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### 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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### 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

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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

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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 symptom is 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

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