Published in final edited form as:
Addict Behav. 2009 ; 34(6-7): 554–560. doi:10.1016/j.addbeh.2009.03.011.

Cognitive-behavioral therapy for panic disorder in patients being treated for alcohol dependence: Moderating effects of alcohol outcome expectancies☆

Matt G. Kushner*, **Sandra Sletten**, **Christopher Donahue**, **Paul Thuras**, **Eric Maurer**, **Antonina Schneider**, **Brenda Frye**, and **Joani Van Demark**
University of Minnesota, Department of Psychiatry, United States

Abstract

Anxiety disorders commonly co-occur with alcohol use disorders and reliably mark a poor response to substance abuse treatment. However, treating a co-occurring anxiety disorder does not reliably improve substance abuse treatment outcomes. Failure to account for individual differences in the functional dynamic between anxiety symptoms and drinking behavior might impede the progress and clarity of this research program. For example, while both theory and research point to the moderating role of tension-reduction alcohol outcome expectancies (TR-AOEs) in the association between anxiety symptoms and alcohol use, relevant treatment studies have not typically modeled TR-AOE effects. We examined the impact of a hybrid cognitive-behavioral therapy (H-CBT) treatment for panic disorder (independent variable) on response to a community-based alcohol dependence treatment program (dependent variable) in patients with higher vs. lower TR-AOEs (moderator). The H-CBT treatment was generally effective in relieving participants' panic symptoms relative to controls. However, TR-AOEs interacted with study cohort (H-CBT vs. control) in predicting response to substance abuse treatment. As expected, the H-CBT was most effective in improving alcohol use outcomes among those with the highest TR-AOEs. The study's primary methodological limitations are related to the quasi-experimental design employed.

Keywords

Comorbidity; Alcohol; Panic disorder; Expectancies; CBT treatment

Everything else being equal, alcohol dependence occurs more frequently among those who have the anxiety syndrome, panic disorder. Regier et al. (1990) reported a three-fold increase in risk for alcohol dependence among those with panic disorder in a community sample. Grant et al. (2004) and Kessler et al. (1997) also found a doubling to quadrupling of risk for alcohol dependence in a community sample of men and women with panic disorder relative to men and women without panic disorder. Because of self and other referral biases (Berkson, 1949), the degree to which panic disorder and alcohol disorder co-occur is even greater in clinical (vs. community) samples (Kushner, Sher, & Beitman, 1990).

Addiction specialists have struggled to understand the implications of co-occurring anxiety disorder for substance abuse treatment (e.g., Kushner, Abrams, & Borchardt, 2000; Tiet &

☆This research was supported, in part, by a grant from the National Institute on Alcoholism and Alcohol Abuse (AA12426 and AA015069) awarded to the first author.

* Corresponding author. University of Minnesota, Department of Psychiatry, Fairview-Riverside Hospital, F-282-2A West, 2450 Riverside Ave., Minneapolis, MN 55455, United States., kushn001@umn.edu (M.G. Kushner).

Mausbach, 2007). Driessen et al. (2001) found that anxiety disorders and depression were predictive of poor substance abuse treatment outcomes. Kushner et al. (2005) obtained similar results, showing that individuals with comorbid anxiety disorders were roughly twice as likely than those without a co-occurring anxiety disorder to relapse to drinking within four months of being treated for alcohol dependence. Based on this and related work, there is an emerging consensus that co-occurring anxiety disorders (and psychopathology more broadly) is a negative prognostic indicator for substance abuse treatment outcome (e.g., Kushner, Donahue, Frye, Book, & Randall, 2007). Even so, poor substance abuse treatment outcomes among those with a co-occurring anxiety disorder do not necessarily imply that treating the latter would improve the former.

Competing models make distinct predictions for how treating a co-occurring anxiety disorder should impact substance abuse treatment outcome (e.g., Kushner, Abrams, & Borchardt, 2000). If, for instance, anxiety symptoms actually promote alcohol use (e.g., via drinking to cope), then successfully treating a co-occurring anxiety disorder should lead to an improvement in substance abuse treatment outcomes. Alternatively, if anxiety symptoms are independent from alcohol dependence, or are actually a result of alcohol dependence, then successfully treating a co-occurring anxiety disorder should have no impact on substance abuse treatment outcomes.

Studies relevant to these competing predictions have produced inconsistent results. Several studies have found that treating a co-occurring anxiety disorder improves substance abuse treatment outcomes (e.g., Fals-Stewart and Schafer, 1992; Kranzler et al., 1994; Tollefson, Montague-Clouse, & Tollefson, 1992). Other studies have found that treating a co-occurring anxiety disorder has no effect on substance abuse treatment outcome (e.g., Bowen, D'Arcy, Keegan, & Senthilselvan, 2000; Malcolm et al., 1992; Randall, Thomas, & Thevos, 2001; Schade et al., 2005).

In addition to methodological variations (e.g., measures, type of anxiety disorder examined, type of treatment employed), uncontrolled individual differences might also increase error variance within and between these studies. For example, social learning models (e.g., Abrams & Niaura, 1987; Marlatt & Gordon, 1980) suggest that drinking to cope with anxiety and negative affect should occur only when two specific conditions are met: a) one experiences negative affect; and, b) one expects alcohol use to serve as an effective means of reducing or eliminating the negative affect. In this model, reducing co-occurring anxiety symptoms via treatment would improve alcohol outcomes robustly only in the subset of patients who expect alcohol to be effective in relieving anxiety/tension.

Consistent with this social learning perspective, there is substantial literature indicating that the strength of the association between anxiety symptoms and alcohol use is greater among those with higher tension-reduction alcohol outcome expectancies (TR-AOEs) (e.g., Cooper, Russell, Skinner, Fone, & Mudar, 1992; Kushner, Sher, Wood, & Wood, 1994). Several studies have confirmed that this moderated association also appears to extend to drinking to cope with the symptoms of various clinical anxiety syndromes including panic disorder (e.g., Abrams & Kushner, 2004; Kushner, Abrams, Thuras, & Hanson, 2000).

These findings support, but do not demonstrate, that TR-AOEs moderate the extent to which treatment for a co-occurring anxiety disorder improves substance abuse treatment outcomes. The only study that we are aware of bearing directly on this hypothesis found that a program designed to reduce high state anxiety was associated with greater improvement in substance abuse treatment outcomes for those with higher (vs. lower) TR-AOEs (Ormrod and Budd, 1991).

In the present work, we replicated and extended this earlier work. First, we developed a hybrid cognitive-behavioral therapy (H-CBT) program by integrating standard CBT treatment elements for panic disorder (e.g., Barlow, Craske, Cerny, & Klosko, 1989) with elements focused on the reciprocal influences linking anxiety and alcohol use (e.g., Kushner, Abrams, & Borchardt, 2000; Kushner, Abrams, Thuras et al., 2000). Recruiting from patients undergoing a standard community-based residential substance abuse program (treatment as usual; TAU), we contrasted four-month clinical outcomes of those receiving the H-CBT plus the TAU (treatment cohort) with those of patients receiving the TAU only (control cohort). We predicted that four months following the intervention, the treatment cohort, relative to the control cohort, would demonstrate: a) greater reduction in panic disorder symptoms; and, b) better drinking outcomes (e.g., higher rates of abstinence). Further, we predicted that the H-CBT will be especially predictive of better drinking outcomes among those with the highest TR-AOEs; i.e., TR-AOEs will moderate the association between study cohort and drinking outcomes.

We tested these predictions utilizing a quasi-experimental design (e.g., Cook & Campbell, 1979) in which serial cohorts of patients undergoing the substance abuse TAU program either did (treatment cohort) or did not (control cohort) also undergo the supplemental H-CBT treatment. For the treatment cohort, the H-CBT program (described below) was administered in parallel to (i.e., over the same time period as) the substance abuse TAU program.

1. Methods

1.1. Participants

All participants were drawn from the incoming patients of a residential community-based 28-day chemical dependence treatment program based within the University-Fairview Medical Center located in Minneapolis (“treatment as usual;” TAU). As described in detail in the Procedure section below, the treatment and control cohorts were obtained at separate times (serially) from the same TAU program. For the treatment cohort, 31 of the 43 individuals (78%) provided follow-up data. For the control cohort,17 of the 23 individuals (74%) provided follow-up data. Suggesting that data losses at follow-up were not systematic, comparisons of those who did vs. did not provide follow-up data showed that they did not differ at baseline on critical study outcome measures.

Eligible patients met diagnostic criteria for panic disorder and alcohol dependence and were being treated for alcohol disorder (vs. drug use disorder). Patients were excluded if they had a current (past month) history of suicidal behavior or psychosis. The total sample, then, consisted of 48 individuals (31 in the treatment cohort and 17 in the control cohort), which included 26 women and 22 men with a mean age of 41.4 years (SD=10.5). The mean age in the treatment cohort was 41.4 years (SD=10.3) with 51.6% who were female vs. 41.2 years in the control cohort (SD=11.1) with 58.8% who were female. The trained research assistant (RA) obtained informed consent from all qualified individuals using a consent form approved by the institution's IRB.

1.2. Measures

1.2.1. Structured Clinical Interview for DSM IV (SCID-I/P Version 2.0)—The SCID-IV I/P (First, Spitzer, Gibbon, & Williams, 1989) is a semi-structured diagnostic interview that determines the presence of specific psychiatric diagnoses during pre-specified time frames according to DSM IV criteria. Trained interviewers ask a series of questions that allow specific diagnostic criteria to be judged as present or absent. Diagnostic decision rules are built into the interview. We utilized the SCID to document the presence of “lifetime” and “current” (last 30 days) diagnosis for panic disorder (including a designation of agoraphobia) and alcohol

dependence. The SCID has been shown to have acceptable to good psychometric properties (e.g., Kranzler, Kadden, Babor, & Tennen, 1996; Zanarini & Frankenburg, 2000).

1.2.2. Time-Line Follow-Back (TLFB)—We used the TLFB interview (Sobell & Sobell, 1995) to estimate participants' daily quantity and frequency of alcohol use over the four months preceding the baseline interview and the time between subsequent assessments. The TLFB interview is a drinking assessment method that identifies daily drinking patterns and has been shown to have favorable psychometric qualities with clinical and non-clinical populations (Sobell & Sobell, 1995). Using a calendar, the respondent provides retrospective estimates of daily drinking over a specified amount of time. Several memory aids can be used to enhance recall (e.g., holidays, important weekends). The TLFB provides information about the participant's drinking pattern, variability and magnitude.

1.2.3. Panic Attack Questionnaire (PAQ)—The PAQ is a 19-item scale which we adapted from the Acute Panic Inventory (Dillion, Gorman, Liebowitz, Fyer, & Klein, 1987). The PAQ assesses the severityof each DSM IV panic symptom on a 5-point scale (“not at all” to “severe”) during a “typical panic attack” in the previous month. The PAQ also assesses the quantity, frequency and intensity of panic attacks during the previous month.

1.2.4. Alcohol Expectancies Questionnaire (AEQ)—The AEQ is a 31-item scale consisting of four factors. In this study we used the “tension-reduction” (TR) factor which includes 10 items (e.g., “Drinking helps me to relax”) (Kushner et al., 1994; Sher, Walitzer, Wood, & Brent, 1991). Each of the 10 items is rated using a five-point Likert-like scale. Favorable psychometric properties for the AEQ tension-reduction factor were obtained and reported by Kushner et al. (1994).

1.2.5. Brief Symptom Inventory (BSI)—The BSI is a 53 item self-report questionnaire that assesses global distress as well as psychological symptoms associated with several different areas of psychopathology (Derogatis & Melisaratos, 1983). The respondents describe how much they have experienced specific symptoms by marking 1–5 on a Likert-type scale (1=not at all, 5=extremely). The General Severity Index (GSI) of the BSI was selected for use in data analyses since it summarizes the overall severity of distress experienced by the rater due to psychological symptoms.

1.3. Procedure

1.3.1. Design—We employed a quasi-experimental design (e.g., Cook & Campbell, 1979). While all participants were recruited from the same substance abuse TAU program using the same procedures, there was approximately one year separating the end of the data collection for the control cohort and the initiation of data collection for the treatment cohort. The control cohort was obtained as part of a larger follow-up study in which patients could participate whether or not they had a co-existing panic disorder (Kushner et al., 2005). Only participants from that study who met diagnostic criteria for panic disorder (n=17) were considered eligible for use in the present study. There were no changes in the substance abuse TAU program's clinical content or patient ascertainment (e.g., catchment area, selection criteria) protocols in the time separating data collection for the two cohorts. This quasi-experimental design can be contrasted with a true experimental design inwhich all participants are assigned to the study groups on a random basis.

1.3.2. Recruitment—All recruitment procedures germane to the present study were identical between the study cohorts. Within three days of admission, new patients in the intensive substance abuse TAU program were given a brief initial screening form to complete. This form asked respondents about recent alcohol and drug use and about the presence of anxiety

symptoms indicative of various anxiety disorders. Approximately one week after admission, seemingly eligible individuals who expressed an interest in participating in the study were invited for a final screening visit in which the trained RA administered the diagnostic interview to determine eligibility.

1.3.3. Baseline assessment—Those individuals meeting full eligibility criteria (above) and who provided their informed consent underwent the baseline assessment.

1.3.4. Hybrid CBT treatment—A detailed description of the H-CBT treatment protocol and its background can be found in Kushner, Donahue, Sletten, Thuras, Abrams, Peterson, & Frye (2006). We developed the H-CBT program by integrating standard CBT panic disorder treatment elements based upon the work of Barlow et al. (1989) with new material focused on the interaction of alcohol consumption and anxiety symptoms drawn from our own work (e.g., Kushner, Abrams, & Borchardt, 2000; Kushner, Abrams, Thuras et al., 2000).

1.3.5. Four-month follow-up assessment—Ninety days following the baseline assessment, the RA began the process of contacting the participant for the follow-up assessment. When necessary, the RA called a contact person (identified during the baseline assessment) to help locate the participant. Upon contact, the participant was offered several possible dates to return to the treatment facility for the assessment. We required that the session take place no earlier than the contact date and no later than 120 days following the baseline assessment. This follow-up assessment consisted of a questionnaire packet and an interview paralleling the baseline assessment. Participants were paid for their participation.

1.4. Statistical approach

We used chi-square tests for categorical cohort comparisons at the follow-up (i.e., any alcohol use and any panic attacks, as well as diagnostic status of alcohol dependence and panic disorder) with Phi (ϕ) to quantify effect sizes. We also examined outcomes involving the number (count) of panic attacks, drinking days and binge drinking episodes in the month preceding the follow-up assessment. The effect of cohort membership on panic attack frequency was also examined using analysis of variance (ANOVA). Because zero was the most common single count for the alcohol variables (i.e., those who remained abstinent), and with a few participants having very high counts (i.e., those with a severe relapse), the distributions of these variables are heavily positively skewed, which is problematic for traditional GLM regression techniques. Such data are typically transformed mathematically with the goal of artificially normalizing the distribution. However, Delucchi and Bostrom (2004) (also see Hutchinson and Holtman, 2005) argue that Poisson regression (based on the Poisson distribution) or negative binomial regression provides a more appropriate analysis for such data. The latter is preferred when data are over-dispersed (variance>mean), as was the case for our data. Therefore, we employed a negative binomial regression using the GENMOD procedure in SAS. In these analyses, we used gender and pre-treatment GSI level as covariates as well as the pre-treatment (baseline) counterpart of the dependent variable.[1] We used eta squared (η^2) to quantify the magnitude of the effect size in these analyses.

For the count-based alcohol outcomes, tests of moderation were based on examination of two-way interactions between the predictor (cohort) and putative moderator (level of TR-AOE) (Baron & Kenny, 1986). For these analyses, we conducted a median split on the expectancy

[1]Drinking behavior reported for the month preceding entry into the chemical dependence TAU program was often not representative of participants' "typical" drinking. For example, some participants had quit drinking in the days or weeks prior to entering treatment for a variety of reasons (e.g., being in jail, being in the hospital, moving to an alcohol-free half-way house, being the focus of an "intervention"). In order to obtain a less biased baseline measure of "typical" drinking behavior, therefore, we generated baseline 30-day measures from timeline data representing the period from 60 days prior to treatment to 90 days prior to treatment.

measure scores to categorize participants into either a “low” or “high” TR-AOE group. For analyses using the categorical alcohol outcomes, it was our original intention to test for moderation similarly using logistic regression. However, our attempts to formally examine interaction effects using logistic regression were challenged operationally by the small sample sizes (zero, in some cases) in some of the interaction cells resulting in unstable or incalculable logistic estimates. Because of these challenges, we tested moderators in these cases by examining the two-by-two associations between the predictor and outcome separately for those with high vs. low TR-AOEs. We tested the statistical significance of these comparisons using the Fisher exact test rather than the chi-square statistic to accommodate the cell counts that were too low for valid inferences using the latter approach.

2. Results

2.1. Baseline characteristics

The cohorts were highly similar regarding both clinical and demographic characteristics at the baseline assessment. Regarding the latter, 88.0% in the control cohort and 91.4% in the treatment cohort were self-identified as Caucasian. Approximately half of each cohort was employed (60.0% for control and 51.4% for treatment). The median income and education level in both cohorts was <$30k annually with a high school/GED degree and “some” (i.e., attendance but no degree) college or vocational training. Table 1 shows additional baseline characteristics for participants in the two study cohorts. As can be seen, there were no baseline differences between the groups on parameters of drinking, panic, TR-AOEs or drug abuse. However, Table 1 also shows that the control cohort was significantly higher on distress from psychiatric symptoms than was the treatment cohort as measured by the GSI index. This unanticipated finding led us to use the GSI index as a covariate in the primary alcohol outcome analyses.

2.2. Main effects

2.2.1. Panic—Because predictions related to our primary hypothesis are conceptually predicated on the effective treatment of co-occurring panic disorder in the treatment cohort relative tothe control cohort, our initial analyses sought to confirm this effect. As shown in Table 2, the H-CBT was associated with reduced rates of both panic disorder and panic attacks at the follow-up. Relative to baseline (Table 1), the frequency of panic attacks at the follow-up decreased by 7.8 attacks/week (85%) in the treatment cohort vs. 2.6 attacks/week (23%) in the control cohort. This effect was statistically significant (Table 2). Similarly, the percent of individuals meeting full diagnostic criteria for panic disorder in the 30 days preceding the follow-up in the treatment condition was less than half of thatin the control condition. (However, it is notable that less than 50% of individuals continued to meet full diagnostic criteria for panic disorder even in the control cohort.) When gender and GSI were included as covariates for the panic attack frequency analyses, neither covariate was significant and the effect for cohort remained essentially the same ($F(1,43)=8.54$, $p=.006$, $\eta^2=.17$).

2.2.2. Drinking—Table 2 also shows drinking outcomes for the 30 days preceding the follow-up in the two study cohorts, including: a) having used any alcohol; and, b) meeting full alcohol dependence criteria. Although the percentage of those in the control cohort meeting the former relapse criteria was more than double of that in the treatment cohort, the cohort effect was not quite statistical significant ($p<.10$). However, the percentage of those who met diagnostic criteria for alcohol dependence in the 30 days preceding the follow-up was significantly greater among the participants in the control cohort. That is, those undergoing the H-CBT treatment were significantly less likely to meet diagnostic criteria for alcohol dependence at the follow-up than those not undergoing the H-CBT treatment. (As with panic disorder rates at the follow-up, we noted that the overall rate of meeting alcohol dependence criteria at the follow-up was

relatively low in both groups.) Table 2 also shows count-based drinking outcomes for the two cohorts in the 30 days preceding the follow-up including: a) the number of drinking days; and b) number of drinking binges (i.e., ≥5 drinks for men and ≥4 drinks for women). As shown, the control cohort reported more than three times the number of drinking days and binges than did the treatment cohort. The difference on the former was significant while that on the latter only approached statistical significance (p=.06).

2.3. Moderator analyses

2.3.1. Categorical alcohol outcomes—Table 3 shows the same alcohol outcomes as examined earlier but separately for cases that were above vs. below the median on TR-AOEs (labeled "high" vs. "low," respectively). As predicted, there was a significant interaction between expectancies and cohort in predicting the percent who had used any alcohol in the month preceding the follow-up (OR=.006, 95% CI=.0 -.19, p=.0 04). As shown, among those with the highest TR-AOE levels (the two columns on the right), H-CBT was associated with significantly (Fisher's Exact=.02, ϕ=.65) and substantially (>7-fold) lower rates of relapse to any drinking relative to the control cohort. Alternatively, there was a much smaller and nonsignificant difference between the cohorts on this outcome measure among those with the lowest TR-AOEs (two columns on the left). A similar pattern emerges when looking at the rate of individuals meeting criteria for alcohol dependence. Among those with the highest TR-AOE levels, H-CBT was associated with significantly (Fisher's Exact=.003, ϕ=.70) and substantially (nearly 60% vs. 0%) lower rates of meeting diagnostic criteria for alcohol dependence in the month preceding the follow-up. By contrast, there was no cohort effect for alcohol dependence at follow-up among those with the lowest TR-AOEs.

2.3.2. Count alcohol outcomes—The bottom two rows of Table 3 show alcohol outcomes involving event counts for the two cohorts separately by those with higher TR-AOEs (right side) vs. those with lower TR-AOEs (left side). For both outcomes, study cohort interacted with TR-AOE (drinking days, χ^2=7.78, p=.005, η^2=.17; binge drinking days, χ^2=5.38, p=.02, η^2= .12). Consistent with study predictions, H-CBT was associated with fewer binges and fewer drinking days for those above but not those below the median onTR-AOEs, while TR-AOE level did not effect outcomes in the control cohort.

3. Discussion

Anxiety disorders in general and panic disorder in particular are common among substance abuse treatment patients and mark those at a high risk for relapse to drinking following treatment for alcohol dependence. These well-replicated findings provide a background to the hypothesis that treating co-occurring panic disorder should improve substance abuse treatment outcomes. However, this hypothesis is not logically necessitated by the earlier findings and, more importantly, it has not been consistently supported across the relevant studies reviewed in the Introduction. In the present work, we focused on this hypothesis while adding two novel elements relative to the previous work. First, we created a hybrid intervention by integrating elements of a standard CBT treatment for panic disorder with information and interventions focused directly on the interface between anxiety symptoms and pathological drinking behavior (H-CBT). Second, we extrapolated from social learning theory and research on alcohol expectancies that the H-CBT should improve drinking outcomes, especially for patients with higher TR-AOEs.

A prerequisite to testing the central hypotheses concerning drinking outcomes is to confirm that the H-CBT treatment reduced panic disorder symptoms relative to the control condition. Past work shows that CBT is effective in psychiatric patients whose panic symptoms are uncomplicated by substance abuse (e.g., Barlow et al., 1989). Although we could not assume

that these past results would apply in our study; we did, in fact, find that the H-CBT program exerted a significant therapeutic effect on the panic symptoms of alcohol dependence treatment patients. While not the central purpose of our work, this finding does demonstrate that CBT panic treatment techniques developed for and validated in psychiatric patients can also be applied beneficially in substance abuse treatment patients. Confirming that the H-CBT actually reduced panic level also allows us to evaluate cohort effects on alcohol outcomes with confidence that the H-CBT manipulation was successful.

Table 2 shows the data and analyses indicating that H-CBT was associated with superior alcohol dependence treatment outcomes; although, the cohort effect for two of the four outcome measures (any alcohol use and number of binges) only approached the conventional statistical significance criterion (i.e., *ps*<.10). Importantly, however, Table 3 shows that those participants with higher TR-AOEs benefited from the H-CBT significantly more in terms of their alcohol treatment outcomes than was true for those with lower TR-AOEs. In fact, individuals with TR-AOEs below the median tended not to benefit at all from the H-CBT.

These findings raise the important practical question of whether treatment for co-occurring panic disorder among patients being treated for alcohol dependence should be reserved for those who have relatively high TR-AOEs. The primary factor in favor of this position is that such cases would, based upon our findings, be more likely (relative to those with lower TR-AOEs) to experience improved alcohol treatment outcomes if treatment for the co-occurring panic disorder is also provided. Against this position, however, is that all cases, regardless of TR-AOE levels, are likely to experience relief of disturbing panic disorder symptoms if H-CBT is added to substance abuse TAU. In this regard, it would seem undesirable and ethically questionable to deny access to anxiety treatment for some but not other anxious patients in the same treatment program when all could benefit from it to one degree or another.

Elsewhere, we argue that panic and other anxiety disorders co-occurring with substance abuse might form a hybrid condition with maintaining factors and treatment requirements that differ from either condition alone (Kushner, Abrams, & Borchardt, 2000; Kushner, Abrams, Thuras et al., 2000). This viewpoint informed our tailoring the H-CBT panic disorder treatment specificallyto individuals who are simultaneously undergoing treatment for alcohol dependence (see description in Method section and reference to Kushner et al., 2006). In pursuing this goal, we made several strategic choices. First, rather than simply adding a CBT treatment that was empirically validated in psychiatric patients, we modified the program to explicitly address the interaction of panic disorder and alcohol use in cases where both conditions co-occur (Kushner et al., 2006). Second, we delivered H-CBT treatment to a patient population already undergoing community-based substance abuse treatment as usual. This decision reflects our belief that the treatment of alcohol dependence, regardless of the presence of a co-occurring disorder, potentially requires traditional substance abuse treatment elements including medically supervised detoxification, family counseling, social work and integration into an abstinent community/philosophy (e.g., AA). Third, we delivered the H-CBT treatment in parallel with the substance abuse TAU program. This decision reflected our earlier observation that untreated panic disorder increases the risk of relapse and patient attrition in the time immediately following alcohol treatment (Kushner et al., 2005). Despite our findings, the optimal sequencing/timing of treatments for co-occurring disorders still remains uncertain (e.g., Kushner et al., 2007).

These various aspects of the H-CBT and its delivery might have made it more effective in relieving both panic symptoms and improving alcohol outcomes than would have been the case for a traditional CBT treatment. For example, Randall et al. (2001) found that a CBT treatment deemed effective in treating social anxiety in psychiatric patients was not effective in treating social anxiety in their alcoholism treatment sample. Consistent with our view that it is the

reduction in anxiety (rather than CBT treatment per se) that promotes improved alcohol treatment outcomes, it is not surprising that Randall et al. (2001) found that alcoholism treatment outcomes were also not improved by the addition of CBT for social anxiety. However, some investigators have found that alcoholism treatment outcomes are unaffected even when co-occurring anxiety symptoms are successfully treated (e.g., Schade' et al., 2005).

Two factors that are unique to the intervention used in this study may have contributed to the success of our CBT program relative to the earlier work. First, as noted above, our intervention was a hybrid treatment that focused both on reducing anxiety symptoms and highlighting and ameliorating pathological interactions between anxiety symptoms and drinking. By creating a treatment in which the nexus of the co-occurring problems is made explicit, we may have increased alcoholism treatment patients' attention to and motivation for controlling their anxiety symptoms. Related to this, we may have benefited both drinking and anxiety outcomes by allowing patients to see how the two problems interacted to promote the other. A second feature unique to this study is our attention to individual differences in TR-AOEs as a moderating feature that distinguishes those whose alcohol treatment outcomes might most benefit from anxiety reduction. Although the H-CBT treatment demonstrated a qualified benefit to drinking outcomes (significantly so in two of four measures), these benefits were more robust and uniformly significant when considering their interaction with TR-AOEs.

Findings from this study require replication both because we employed a relatively novel approach in an underdeveloped field of treatment research (i.e., that involving co-occurring disorders) and because of several methodological limitations to our study. The primary limitations relate to our use of a quasi-experimental vs. a fully experimental (i.e., randomized) design. At the baseline, the control cohort displayed significantly more psychological distress than the treatment cohort based on the GSI index. Randomization would have made such differences between the groups less likely. (Such group differences, however, would remain possible regardless of the design; especially with smaller sample sizes.) The important question is whether this unexpected baseline difference threatens the inference that cohort differences at follow-up were due to the H-CBT intervention. Two pieces of evidence leave us confident that this key scientific inference remains valid in spite of the baseline group difference on the GSI. First, the two cohorts did not differ at baseline on the two central study parameters, panic and drinking. Since the baseline GSI difference did not affect panic attack rates or drinking parameters at baseline, it seems reasonable to assume that it would not affect these parameters at follow-up. Second, the hypothesized effects remained significant even after including the baseline GSI as a statistical covariate in predictive models. These considerations leave us confident that baseline GSI differences did not impact significantly on study outcomes and the inference that differences between the groups on these outcomes were due to the H-CBT intervention.

In addition to the cohort differences that were measured, we must also be concerned about the possibility of cohort differences that were not measured. Threats to validity from unmeasured sources are of less concern in quasi-experimental designs to the extent that factors that could influence the dependent variable (other than the independent variable) are similar for study cohorts. For example, the fact that participants in both of our study cohorts came from the same chemical dependence program reduces concerns that the types of patients placed in the two cohorts differed as a function of the CD treatment content each received, selection criteria for treatment inclusion or the treatment catchment area. Even within the same program, however, the time between recruitment of the cohorts offers the potential for changes in programming, patient selection criteria, etc. that could threaten validity. Importantly, the programming, treatment philosophy, treatment content, catchment area, referral patterns and funding issues (e.g., budget, fees, third party payer mix) remained unchanged in the time between the data

collection for the two cohorts according to the program director. These observations support our conclusion that any differences in outcomes between the cohorts were not due to changes in the TAU program or due to differences in the types of patients included. Finally, it is worth noting that a randomized experimental design might have actually had a greater risk of cross-contamination among participants in different conditions than was true in our quasi-experimental design. This is because the former would have patients participating in different groups in the TAU at the same time, thereby allowing them to discuss their differing study experiences with one another.

There are also several methodological limitations in the current work that are unrelated to quasi-experimental design. Patients in the control cohort underwent the substance use TAU program while those in the treatment cohort underwent the TAU and the H-CBT. Ideally, the control cohort would have also been exposed to an additional activity to balance the extra clinical time and attention received by patients undergoing the H-CBT. Also, since we did not obtain information on those who chose not to participate in the study, we cannot be assured that those who did participate were fully representative of all otherwise eligible cases. Although we did determine that those who failed to provide follow-up data were not different at the baseline on key parameters from those who did provide follow-up data. Another feature that could limit generalizability is our focus on panic disorder (vs. other anxiety disorders such as social phobia) and our exclusion of substance abusers other than those who are alcohol dependent. Finally, the study was limited by being adequately powered only for relatively large effects (especially with regard to the predicted interactions), which introduces an increased risk for Type 2 errors. As a limited guard against this risk, we were especially cautious in interpreting negative findings and have reported effect sizes.

This work has several implications for future research. For example, we are currently conducting a study that addresses the primary methodological concerns with the aim of replicating and extending the findings reported herein. This project employs a true experimental design, an active control condition and an expanded range of anxiety disorders beyond panic disorder. More generally, this work indicates that alcohol outcome expectancies and CBT programs that are tailored to the synergistic elements of co-occurring disorders are likely to be important in developing and targeting treatments in this population.

Acknowledgments

We acknowledge and thank the director (Jeff Powers) and staff of the Fairview-University Medical Center's Chemical Dependency Treatment Program for their support in the conduct of this work.

References

Abrams K, Kushner MG. The moderating effects of tension-reduction alcohol outcome expectancies on placebo responding in individuals with social phobia. Addictive Behaviors 2004;29:1221–1224. [PubMed: 15236826]

Abrams, DB.; Niaura, RS. Social learning theory. In: Blane, HT.; Leonard, KE., editors. Psychological theories of drinking and substance abuse. New York, NY: Guildford Press; 1987. p. 131-178.

Barlow DH, Craske MG, Cerny JA, Klosko JS. Behavioral treatment of panic disorder. Behavior Therapist 1989;20:261–282.

Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. Journal of Personality and Social Psychology 1986;51:1173–1182. [PubMed: 3806354]

Berkson J. Limitations of the application of four-fold tables to hospital data. Biological Bulletin 1949;2:47–53.

Bowen RC, D'Arcy C, Keegan D, Senthilselvan A. A controlled trial of cognitive behavioral treatment of panic in alcoholic inpatients with comorbid panic disorder. (Brief Report). Addictive Behaviors 2000;25:593–597. [PubMed: 10972451]

Cook, TD.; Campbell, DT. Quasi-experimentation: Design and analysis issues for field settings. Boston: Houghton Mifflin Company; 1979.

Cooper ML, Russell M, Skinner JB, Frone MR, Mudar P. Stress and alcohol use: Moderating effects of gender, coping, and alcohol expectancies. Journal of Abnormal Psychology 1992;101:139–152. [PubMed: 1537960]

Delucchi KL, Bostrom A. Methods for analysis of skewed data distributions in psychiatric clinical studies: Working with many zero values. American Journal of Psychiatry 2004;161:1159–116. 8. [PubMed: 15229044]

Derogatis LR, Melisaratos N. The Brief Symptom Inventory: An introductory report. Psychological Medicine 1983;13:595–605. [PubMed: 6622612]

Dillion DJ, Gorman JM, Liebowitz MR, Fyer AJ, Klein DF. Measurement of lactate-induced panic and anxiety. Psychiatry Research 1987;20:97–105. [PubMed: 3575564]

Driessen M, Meier S, Hill A, Wetterling T, Lange W, Junghanns K. The course of anxiety, depression and drinking behaviours after completed detoxification in alcoholics with and without comorbid anxiety and depressive disorders. Alcohol and Substance abuse 2001;36:249–255.

Fals-Stewart W, Schafer J. The treatment of substance abusers diagnosed with obsessive–compulsive disorder: An outcome study. Journal of Substance Abuse Treatment 1992;9:365–370. [PubMed: 1479631]

First, MB.; Spitzer, R.; Gibbon, M.; Williams, J. Structural Clinical Interview for Axis-I DSM-IV Disorders Patient Edition (SCID-I/P Version 2.0). New York State: Biometrics Research Department, Psychiatric Institution; 1989.

Grant BF, Stinson FS, Dawson DA, Chou SP, Dufour MC, Compton W, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Archives of General Psychiatry 2004;61:807–816. [PubMed: 15289279]

Hutchinson MK, Holtman MC. Analysis of Count Data using Poisson Regression. Research in Nursing and Health 2005;28:408–418. [PubMed: 16163676]

Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC. Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comobidity Survey. Archives of General Psychiatry 1997;54:313–321. [PubMed: 9107147]

Kranzler HR, Burleson JA, Del Boca FK, Babor TF, Korner P, Brown J, et al. Buspirone treatment of anxious alcoholics: A placebo-controlled trial. Archives of General Psychiatry 1994;51:720–731. [PubMed: 8080349]

Kranzler HR, Kadden RM, Babor TF, Tennen H. Validity of the SCID in substance abuse patients. Addiction 1996;91:859–868. [PubMed: 8696248]

Kushner MG, Abrams K, Borchardt C. The relationship between anxiety disorders and alcohol use disorders: A review of major perspectives and findings. Clinical Psychology Review 2000;20:149–17. 1. [PubMed: 10721495]

Kushner MG, Abrams K, Thuras P, Hanson K. Individual differences predictive of drinking to manage anxiety among non-problem drinkers with panic disorder. Alcoholism: Clinical and Experimental Research 2000;24:448–458.

Kushner MG, Abrams K, Thuras P, Hanson KL, Brekke M, Sletten S. A follow-up study of anxiety disorder and alcohol dependence in comorbid substance abuse treatment patients. Alcoholism: Clinical and Experimental Research 2005;29:1432–1443.

Kushner MG, Donahue C, Frye B, Book SW, Randall CL. Which to treat first: Comorbid anxiety or alcohol disorder. (Invited Review). Current Psychiatry 2007;6(8):55–64.

Kushner MG, Donahue C, Sletten S, Thuras P, Abrams K, Peterson J, et al. Cognitive behavioral treatment of comorbid anxiety disorder in substance abuse treatment patients: Presentation of a prototype program and future directions. Journal of Mental Health 2006;15:697–708.

Kushner MG, Sher KJ, Beitman BD. The relation between alcohol problems and the anxiety disorders. American Journal of Psychiatry 1990;147:685–695. [PubMed: 2188513]

Kushner MG, Sher KJ, Wood MD, Wood PK. Anxiety and drinking behavior: Moderating effects of tension-reduction alcohol outcome expectancies. Alcoholism: Clinical and Experimental Research 1994;18:852–860.

Malcolm R, Anton RF, Randall CL, Johnston A, Brady K, Thevos A. A placebo-controlled trial of buspirone in anxious inpatient alcoholics. Alcoholism: Clinical and Experimental Research 1992;16:1007–1013.

Marlatt, GA.; Gordon, JR. Determinants of relapse: Implications for the maintenance of behavior change. In: Davidson, P.; Davidson, S., editors. Behavioral Medicine: Changing health lifestyles. New York, NY: Brunner/Mazel; 1980. p. 410-452.

Ormrod J, Budd R. A comparison of two treatment interventions aimed at lowering anxiety levels and alcohol consumption amongst alcohol abusers. Drug and Alcohol Dependence 1991;27:233–243. [PubMed: 1884666]

Randall CL, Thomas S, Thevos AK. Concurrent substance abuse and social anxiety disorder: A first step toward developing effective treatments. Alcoholism: Clinical and Experimental Research 2001;25:210–220.

Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, et al. Comorbidity of mental disorders with alcohol and other drug abuse: Results from the Epidemiologic Catchment Area (ECA) Study. Journal of the American Medical Association 1990;264:2511–2518. [PubMed: 2232018]

Schade A, Marquenie LA, van Balkom AJLM, Koeter MWJ, de Beurs E, van den Brink W, et al. The effectiveness of anxiety treatment on alcohol dependent patients with a comorbid phobic disorder: A randomized controlled trial. Alcoholism: Clinical and Experimental Research 2005;29:794–800.

Sher KJ, Walitzer KS, Wood PK, Brent EE. Characteristics of children of alcoholics: Putative risk factors, substance use and abuse, and psychopathology. Journal of Abnormal Psychology 1991;100:427–448. [PubMed: 1757657]

Sobell, LC.; Sobell, MB. Alcohol Time-Line Follow-Back user's manual. Toronto, Canada: Addiction Research Foundation; 1995.

Tiet QQ, Mausbach B. Treatments for patients with dual diagnosis: A review. Alcoholism: Clinical and Experimental Research 2007;31:513–536.

Tollefson GD, Montague-Clouse J, Tollefson SL. Treatment of comorbid generalized anxiety in a recently detoxified alcoholic population with a selective serotonergic drug (buspirone). Journal of Clinical Psychopharmacology 1992;12:19–26. [PubMed: 1552035]

Zanarini MC, Frankenburg FR. Attainment and maintenance of reliability of Axis I and II disorders over the course of a longitudinal study. Comprehensive Psychiatry 2000;42:369–374. [PubMed: 11559863]

Table 1

Baseline comparisons by study cohort.

	Treatment cohort (*N*=31)		Control cohort (*n*=17)		Statistic	*p* value
Variable	**Mean**	**SD**	**Mean**	**SD**		
Drinking days in month prior to treatment	20.5	11.7	21.6	8.5	$F(1,46) = 0.11$	0.74
Binge days in month prior to treatment	18	12.2	19.4	8.9	$F(1,43) = 0.17$	0.68
Panic attacks per week in month prior to treatment	9.2	7.4	11.2	11.1	$F(1,46) = 0.57$	0.46
Alcohol outcome expectancies for tension reduction	3.3	1.0	3.0	1.0	$F(1,46) = 0.84$	0.36
BSI — Global Severity Index	1.75	0.62	2.3	0.72	$F(1,46) = 8.1$	0.01
Illegal drug use	39.3%		47.1%		$\chi^2 = .26$	0.61
Anti-anxiety medication use (%)	64.7%		51.6%		$\chi^2 = .77$	0.38

Table 2

Panic and alcohol outcomes (30 days prior to follow-up) by study cohort.

	Treatment cohort (*N*=31)		Control cohort (*n*=17)		Statistic	*p* and ϕ values
	Mean	**SD**	**Mean**	**SD**		
Panic variables						
Panic attacks per week	1.4	4.9	8.6	9.9	$F(1,46) = 11.29$	$p = .002$, $\eta^2 = .20$
Panic disorder criteria	16%		41%		$\chi^2 = 3.67$	$p = .05$, $\phi = .28$
Drinking variables						
Any alcohol	22.6%		47.1%		$\chi^2 = 3.06$	$p = .08$, $\phi = .25$
Alcohol dependence	9.7%		35.3%		$\chi^2 = 4.73$	$p = .03$, $\phi = .31$
Number of drinking days	2.2	6.2	6.9	10.8	$\chi^2 = 5.18$	$p = .03$, $\eta^2 = .11$
Number of binges	1.8	5.8	6.1	10.1	$\chi^2 = 3.59$	$p = .06$, $\eta^2 = .08$

Table 3

Alcohol outcomes by study cohort and expectancy level.

	Low TR-AOEs (below median)				High TR-AOEs (above median)			
	Treatment cohort (*N*=14)		Control cohort (*N*=10)		Treatment cohort (*N*=17)		Control cohort (*N*=7)	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Any drinking	35.7%		20.0%		11.8%		85.7%	
Alcohol dependence	21.4%		20.0%		0.0%		57.1%	
# binges	3.7	8.3	2.8	6.5	0.2	0.7	10.9	12.8
# drinking days	4.5	8.8	3.1	7.4	0.2	0.7	12.4	13.1