Published in final edited form as:

Drug Alcohol Depend. 2016 February 1; 159: 93–100. doi:10.1016/j.drugalcdep.2015.11.031.

Drinking to cope with negative emotions moderates alcohol use disorder treatment response in patients with co-occurring anxiety disorder

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Abstract

Background—Epidemiological studies and theory implicate drinking to cope (DTC) with anxiety as a potent moderator of the association between anxiety disorder (AnxD) and problematic alcohol use. However, the relevance of DTC to the treatment of alcohol use disorder (AUD) in those with a co-occurring AnxD has not been well studied. To address this, we examined whether DTC moderates the impact of two therapies: (1) a cognitive behavioral therapy (CBT) designed to reduce DTC and anxiety symptoms; (2) a progressive muscle relaxation training (PMRT) program designed to reduce anxiety symptoms only.

Methods—Patients undergoing a standard AUD residential treatment with a co-occurring AnxD ($N = 218$) were randomly assigned to also receive either the CBT or PMRT. DTC in the 30 days prior to treatment was measured using the Unpleasant Emotions subscale of the Inventory of Drinking Situations.

Results—Confirming the predicted moderator model, the results indicated a significant interaction between treatment group and level of pre-treatment DTC behavior. Probing this interaction revealed that for those reporting more pre-treatment DTC behavior, 4-month alcohol outcomes were superior in the CBT group relative to the PMRT group. For those reporting less pre-treatment DTC behavior, however, 4-month alcohol outcomes were similar and relatively good in both treatment groups.

Conclusions—These findings establish a meaningful clinical distinction among those with co-occurring AUD-AnxD based on the degree to which the symptoms of the two disorders are functionally linked through DTC. Those whose co-occurring AUD-AnxD is more versus less strongly linked via DTC are especially likely to benefit from standard AUD treatment that is augmented by a brief CBT designed to disrupt this functional link.

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Contributors

Matt Kushner and Justin Anker were involved in the design of the experiment, data analysis, graphic presentation, and manuscript preparation. Paul Thuras and Jeremiah Menk were involved in data analysis and Amanda Unruh contributed to data collection, manuscript preparation and data management. All authors were involved in the final preparation of the manuscript, and have approved the final version.

Conflict of interest

The authors have no conflicts to declare.

Keywords

Alcohol; Anxiety disorder; Comorbidity; CBT treatment; Drinking motives

1. Introduction

Individuals undergoing treatment for alcohol use disorder (AUD) who have a co-occurring anxiety disorder (AnxD) relapse to drinking at a substantially higher rate than do those with no co-occurring AnxD (Driessen et al., 2001; Falk et al., 2008; Kushner et al., 2005). Much of the clinical research aimed at remediating this problem has pursued the agenda of augmenting standard AUD treatment with an established AnxD treatment. This approach reasonably assumes that reducing AnxD symptoms should reduce the AUD relapse risk associated with AnxD. It has become increasingly clear, however, that this common sense approach has largely failed to improve AUD outcomes significantly for those with a co-occurring AnxD (Book et al., 2008; Bowen et al., 2000; Hobbs et al., 2011; Randall et al., 2001; Schade et al., 2005; Thomas et al., 2008). For example, Hobbs et al. (2011) conducted a meta-analysis of 15 controlled randomized studies testing the value of augmenting AUD treatment with either cognitive behavioral therapy (CBT) or medications for a co-occurring AnxD. Although the treatment effect for the AnxD was moderate in size, the collateral benefit this conferred on AUD outcomes, while significant, was small in size. Hobbs et al. (2011) concluded from this finding that processes beyond AnxD symptom levels are operating to promote alcohol relapse in this patient group.

One process that is not directly addressed by standard AnxD treatment, but is associated with problematic alcohol use among those with AnxD, is drinking to cope (DTC). Menary et al. (2011) examined the relationship of AnxD and alcohol use/problems between those who did versus did not endorse DTC behavior in a large ($N \sim 44,000$) prospective and nationally representative sample (NESARC). They reported that compared to those with an AnxD in the absence of DTC, individuals with an AnxD who endorsed DTC: (1) drank significantly more alcohol; (2) were more likely to have an AUD at the initial assessment wave; and (3) were more likely to develop a new AUD by the second assessment wave approximately 3 years later (also see Crum et al., 2013a,b). Although those with an AnxD who reported no DTC experienced some increase in cross-sectional risk for AUD at the baseline relative to those with no AnxD, their prospective risk was similar and their daily drinking volume was less compared to those with no AnxD.

These findings align with the theoretical (Kushner et al., 2000a) and clinical (Kushner et al., 2013) importance we assign to DTC in the development and maintenance of a functional linkage between AnxD and AUD. They are also generally consistent with the neurobiological model of allostatic adaptation in addiction (Koob, 2013; Koob and Le Moal, 2006) and various learning-based models linking negative affect to maintenance of AUD (c.f., Stasiewicz and Maisto, 1993). Additionally, several of these complementary views, including ours, emphasize bi-directional feed-forward linkages between drinking and negative affect where DTC serves as a central goal-directed behavior with attendant negative reinforcement maintaining and promoting additional drinking. This, in turn,

worsens anxiety and other negative affect via neurobiological dysregulations and environmental disruptions/consequences (the “vicious cycle”). Based on this perspective, the reduction of AnxD symptoms alone may not be sufficient to overcome established behavioral patterns and learned response dispositions that may serve to link even subclinical anxiety symptoms (and, perhaps, even normative stress responding) to relapse following treatment in those with both AnxD and AUD.

Consistent with this model, Kushner et al. (2013) found that augmenting AUD treatment with a CBT-based treatment designed to reduce both DTC behavior and anxiety symptoms produced better AUD outcomes than did a treatment designed to reduce anxiety symptoms alone (i.e., progressive muscle relaxation training; PMRT). The present study reanalyzed data from the Kushner et al. (2013) study to evaluate whether level of pre-treatment DTC behavior moderates response to the two treatments studied. Specifically, we predicted a significant interaction between level of pre-treatment DTC behavior (i.e., the moderator) and treatment group (i.e., the independent variable) in predicting 4-month post-treatment alcohol outcomes (i.e., the dependent variables).

Based on the findings and theories reviewed, we predicted that among those higher in pre-treatment DTC, the CBT aimed at reducing both DTC and anxiety symptoms would be associated with superior alcohol outcomes compared to those who received the PMRT aimed at reducing anxiety alone. Among those lower in pre-treatment DTC behavior, however, we expected comparable treatment effects for the two study treatments either because: (a) the anxiety-reduction components included in both study treatments would confer similar AUD-outcome benefits, with the DTC-reducing components of the CBT being relatively neutral in the low DTC subgroup; or, (b) both the anxiety reduction and DTC reduction components of the study treatments would be unrelated to standard AUD treatment outcomes in the low DTC subgroup. Although our study design cannot distinguish these two explanations, the predictions they make in terms of the hypothesized moderator effect are the same.

Confirming the hypothesized moderator model would provide an empirical basis for separating AUD-AnxD cases into two distinct clinical subtypes. Moreover, if the hypothesized pattern of the moderator effect is confirmed, the study findings would point to specific intervention approaches best suited to each of the clinical subtypes.

2. Methods

2.1. Participants

2.1.1. Inclusion/exclusion criteria—Participants were selected from a 61-bed, 21-day, community-based residential chemical dependency (CD) treatment program. Inclusion criteria were current DSM-IV diagnosis of alcohol dependence and at least one of the following anxiety disorders: panic, social anxiety, and/or generalized anxiety. Exclusion criteria were a history of bipolar disorder, psychosis or schizophrenia, ongoing acute suicidality, inability to read or speak English, or the presence of cognitive impairments that would impede study participation. Patients with a diagnosis of drug dependence were not excluded; however, alcohol had to be the primary reason for their treatment. Major

depression and posttraumatic stress disorder were also assessed and recorded. Eligible participants provided written informed consent. The study was approved by the University of Minnesota's Institutional Review Board and was funded by a grant from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) awarded to the second author.

2.1.2. Recruitment—A full description of the recruitment methods is reported in Kushner et al. (2013) and is briefly summarized here. Participants were recruited during their first week of the CD treatment program in 3 screening steps. In Step 1, a screening questionnaire was offered to 100% of the patients entering the CD treatment. In Step 2, responding patients who reported alcohol as their primary addiction and who endorsed significant symptoms of social anxiety, panic, and/or generalized anxiety on the questionnaire were invited to a screening interview where they were asked to elaborate on their endorsements. The clinical team (including a staff psychologist) then evaluated these responses to determine if the candidate fit the inclusion/exclusion criteria. Qualified candidates proceeded to Step 3 where psychiatric diagnoses were formally established using the Structured Clinical Interview for DSM-IV (SCID; First et al., 1989). A clinical consensus method involving at least two Ph.D. psychologists, with the principle investigator (author, MGK) adjudicating disagreements, was used to make all diagnostic decisions.

2.1.3. Participant demographics—Data were analyzed from an original sample of 247 individuals. Of the 247 individuals, 218 had complete data and were used in analyses in the present study (see Table 1 for demographic and clinical information from the study sample).

2.2. Internalizing symptom assessments: pre-treatment

2.2.1. Inventory of drinking situations (IDS)—The IDS-100 (Annis, 1982) is a psychometrically reliable and valid 100-item self-report questionnaire that assesses the frequency of heavy drinking in relation to Marlatt's eight high-risk situations/categories (Cannon et al., 1990; Marlatt, 1979; Parra et al., 2005). Index scores for the Unpleasant Emotions (IDS-UE) subscale served as the primary measure of DTC as it was designed to capture DTC behavior associated with negative affect situations (e.g., "When I was angry at the way things had turned out", "When I felt under a lot of pressure") and typifies differences in drinking motives among alcohol-dependent individuals with versus without a co-occurring AnxD (Norton et al., 1989; Waldrop et al., 2007). Participants were instructed to mark the response (1 = "Never", through 4 = "Almost Always") that most accurately described the extent they drank heavily in IDS-UE situations during the 30 days leading up to their CD treatment. The IDS-UE index score was derived by summing the 20 UE-related IDS items and ranged from 20 to 80 (median = 63). Participants were divided into a "High Unpleasant Emotions" (High IDS-UE; above the median) or "Low Unpleasant Emotions" (Low IDS-UE; below the median) group based on their score on the IDS-UE subscale at baseline/pre-treatment. The distribution of IDS-UE scores is shown in Fig. 1. The distribution was slightly skewed to the left reflecting the tendency for drinking to manage negative affect among comorbid individuals.

2.2.2. Trait anxiety and depression severity assessments—The Spielberger Trait Anxiety Inventory (STAI) served as a measure of trait anxiety (Spielberger and Sydeman,

1994). Participants were instructed to complete the STAI by rating response items (e.g., “I feel nervous and restless”) in terms of how they “generally” feel on a 4-point scale (1 = “Not at all” to 4 = “Very much so”). Summed scores on the STAI can range from 20 to 80, with higher scores indicating greater trait anxiety. The Beck Depression Inventory (BDI; Beck et al., 1988) served as a measure of depression severity. Participants were instructed to rate descriptions that correspond to specific symptoms of depression on a 4-point scale (0 = symptom is not present through 3 = symptom is severe). Summed scores on the BDI can range from 0 to 63, with higher scores indicating greater depression.

2.3. Alcohol use assessment: pre- and post-treatment

2.3.1. Time line follow-back (TLFB) interview and alcohol use outcomes—

Alcohol use outcomes 4 months before (baseline) and 4 months after (follow-up) the completion of study treatments were based on the TLFB (Sobell and Sobell, 1995). In the TLFB, an interviewer uses a calendar to document a participant’s estimate of the number of alcoholic drinks they consumed on each day of the assessment period. A standard alcoholic drink was defined as one ounce of alcohol spirits, four ounces of wine, or 12 ounces of beer and a “binge day” was defined as a day in which four or more drinks were consumed by women and five or more drinks consumed by men. The TLFB has been deemed a psychometrically reliable and valid instrument for collecting drinking history in clinical populations (Pedersen and LaBrie, 2006; Sobell and Sobell, 1995). Total number of drinking days, number of binge days, and total number of drinks consumed were used as primary alcohol use outcome measures as they allowed for the assessment of cumulative alcohol consumption over the entire 4-month follow-up period. We concluded that these cumulative measures better represented total alcohol exposure over the follow up compared to other standard alcohol outcome measures such as drinks per drinking day because there were a number of cases in which there was a high volume of drinking on a small number of (in some cases, only one) drinking days.

2.4. Treatments

2.4.1. AUD treatment as usual (TAU)—All participants were patients in a community-based 21-day residential CD program based on the “Minnesota Model” of care emphasizing abstinence, the 12-step recovery approach, family involvement, and spiritual growth. During treatment, patients lived on-site in one- or two-person rooms and attended therapy programming from 8 a.m. to 3 p.m., Monday through Friday.

2.4.2. Study treatments: general—Consented participants were randomly assigned to receive six daily one-hour sessions of either CBT or PMRT. Study treatments were conducted at 3 p.m. following standard residential programming. The delivery of both study therapies was fully manualized and standardized (see below). Participants were instructed to practice newly introduced techniques during their own free time between sessions.

2.4.3. Study treatments: CBT—Content for the CBT was organized around three intervention domains: psychoeducation (introduction to the basics of the CBT model), cognitive restructuring (recognizing and modifying inaccurate beliefs related to alcohol and anxiety), and imagination-based exposure practice (applying newly-learned cognitive and

behavioral coping skills while imagining relevant stressful situations). Two sessions were devoted to each of these domains; one focused on anxiety symptoms alone and one focused on the association between anxiety symptoms and alcohol use. All therapy content was presented via a slide presentation to maximize participant understanding and to further standardize content delivery. Participants were instructed to practice new skills between sessions using structured worksheets that were reviewed with the therapist at the following session. All CBT therapy sessions were delivered by a doctoral-level psychologist with supervision provided by the second author.

2.4.4. Study treatments

PMRT: PMRT served as an active control and comparison treatment for the CBT. In contrast to CBT, PMRT focuses on anxiety and stress management without reference to the association between anxiety and alcohol use. Content for PMRT was adapted from *Progressive Relaxation Training: A Manual for the Helping Professions* (Bernstein and Borkovec, 1973) and was modified to match the CBT in terms of number and duration of sessions. PMRT sessions contained muscle-tension-release routines aimed at reducing muscular tension and has been shown to reduce AnxD symptoms (Manzoni et al., 2008; Siev and Chambless, 2007). The PMRT routines were delivered directly from a script by a post-bachelorette research therapist and participants were instructed to practice the relaxation techniques between each session.

2.5. Analytic approach

Analysis of variance was used to contrast High (above the median) vs. Low (below the median) IDS-UE groups on continuously measured demographic and clinical variables and chi-square tests were used for comparisons of the groups on categorical demographic and clinical variables. Moderation of 4-month treatment effects by level of baseline IDS-UE was assessed using logistic regression for binary outcomes (e.g. relapse vs. abstinence) and negative binomial regressions for continuous (i.e., count) outcomes (drinking days, binge days, and total drinks). Negative binomial regression was used due to the non-normal (over-dispersed Poisson) nature of drinking outcome count-based data (Horton et al., 2007). Given our hypothesis that DTC moderates treatment outcome, we highlight results that include two-way interactions between DTC and treatment; i.e., versus main effects. The time between treatment discharge and the 4-month follow-up represented the timeframe for all drinking outcomes data.

3. Results

3.1. Demographic and baseline clinical variable comparisons by IDS-UE group

The IDS-UE groups were compared on baseline demographic and clinical measures (Table 1). Regarding psychiatric diagnoses, the High (vs. Low) IDS-UE group had a significantly greater proportion of participants with major depression ($\chi^2(1) = 5.32, p < .05$), as well as more than one AnxD ($\chi^2(1) = 5.39, p < .05$). Additionally, the High (vs. Low) IDS-UE group reported significantly higher levels of drinking in the 4 months prior to treatment entry including drinking days (83.5 vs. 72.1, $F(1,209) = 5.57, p < .05$), binge days (81.2 vs. 66.8, $F(1,209) = 8.33, p < .01$), and total drinks (1876 vs. 1341, $F(1,209) = 8.62, p < .01$).

Those in the High IDS-UE group were also significantly higher on STAI (59.4 vs. 53.7, $F(1,215) = 17.67, p < .001$) and the BDI (22.7 vs. 17.3, $F(1,216) = 24.47, p < .001$). Not surprisingly given the median split forming the groups, the High IDS-UE group had significantly higher IDS-UE subscale scores than did the Low IDS-UE group (72.73 vs. 52.24, $F(1,216) = 410.02, p < .001$). The two IDS-UE groups were not significantly different in age, nor were there significant differences in distribution by treatment assignment, treatment completion rates, ethnicity, marital status, illicit drug use at baseline, use of prescribed psychiatric medications, or order of onset of alcohol and anxiety problems (see Table 1). Although not significant, there was a somewhat higher proportion of women in the High IDS-UE group as compared to the Low IDS-UE group ($\chi^2(1) = 2.66, p = .103$); however, the mean IDS-UE score did not significantly differ between women 64.39 (SD = 12.79) and men 61.06 (SD = 12.49).

3.2. IDS-UE as a moderator of treatment effects on alcohol outcomes: unadjusted analyses

Prior to testing moderator models adjusted for baseline clinical differences, we tested the unadjusted models for all outcomes with treatment group, IDS-UE group, and their interaction as predictors. Results from unadjusted models indicated significant interactions between IDS-UE group and treatment group for drinking days (Wald $\chi^2 = 14.12; p < .001$), binge days (Wald $\chi^2 = 26.79; p < .001$), and total drinks (Wald $\chi^2 = 40.94; p < .001$), suggesting IDS-UE moderated the effects of treatment on continuous drinking measures. However, the interaction between treatment group and IDS-UE group was not significant for the categorical measure of no drinking (“abstinence”) versus any drinking (“relapse”). Of the 218 total participants in the sample, 49% ($N = 106$) reported a relapse to any drinking during the 4 months following treatment. For those in the High IDS-UE group, 60.4% vs. 43.6% relapsed to any drinking after receiving PMRT versus CBT, respectively. For those in the Low IDS-UE group, 50.8% versus 38.3% relapsed to any drinking after receiving the PMRT versus CBT, respectively.

3.3. IDS-UE as a moderator of treatment effects on alcohol outcomes: adjusted analyses

To refine our understanding of the results from unadjusted analyses, demographic and baseline clinical variables that significantly differed between the Low and High IDS-UE groups (see Table 1), we entered these variables as covariates in analyses examining IDS-UE moderation of treatment effects on 4-month drinking outcomes. Gender was also included as a covariate to be consistent with the analytic approach of previous work on the IDS-UE subscale that included both men and women (Annis et al., 1987; Lau-Barraco et al., 2009).

As in the unadjusted analyses, results from the binary logistic regression indicated no significant interaction between IDS-UE and treatment group on relapse to the binary outcome of any drinking at 4 months, suggesting that IDS-UE failed to moderate the association between treatment group and this binary relapse parameter. Negative binomial regression results for continuous count alcohol outcome measures indicated the IDS-UE group by treatment group interaction approached the $p < .05$ criterion for statistical significance in terms drinking days (Wald $\chi^2 = 2.81; p = .09$) and was significant for binge days (Wald $\chi^2 = 6.95; p < .01$) and total drinks (Wald $\chi^2 = 8.64; p < .01$). To interpret

interaction effects, estimated means of alcohol outcome measures were plotted as a function treatment group and level of IDS-UE (see Fig. 2). As predicted, in the High IDS-UE group there were substantially fewer binge days after 4 months following treatment for those receiving the CBT compared to those receiving the PMRT while this treatment outcome difference was much smaller in the Low IDS-UE group (see Fig. 2B). As shown in Fig. 2C, comparison of estimated means of total drinks paralleled the results with binge days. Specifically, in the High IDS-UE group, those treated with CBT (vs. PMRT) reported having substantially fewer drinks over the 4-month follow-up period, while this difference was substantially smaller among those in the Low IDS-UE group.

4. Discussion

Consistent with study predictions, level of pre-treatment DTC behavior marked an important difference in the way patients with co-occurring AUD and AnxD responded to the two study treatments. For those reporting higher levels of pre-treatment DTC behavior, better outcomes were obtained from a CBT-based treatment targeting both anxiety symptoms and DTC, as compared to a treatment targeting anxiety management alone. By contrast, for those reporting lower levels of pre-treatment DTC behavior, outcomes were comparable and relatively good for both treatment approaches. These findings are consistent with the “vicious cycle” model of comorbidity that forms the conceptual and technical basis of the CBT employed in this study (Kushner et al., 2000a). As noted in Section 1, this model specifies that anxiety symptoms and alcohol use can become linked by reciprocal psychosocial and biological factors that concomitantly maintain and exacerbate symptoms of both conditions. Extrapolating from this model, identification and disruption of processes connecting anxiety symptoms with drinking behavior should result in improved drinking outcomes beyond reducing anxiety alone. Findings from Kushner et al. (2013) supported this prediction, while findings from the present study refine this hypothesis by showing that such treatments (and the model itself) may be most applicable to the subset of AUD-AnxD cases with higher versus lower levels of DTC behavior.

These findings, as well as the epidemiological studies showing that DTC behavior moderates the association of AnxD and risk for the development of AUD (Menary et al., 2011), prod us to consider further the broader implications of individual differences in the degree to which co-occurring AnxD and AUD are functionally related. We consider it relevant to this issue that the term “comorbidity,” as originally coined by Feinstein (1970), referred to co-occurring medical conditions that interact in some way effecting the development, maintenance, treatment response or relapse in the index condition. From this viewpoint, comorbidity of AnxD and AUD would refer more properly to the subset of those cases that have a meaningful functional link between these disorders. We operationalized “functional link” in the present study by distinguishing cases with more versus less DTC behavior; although it should be kept in mind that DTC is not the only conceivable functional link between AnxD and AUD. Nonetheless, our findings point to the potential clinical value of subdividing individuals with co-occurring AUD-AnxD based on the extent to which higher levels of DTC meaningfully relate the symptoms of the two conditions. Based on these findings, it may be clinically useful to reserve the “comorbid” designation for the

subset of those with co-occurring AUD and AnxD that demonstrates a substantial functional link between the two conditions.

In line with this distinction, Schuckit et al. (2013) conducted a 30-year follow-up of young adults to track the development and course of major depression and AUD. They found a significantly elevated association between depression and AUD among those reporting temporal proximity between their depressive episodes and bouts of heavy drinking (about 30% of all depressive episodes) but no significant elevation for AUD among those whose depressive episodes were not temporally proximal to heavy drinking. Importantly, this does not suggest that those whose depressive episodes were uncorrelated with heavy drinking did not develop AUD, just that the percentage developing AUD in this group did not significantly exceed the percentage that developed AUD among non-depressed individuals in the study. This seems to parallel epidemiological findings noted in Section 1 showing that among those with an AnxD, only those with DTC demonstrated an increased prospective risk for AUD relative to those with no AnxD (Menary et al., 2011).

AnxD and AUD are both among the most common mental disorders in the general community (Kessler et al., 2005, 1997) and would be expected to co-occur frequently by chance alone. For example, it would be expected that approximately 18% (a commonly accepted estimate of AnxD base rate in the general community) of those with AUD (nearly 1 in 5) would have an AnxD by chance alone. However, the rate of AnxD among AUD treatment patients is actually estimated to be closer to 50% (Kushner et al., 2005). Perhaps, the excess risk (i.e., beyond chance association) evidenced for AnxD and AUD when the other is present (also see Kushner et al., 2009) is a combination of distinct clinical groups; i.e., a “dually diagnosed” subgroup whose co-occurring disorders result by chance or perhaps from a shared vulnerability (e.g., temperament, neuro-function) in the absence of an explicit functional link versus a “comorbid” subgroup whose co-occurring disorders were promoted and/or maintained by a functional link such as DTC. Of course, one may experience multiple disorders by chance but then develop a functional link between them later in time. Under this scenario, an important clinical consideration is whether identifying and targeting risk factors that promote the development of a functional connection could mitigate the transition to “comorbid” AUD-AnxD. Similarly, one may also have a functional link between co-occurring disorders that weakens later in time; in fact, it is this scenario that the CBT tested seeks to instantiate. In any case, the primary possibility supported by our findings is that at the point in time treatment is sought, individuals with co-occurring disorders can be sub-divided into those with a stronger versus a weaker functional link between the symptoms of the two disorders based on level of DTC and that this distinction affects the patient’s treatment needs and response.

We can extrapolate from this perspective and our findings the conclusion that it is only the subgroup of dually diagnosed individuals who are “comorbid” in the Feinsteonian sense (i.e., those demonstrating a more substantial functional link between the co-occurring disorders) that require a specialized intervention for AUD beyond treatment as usual. In this regard, we can think of no reason why those who are dually diagnosed with no or minimal functional association between the conditions would have a worse AUD treatment outcome than those with no co-occurring AnxD. This conjecture is consistent with our findings showing that it

was those whose co-occurring disorders had a stronger functional link in terms of DTC who demonstrated a differential treatment response favoring the CBT. Of course, this is not to say that there would be no clinical value in treating an AnxD that is not functionally related to a co-occurring AUD, only that we would not expect this to directly improve AUD treatment outcomes.

The conceptual and clinical conjectures raised by these results beg the question of why some individuals with co-occurring disorders manifest a strong functional link between the conditions while others do not. This important question goes well beyond the scope and purpose of our study; however, there are some signals in our data that may be relevant to this question. For example, a significantly greater proportion of the High (vs. the Low) IDS-UE group had more than one AnxD and/or a diagnosis of major depression. The High (vs. Low) IDS-UE group also demonstrated more severe pre-treatment alcohol use at baseline. It is important to note that IDS-UE group moderation of the CBT treatment effect in the present study was demonstrated even after accounting for these baseline differences. This shows that DTC, once present, can exert effects that are independent of internalizing symptom severity but does not rule out the likely possibility that more severe internalizing symptoms may have promoted the development of DTC in the High IDS-UE group.

In addition to more extreme levels of internalizing symptoms, it also seems likely that poorer affect regulation and coping skills increase the likelihood of DTC behavior in response to even modest levels of internalizing symptoms. Consistent with this, DTC has been associated with life stressors such as poverty and work difficulties (c.f., Kushner, 2014) in the absence of AnxD. Further, affect regulation training (ART) has been shown to significantly improve abstinence rates among AUD treatment outpatients who endorse DTC in the absence of an AnxD (Stasiewicz et al., 2013). Taken together, the present study and past findings suggest that higher levels of internalizing symptoms, as well as weaker affect regulation and coping skills may contribute to the development and perpetuation of DTC behavior.

As implied in our model, reduction of DTC proneness is a presumptive mediator of the CBT's effectiveness. Unfortunately, we could not obtain explicit measure of change in DTC behavior in response to treatment in patients who remained abstinent; i.e., it would make no sense to ask about drinking situations or motives when no drinking occurred. We could have asked all patients to rate post-treatment drinking motives in terms of urges to drink or likelihood of drinking in hypothetical situations (e.g., situational confidence). However, when planning the study we decided that this would not necessarily provide an accurate measurement of actual change in drinking motives and would not provide a measure of actual DTC behavior that paralleled the IDS. Therefore, it can be seen as a limitation of the present work that the putative causal (mediator) model of the CBT (i.e., reduction in DTC behavior as the mediator) that informed the moderator hypothesis tested was not itself tested. With that said, the moderator tests conducted do have straightforward clinical implications (above) and provide data that are consistent with (but do not establish) the mediator model implied.

An additional challenge in interpreting our findings and planning future studies stems from the conceptual overlap in several common constructs potentially related to DTC such as drinking situations, drinking motives, and drinking expectancies. Negative affect alcohol outcome expectancies have been studied extensively by our group and others (Agrawal et al., 2008; Goldsmith et al., 2009; Ham et al., 2007; Kushner et al., 2000b; Terlecki and Buckner, 2015). Conceptually, such expectancies (the effect one anticipates drinking would have on negative affect) can be distinguished from drinking motives (why one might chose to drink in a given situation). In our view, the latter is a more complex phenomenon comprising an admixture of inputs such as: outcome expectancies (e.g., “alcohol would be likely to make me feel more relaxed”), competing contingencies (e.g., “I often get in trouble when I drink”), value judgments (e.g., “I’ve committed to myself and others not to drink”) and self-efficacy (e.g., “I can handle this situation without drinking”). We believe the CBT treatment used in this study is more likely to have impacted elements of drinking motives other than alcohol outcome expectancies, which, in our view, are a relatively stable function of one’s actual drinking experiences. One exception to this is that the CBT devotes significant attention to shifting the focus for judging alcohol’s likely effects from primarily proximal drinking effects (where anxiety reduction is typical) to primarily distal drinking effects (where exacerbation of anxiety and stress is typical; Kushner et al., 2000b). With that said, the drinking situations measured by the IDS are behaviorally anchored and therefore do not technically measure either drinking expectancies or drinking motives. Clearly, however, the original impetus for and purpose of the IDS was to capture these motivational phenomena in a behavioral context (Annis, 1982; Annis et al., 1987). In terms of future research, incorporating a combination of measures that assess expectancies, motives, and behaviors, as well as neuro-cognitive measures that tap anxiety-drinking associations in memory would all be relevant to elucidating the functional relationship between DTC and treatment outcomes.

While the predicted moderator of treatment effect by IDS-UE level was obtained for measures of relapse intensity, it was not evident for the categorical outcome of abstinence (no use). In addition to not being significant, the pattern evident in the data did not even show trends consistent with the predicted moderator effect. This could indicate that the processes related to a return to any alcohol use are different from those related to the severity or extent of relapse once alcohol is used. It is notable that studies of other AUD treatments, such as naltrexone, have shown similar distinctions between treatment effects on any relapse versus relapse intensity outcome measures (O’Malley, 1996; Pettinati et al., 2006).

We would contrast the non-significant effect for the binary “any use” outcome with the marginally significant effect for the number of drinking days outcome. Unlike the “any use” outcome measure, this effect approached statistical significance (p value $< .10$) and did conform to the predicted moderator pattern. In interpreting this result, we take into account the work of McClelland and Judd (1993) concerning the structural difficulty of detecting moderator (interaction) effects in field research and the risk for Type II errors this poses. Although those authors have a number of recommendations for overcoming this problem, the only one that can be applied to these data is employing a somewhat relaxed alpha value

in interpreting interaction effect. Based on this recommendation, the overall pattern of the findings, the fact that this effect was significant in the unadjusted models, and some alternative analytic checks described just below, we concluded that the marginally significant moderator effect for the number of drinking days outcome ($p = .09$) in the adjusted model was most likely not due to chance.

A potentially important aspect of our analytic approach was the decision to treat the continuously measured IDS-UE subscale as a two-level variable using a median split. The primary rationale for this was to increase the interpretability of the results. McClelland and Judd (1993) suggest that while reducing the levels of a continuously measured moderator (e.g., the median split used here for the IDS scale) can reduce some problems of moderator detection, it can introduce others; e.g., a potential loss of power and the possibility of spurious effects associated with non-linearity. As a check against these concerns, we re-ran all key hypothesis-testing analyses in two ways: (1) using the IDS-UE subscale as a continuous variable as originally measured; and, (2) using a tertile rather than median split on the measure. These checks confirmed the robustness of the findings reported and also rendered the marginally significant treatment group by DTC behavior interaction as significant for the number of drinking days outcome. These checks, along with the significant effect for this outcome obtained in the unadjusted models, help to reduce concerns about spurious effects due to non-linearity and supports our interpretation of the marginally significant moderator effect for the drinking-days outcome as supportive of the predicted moderator effect.

To conclude, this study is the first of which we are aware to demonstrate that a large and difficult to treat group of individuals with AUD – those with co-occurring AnxD – can be meaningfully differentiated in terms of their treatment needs based on level of pre-treatment DTC. Based on this, we have suggested that the term “comorbid” – commonly used interchangeably with “co-occurring” and “dually-diagnosed” – be reserved for those cases in which the co-occurring disorders manifest a substantial functional link via processes such as DTC. This distinction relates to important clinical differences not otherwise identified in strictly diagnostic terms. Finally, these findings shed new light on the clinical mystery of why effective anxiety reduction strategies alone do not substantially improve AUD treatment outcomes when deployed in groups of patients with co-occurring AnxD and AUD that are undifferentiated by their level of DTC.

Acknowledgments

Role of funding source

This research was supported by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) grant R01-AA015069 awarded to Matt G. Kushner as well as a National Institute of Drug Abuse (NIDA) training grant supporting the work of Justin Anker (T32DA037183). NIAAA and NIDA had no further role in the study design; in the collection, analysis, and interpretation of data; in writing; nor in the decision to submit the manuscript for publication.

The authors wish to acknowledge and thank Christopher Hickman and his staff at the Fairview-Riverside Lodging Plus Chemical Dependency program for their continued support of this and other work. The authors would also like to thank Joani Van Demark, Marc Mooney, Sheila Specker, Mallory Mahaffey, Kari Knefelkamp, and Hoa Le for their technical assistance.

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Fig. 1. Distribution of participant IDS-UE scores within the sample of treatment seeking AUD patients with comorbid AnxD. The solid vertical line represents the median used to split High and Low IDS-UE groups.

Fig. 2.

Estimated means ($\pm$ SEM) for drinking days (A) binge days (B), and total drinks(C) at the 4-month follow-up as a function of treatment and IDS-UE.

Table 1

Baseline demographics and clinical characteristics by IDS-UE group.

Variables	Low IDS-UE (<i>n</i> = 110)	High IDS-UE (<i>n</i> =108)	<i>p</i>
IDS-UE subscale score <i>M</i> (<i>SD</i>)	52.24 (9.24)	72.73 (5.08)	<.01
Gender (% female)	35%	45%	.10
Race			.52
African American	9%	14%	
American Indian	7%	10%	
Asian	1%	0%	
Hispanic	3%	1%	
White	78%	72%	
Other	3%	3%	
Marital status			.15
Never married	49%	39%	
Separated	10%	11%	
Divorced	16%	30%	
Married	24%	20%	
Widowed	1%	0%	
Illicit drug use	60%	57%	.64
Prescribed psychiatric medications	66%	66%	.97
Major depression diagnosis	36%	51%	<.05
Principal anxiety disorder			.20
Generalized anxiety disorder	41%	39%	
Panic disorder	11%	19%	
Social anxiety disorder	48%	42%	
Number of anxiety disorders			<.05
=1	54%	38%	
>1	46%	62%	
Order of onset			.95
Problems with anxiety first	79%	79%	
Problems with alcohol first	21%	21%	
Treatment group			.23
CBT	43%	51%	
PMRT	57%	49%	
Completed study treatment	96%	91%	.17
Completed 4 month follow-up	78%	75%	.48
STAI <i>M</i> (<i>SD</i>)	53.7 (8.88)	59.4 (10.86)	<.01
BDI <i>M</i> (<i>SD</i>)	17.3 (7.22)	22.7 (9.13)	<.01
Baseline drinking measures during the 4 months before treatment			
Drinking days <i>M</i> (<i>SD</i>)	72.1 (36.00)	83.5 (34.00)	<.01
Binge days ^a <i>M</i> (<i>SD</i>)	66.8 (37.76)	81.2 (34.63)	<.05
Total drinks <i>M</i> (<i>SD</i>)	1340.8 (1312.01)	1876.4 (1338.18)	<.01

Variables	Low IDS-UE (<i>n</i> = 110)	High IDS-UE (<i>n</i> =108)	<i>p</i>
	<u>Years</u>	<u>Years</u>	
Age <i>M</i> (<i>SD</i>)	38.9 (11.87)	40.2 (8.51)	.34
Age of principal anxiety onset <i>M</i> (<i>SD</i>)	17.6 (10.92)	17.5 (11.43)	.93
Age of first regular drinking <i>M</i> (<i>SD</i>)	19.1 (6.11)	18.7 (4.58)	.65

CBT = cognitive behavioral therapy; PMRT = Progressive Muscle Relaxation Training; STAI = Spielberger Trait Anxiety Inventory; BDI = Beck Depression Inventory.

^aBinge drinking is defined as four drinks per drinking episode for women and five drinks per drinking episode for men (National Institute on Alcohol Abuse and Alcoholism).