Early-childhood trauma is strongly associated with developing mental health problems, including alcohol dependence, later in life. People with early-life trauma may use alcohol to help cope with trauma-related symptoms. This article reviews the prevalence of early-childhood trauma and its robust association with the development of alcohol use disorders and posttraumatic stress disorder. It also examines the potential biological mechanisms by which early adverse experiences can result in long-lasting changes in neurobiology underlying this vulnerability, as well as pharmacological and behavioral interventions. Recent investigations highlight the importance of assessing trauma among patients with alcohol use disorders and the positive benefits associated with the application of integrative psychosocial interventions that target both trauma-related symptoms and alcohol dependence.

Keywords: Alcohol dependence; alcohol use disorders; childhood; childhood trauma; trauma-related symptoms; posttraumatic stress disorder; coping with stress or anxiety; neurobiology; biological mechanisms; treatment; pharmacological intervention; behavioral intervention; integrative psychosocial intervention; adverse child-rearing environment

Prevalence

There is little doubt that severe childhood adversity may place an individual at life-long risk for a variety of problems, including those related to mental health, physical health, employment, and legal difficulties (Putnam 2006). In a study conducted by the Centers for Disease Control and Prevention and Kaiser Permanente (Adverse Childhood Experiences [ACE] study; Felitti et al. 1998), a sample of 17,337 adults recruited from a large health maintenance organization were surveyed concerning a range of adverse events that might occur during childhood (e.g., physical or sexual abuse, incarcerated household member, emotional neglect) and adult risk behaviors, health status, and disease. The investigators found a graded relationship between the number of adverse childhood experiences (i.e., ACE score), risk behaviors during adulthood, and leading causes of morbidity and mortality in the United States, including heart disease, diabetes, liver disease, and emphysema. It is possible that these increased rates of medical conditions are not a direct result of...
childhood adversity but rather the result of dysfunctional and unhealthy behaviors in which many victims of childhood abuse engage.

A number of studies also report that victims of child maltreatment are more likely to have emotional difficulties and psychiatric disorders. One of the most consistent results across these studies is the finding that childhood maltreatment is associated with an increased risk for alcohol and drug use disorders (Enoch 2011). In a population-based sample of 1,411 female adult twins, self-reported childhood sexual abuse was positively associated with a number of psychiatric disorders, but the strongest associations were with alcohol and drug dependence (Kendler et al. 2000). In the ACE study, the risk of alcohol dependence increased 7.2-fold, and illicit drug use increased 4.5-fold for people with four or more ACEs (Anda et al. 2006). People with a history of childhood abuse or neglect are vulnerable to using alcohol in order to cope with stressful situations, which in turn may lead to excessive alcohol use (Schuck and Widom 2001). An investigation by Widom and colleagues (2007) demonstrates that the increased risk of excessive alcohol use among victims of childhood abuse or neglect is consistent and stable into middle adulthood (e.g., age 40). Furthermore, research has shown that alcohol-dependent patients with a history of sexual abuse are more likely than nonabused patients to relapse to alcohol use (87.5 vs. 63.3 percent) and to relapse more quickly (median time to first drink = 60 vs. 115 days) in the first year following inpatient treatment for alcohol dependence (Greenfield et al. 2002).

In addition to alcohol use disorders, childhood adversity is associated with an increased risk of PTSD (Widom 1999). Data from a number of studies over the last 20 years have emphasized the high co-occurrence of PTSD and alcohol disorders. For example, among 3,768 female twins participating in the longitudinal Missouri Adolescent Female Twin Study (MOAFTS), Sartor and colleagues (2010) found that women exposed to trauma were nearly twice as likely to develop alcohol dependence (hazard ratio 1.85), and women exposed to trauma who also had PTSD were even more likely to develop alcohol dependence (hazard ratio 3.54; significantly higher than women with trauma exposure alone) when compared with women who had not experienced trauma. Studies of samples of individuals seeking treatment for alcohol use disorders also find a high prevalence of reported childhood adversity and PTSD. In a study of men and women in treatment for addictions, 62 percent reported having been victims of childhood physical or sexual abuse (Grice et al. 1995). A review of studies of individuals seeking treatment for addictions reveals rates of PTSD as high as 50 percent or greater (Dansky et al. 1994). In the majority of cases, the development of PTSD precedes the development of the substance use disorder.

These high rates of childhood victimization in individuals with PTSD and alcohol and other substance-related problems suggests that there is a link between childhood adversity and the development of these disorders, although it is impossible to establish a direct causal relationship. However, even when studies control for demographic differences, family discord, and parental pathology, the specific relationship between childhood abuse and the development of substance use disorders holds true. Several theoretical connections have been postulated (Miller et al. 1993). Childhood victimization may lead to low self-esteem and the subsequent use of alcohol to deal with negative cognitions. It also is possible that victims of childhood abuse feel that their experiences make them “different” from other children and lead them to withdraw from healthier social circles toward fringe groups, where alcohol use is more accepted. In any case, given that victims of child abuse are more likely to develop alcohol use disorders as adults, early intervention, prevention, and training for parents are all important in interrupting this cycle of violence and alcohol problems.

### Neurobiology

Recognizing the pervasive and detrimental effects of adverse childhood experiences on quality of life and health outcomes has led to the exploration of potential biological mechanisms by which early experiences can produce long-lasting changes. Evidence from both animal and human research suggests that early stressors can lead to neurobiological changes in systems known to be involved in the pathophysiology of depression, anxiety, and substance use disorders (De Bellis et al. 1999; Heim and Nemeroff 2001). The hypothalamic–pituitary–adrenal (HPA) axis plays a critical role in the stress response and is involved in the pathophysiology of addictive disorders. Early stressors cause long-term increases in the stress response of the hormone cortisol (Plotsky and Meaney 1993) as well as decreased genetic expression of cortisol receptors and increased expression of corticotropin-releasing factor in the hypothalamus, both of which may contribute to dysregulation of the HPA axis (Ladd et al. 1996). The noradrenergic system also plays a key role in stress (Bremner 2003), and early stressors can lead to long-term decreases in α-2 noradrenergic receptors in the locus coeruleus, which may lead to loss of feedback inhibition of noradrenergic activity with associated increases in the noradrenergic stress responses (Caldji et al. 1998; Sanchez et al. 2001).

In addition to the long-lasting effects of early trauma on the stress response, a number of studies indicate that early trauma has specific effects on the neurotransmitter systems involved in the positive reinforcing effects of alcohol and drugs, particularly the brain pathway for dopamine (i.e., the mesocorticolimbic dopamine system (Meaney et al. 2002). Higley and colleagues (1991) found that adult rhesus monkeys raised in peer groups without maternal care showed increased HPA response to stress and increased alcohol consumption during periods of stress (Higley et al. 1991). In a series of studies, Meaney
and colleagues (2002) demonstrated that repeated periods of maternal sepa-
ration in the early life of rats decreased dopamine transporter expression and
increased dopamine responses to stress and behavioral responses to stress,
cocaine, and amphetamine. These findings suggest that early-life experi-
cences can affect the development of the mesocorticolimbic dopamine system
and lead to a vulnerability to addiction in later life. Thus, in addition to effects
on stress reactivity, early-life events might predispose individuals to the develop-
ment of alcohol use disorders by directly influencing the reinforcing effects of
alcohol. Other neurotransmitter systems involved in the pathophysiology of
alcohol dependence, such as brain-derived neurotrophic factor (BDNF),
serotonin, and γ-aminobutyric acid (GABA) systems also are affected by
early-life trauma in ways that may influence vulnerability to the develop-
ment of alcohol dependence, but the mechanistic connections in these systems
are under active investigation and are not as well understood (Enoch 2011).

Not all children exposed to early-life trauma develop alcohol dependence or other significant pathology, clearly sug-
gest that resilience and mediating factors play a role (Enoch 2011).

The genetic risk for alcohol and drug dependence involves multiple genes. Emerging evidence suggests that varia-
tion in some stress-related genes may determine the risk for psychopathology
or resilience in people exposed to early-life trauma. In particular, it seems that there are important variations in the
genes encoding the CRF system that can influence the development of alcohol dependence following an early-
life trauma in a gene-by-environment interaction. One study of at-risk children
found an interaction between a particu-
lar genetic variant coding for the CRF
receptor (i.e., CRHR1) and sexual trauma in adolescents that predicted an
earlier age of onset of drinking and
heavy alcohol consumption (Blomeyer
et al. 2008). This finding is supported by animal studies demonstrating that
the CRHR1 genotype and expression
interact with environmental stress to
reinstate alcohol-seeking in rodents
(Hansson et al. 2006), and a functional
CRF promoter variant in monkeys
conferred increased stress reactivity and
was associated with increased alcohol
consumption in animals reared under
stressful conditions (Barr et al. 2009).
These findings suggest that the interac-
tion of genetic susceptibility and envi-
ronmental exposure can lead to a
pathologically activated CRF system,
which increases the risk for the devel-
opment of alcohol dependence in
some people.

**Treatment**

Both behavioral and pharmacological interventions are important to consider
in the treatment of alcohol dependence and trauma/PTSD (Davis et al. 2006;
Weiss and Kuepennenbender 2006). To date, most empirical studies of behav-
ioral or pharmacological agents have investigated the treatment of either
alcohol dependence or PTSD alone.

**Psychosocial Interventions**

With regard to psychosocial interven-
tions, cognitive–behavioral therapies
(CBTs) are the most widely studied
and empirically valid treatments for
both PTSD and alcohol use disorders.
The CBTs used to treat PTSD fall into
three main categories: (1) exposure-based
therapies, (2) cognition-focused ther-
apy, and (3) anxiety/stress-management
therapy. Exposure-based therapies
are considered the gold standard treatment
for PTSD (Institute of Medicine 2008)
and involve having patients confront
safe, but anxiety-provoking situations
(i.e., physical location where childhood
abuse occurred), known as in vivo
exposure; and the memory of the trau-
matic experience, known as imaginal
exposure (Foa et al. 2006). With pro-
longed, repeated in vivo and imaginal
exposure, the trauma-related anxiety is
extinguished. Cognition-focused therapy
includes cognitive therapy, which
addresses the meaning that people
assign to early-life trauma; and cognitive-

processing therapy, which combines a
narrative element of exposure therapy
with efforts to identify and modify
unhelpful cognitions related to the
themes of safety, trust, power, esteem,
and intimacy (Resick and Schnicke
1992). Finally, stress inoculation train-
ing (Meichenbaum and Novaco 1985),
one of the most widely used and
empirically investigated forms of anxiety
management therapies, aims to provide
a sense of mastery over PTSD symptoms
by teaching patients a variety of coping
skills. Stress inoculation training also
has been incorporated into CBTs for
substance use disorders and includes
relaxation training, breathing retrain-
ing, thought stopping, self-instruction
training, assertiveness training, cogni-
tive restructuring, anger management,
and problem solving.

Recently, integrative psychosocial
interventions have been developed to
address both trauma/PTSD and sub-
stance use disorders simultaneously
(Back 2010). Clinicians previously
believed that trauma interventions
were inappropriate until after a patient
had been abstinent from alcohol or
drugs for a sustained period of time
(e.g., 3 months). This model, known as
the “sequential” model, posits that
continued alcohol use impedes thera-
peutic efforts to address and process
the trauma, and that trauma interven-
tions commenced before sustained
abstinence would result in increased
risk of relapse. Contrary to these beliefs,
however, recent data reported by several
different investigators in the United
States and Australia show that treatment
outcomes of substance dependent patients
who engage in integrative CBT inter-
ventions typically experience signifi-
cant improvements in both conditions
and that rates of relapse are not increased
by the introduction of therapy for
trauma (Brady et al. 2001; Hien et al.
2004; McGovern et al. 2009; Najavits
2002; Triffleman et al. 1999). Proponents
of integrative treatments posit that
unprocessed trauma-related memories
and PTSD symptoms may, at least in
part, drive alcohol use. Thus, attending
to and treating the trauma-related
symptoms early in the process of therapy may improve the chances of long-term recovery from alcohol (Back et al. 2006; Hien et al. 2010). Although more randomized controlled trials of integrative treatments are needed, the studies to date clearly demonstrate that for the majority of alcohol-dependent patients with trauma/PTSD, the inclusion of trauma interventions confers substantial therapeutic benefits.

Pharmacological Interventions

There are several general issues to consider when treating co-occurring alcohol dependence and trauma/PTSD. When pharmacological agents are used, treatment should generally follow routine clinical practice for the treatment of PTSD. Regardless, relapse is common, and it is critical to consider the potential toxic interactions that may occur between the prescribed medication and alcohol. Given the high co-occurrence of alcohol and illicit drug use, potential toxic interactions between the prescribed medication and other substances of abuse must also be addressed. The pharmacological agent with the least abuse liability potential should be chosen for this population. Although benzodiazepines are effective in providing immediate relief of anxiety symptoms, they are generally not considered a first-line treatment for patients with alcohol dependence given the abuse potential of benzodiazepines. During the initial phase of treatment, when latency of onset of antidepressants is an issue, benzodiazepines may be considered as adjunctive medication. The amount of benzodiazepines prescribed to the patient should be limited, and the patient should be closely monitored for relapse or nonmedical use of benzodiazepines or other medications.

The use of pharmacological agents to specifically target alcohol dependence and PTSD is underexplored. Most studies to date, however, show promise and suggest that patients with co-occurring alcohol dependence and trauma/PTSD respond well to standard PTSD pharmacotherapies. Sertraline, a serotonin-specific reuptake inhibitor, has been investigated in patients with comorbid alcohol dependence and PTSD. The first study was a small (n = 9) open-label, 12-week trial, which demonstrated significant pre–post decreases in alcohol use severity (e.g., number of drinking days, number of drinks per day), as well as PTSD symptoms of re-experiencing the trauma, avoidance, and hyperarousal (Brady et al. 1995). A second study examined the efficacy of 12 weeks of sertraline compared with placebo in 94 patients with alcohol dependence and PTSD (Brady et al. 2005). The primary outcome analysis indicated no significant effect of sertraline on alcohol-related outcomes and only trend-level findings for the PTSD outcomes. The sertraline-treated group showed statistical trends for greater improvement in the experience of sudden flashbacks of the traumatic event and hyperarousal symptoms (e.g., insomnia, inability to concentrate). Follow-up cluster analyses suggested that individuals with primary PTSD, compared with primary alcohol dependence, derived more benefit from sertraline treatment as evidenced by significantly less severe alcohol use. The results suggested that patients with early-onset alcohol dependence actually had worse alcohol-related outcomes with sertraline treatment compared with placebo (Brady et al. 2005).

In another study of 254 veterans with alcohol dependence and a variety of co-occurring mood and anxiety disorders (Petrakis et al. 2005), naltrexone, disulfiram, or a combination of both was added to treatment as usual. A high percentage (42.9 percent) of the study participants had PTSD, although data analysis for specific disorders was not conducted. Alcohol-related outcomes improved significantly in patients treated with either medication alone or with combination therapy, compared with placebo, but there was no added improvement with combination therapy when compared with monotherapy. This study strongly suggests that alcohol-dependent patients with co-occurring PTSD should receive medications targeting alcohol consumption.

There is good rationale for the exploration of a number of other compounds in the treatment of co-occurring PTSD and alcohol dependence. Prazosin blocks a specific α1-adrenergic receptor and has shown promise in several well-controlled trials for the treatment of PTSD, particularly in decreasing PTSD-related sleep disturbance and nightmares (Raskin et al. 2007). In a preliminary study, prazosin decreased alcohol consumption in an alcohol-dependent population (Simpson et al. 2009). This inexpensive and relatively safe drug warrants investigation in the treatment of co-occurring PTSD and alcohol dependence. In addition, several anticonvulsant agents, such as topiramate, have shown promise in the treatment of alcohol dependence (Johnson et al. 2003). It is hypothesized that actions on the glutamatergic systems might be responsible for these agents’ therapeutic actions. PTSD also has been associated with glutamatergic dysregulation, and anticonvulsant agents have shown promise in small-number, open-label studies in the treatment of PTSD. This is another area in which additional investigation is warranted. More research clearly is needed to help advance the behavioral and pharmacological treatment of co-occurring trauma/PTSD and substance use disorders.

Conclusions

Epidemiologic studies as well as studies in treatment-seeking populations converge to support the finding that early-life trauma is common in people with alcohol dependence. There are a number of potential mechanistic explanations for the connection between early-life trauma and the development of alcohol dependence. These include psychological and developmental issues that are affected by trauma, as well as neurobiological effects of early trauma that can lead to increased vulnerability to the development of alcohol and other substance use disorders. These explanatory
hypotheses are not mutually exclusive. There is a growing literature on efficacious psychosocial and pharmacotherapeutic treatments for individuals with co-occurring PTSD and alcohol dependence. Integrative psychosocial interventions combining efficacious interventions from the alcohol and PTSD fields have shown promise. Evidence suggests that agents targeting alcohol consumption (i.e., disulfiram, naltrexone) can be useful in patients with co-occurring PTSD and alcohol dependence, but additional investigation clearly is needed.

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