Carroll et al., 1993, 1994; Siqueland et al., 1998). Siqueland (1998) suggested that individuals with higher levels of depression may be more motivated to stay in treatment in order to alleviate these symptoms. Several other potential explanations exist, such as gender socialization differences, which may influence levels of compliance, and the fact that men attended a greater number of outside groups during therapy. The attendance at outside groups by men may have reduced their commitment or desire to continue in individual therapy.

Limitations of the Study

Several limitations of the current study warrant consideration. This study included treatment-seeking individuals with alcohol dependence and PTSD. The findings from this study may not generalize to non-treatment seeking individuals, or to individuals with PTSD and other comorbid substance use disorders. In addition, recall bias may exist with regard to age of onset of alcohol dependence or PTSD. Because this study was not designed to examine differences in treatment response by order of onset, it is difficult to draw final conclusions from this study. Rather, the results are considered to represent an initial step toward increasing awareness of order of onset differences, the potential clinical utility of establishing the temporal order of onset among individuals with alcohol dependence and PTSD, and toward encouraging future research in this area.

Conclusions

The findings from the current study add to the literature on the relevance of considering the temporal order of onset among individuals with SUDs and PTSD. To date, little research has been conducted in this area. Prior research has focused mainly on 1) establishing that SUDs and PTSD frequently co-occur and 2) on the development and implementation of integrated treatments. Very little research has been conducted on

intradiagnostic distinctions within the SUD-PTSD dual diagnosis group. The findings from the current study increase our understanding of variations within this heterogeneous group and demonstrate that SUD-PTSD clients do present with varying levels of distress at treatment entry and they do respond differently to treatment based on their order of onset. This finding brings into question current practices of offering the same form of treatment to these individuals, regardless of their order of onset. The findings also highlight that differences in clinical presentation and treatment response may differ among men and women, and that gender needs to be considered when deciding how to best treat individuals with comorbid alcohol dependence and PTSD.

With regard to PTSD improvement, the findings from this study suggest that addressing alcohol use *is* beneficial with regard to improving concurrent PTSD symptoms. For the majority of participants in this sample, regardless of their order of onset, PTSD symptoms improved during the course of CBT for substance use. This finding provides some support for sequential psychotherapies in which the alcohol use is targeted first in therapy and is then followed by treatment targeting the PTSD. Because the current study did not include any psychotherapy for PTSD, it is not possible to comment directly on whether or not including PTSD treatment concurrently or after alcohol use treatment would have provided additional benefits or would have helped to maintain treatment gains. This would be a very useful area of future research.

Although the findings from this study are preliminary in nature and future research is needed to replicate the findings, the results suggest that CBT for substance use is a beneficial form of treatment for individuals with alcohol dependence and PTSD. The majority of participants demonstrated significant improvement in their alcohol use and PTSD symptoms. Increases in PTSD symptoms were not observed. In addition, it appears that there are intradiagnostic groups, based on temporal order of onset and gender, that benefit more or less from this form of treatment.

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Future Studies

Future research is needed to help increase understanding of the mechanisms involved in the improvement of symptoms (e.g., PTSD) that are not directly targeted in therapy. In addition, continued work in the area of gender differences in initiation to substance use, maintenance and exacerbation of use, treatment-seeking decisions, treatment response, and perceptions of treatment care providers is needed.

At present, there is a strong movement in the field of psychology toward integrated treatments for individuals with comorbid SUDs and PTSD. More work is needed to help treatment care providers identify individuals who are good candidates for integrated treatments and those for whom integrated treatments may be countertherapeutic. Thus far, little if any attention has been paid to order of onset differences in response to integrated treatment. It is also unclear when in the process of integrated therapy PTSD should be targeted, and what "treatment" should constitute (e.g., psychoeducation, narrative exposure, imaginal or invivo exposure, assessment, some combination of these).

Research has shown that it is not necessarily the exposure to traumatic events, but rather the development of PTSD that places individuals at greater risk for developing a SUD (Chilcoat & Breslau, 1998; Stewart & Conrod, 2003). Further research is needed to help increase understanding of why and how the development of PTSD increases risk for substance use problems. Moreover, it is clear that not everyone who goes on to develop PTSD subsequently develops a SUD. Studies examining the protective factors involved in this would also be of great benefit to the field.

More specific to this study, future research is needed to help increase knowledge of whether including additional psychotherapy for PTSD, or following CBT for substance use with psychotherapy for PTSD would result in additional treatment gains. More research is also needed to help design effective treatments for individuals who do not respond as well to this form of treatment (e.g., individuals with primary alcohol dependence). Finally, more research in the area of client preferences would be beneficial. That is, increasing our knowledge of what types of treatment clients with alcohol dependence and PTSD prefer, how these preferences relate to treatment outcome, and if they differ by order of onset or gender.

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