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Effect of Cognitive Bias Modification on Early Relapse Among Adults Undergoing Inpatient Alcohol Withdrawal Treatment
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IMPORTANCE More than half of patients with alcohol use disorder who receive inpatient withdrawal treatment relapse within weeks of discharge, hampering subsequent uptake and effectiveness of psychological and pharmacologic interventions. Cognitive bias modification (CBM) improves outcomes after alcohol rehabilitation, but the efficacy of delivering CBM during withdrawal treatment has not yet been established.

OBJECTIVE To test the hypothesis that CBM would increase the likelihood of abstaining from alcohol during the 2 weeks following discharge from inpatient withdrawal treatment.

DESIGN, SETTING, AND PARTICIPANTS In a randomized clinical trial, 950 patients in 4 inpatient withdrawal units in Melbourne, Australia, were screened for eligibility between June 4, 2017, and July 14, 2019, to receive CBM or sham treatment. Patients with moderate or severe alcohol use disorder aged 18 to 65 years who had no neurologic illness or traumatic brain injury were eligible. Two-week follow-up, conducted by researchers blinded to the participant's condition, was the primary end point. Both per-protocol and intention-to-treat analysis were conducted.

INTERVENTIONS Randomized to 4 consecutive daily sessions of CBM designed to reduce alcohol approach bias or sham training not designed to modify approach bias.

MAIN OUTCOMES AND MEASURES Primary outcome was abstinence assessed using a timeline followback interview. Participants were classified as abstinent (no alcohol use in the first 14 days following discharge) or relapsed (any alcohol use during the first 14 days following discharge or lost to follow-up).

RESULTS Of the 950 patients screened for eligibility, 338 did not meet inclusion criteria, 108 were discharged before being approached, and 192 refused. Of the 312 patients who consented (referred sample), 12 withdrew before being randomized. In the final population of 300 randomized patients (CBM, n = 147; sham, n = 153), 248 completed the intervention and 272 completed the follow-up. Of the 300 participants (173 [57.7%] men; mean [SD] age, 43.47 [10.43] years), 7 patients (3 controls, 4 CBM) withdrew after finding the training uncomfortable. Abstinence rates were 42.5% (95% CI, 34.3%-50.6%) in controls and 54.4% (95% CI, 46.0%-62.8%) in CBM participants, yielding an 11.9% (95% CI, 0.04%-23.8%; $P = .04$) difference in abstinence rates. In a per-protocol analysis including only those who completed 4 sessions of training and the follow-up, the difference in abstinence rate between groups was 17.0% (95% CI, 3.8%-30.2%; $P = .008$).

CONCLUSIONS AND RELEVANCE The findings of this clinical trial support the efficacy of CBM for treatment of alcohol use disorder. Being safe and easy to implement, requiring only a computer and joystick, and needing no specialist staff/training, CBM could be routinely offered as an adjunctive intervention during withdrawal treatment to optimize outcomes.

TRIAL REGISTRATION Australian New Zealand Clinical Trials Registry Identifier: ACTRN12617001241325

Supplemental content

CME Quiz at jamacmelookup.com and CME Questions page 228

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Worldwide, 2.3 billion people consume alcohol, with 283 million meeting alcohol use disorder (AUD) criteria,[1] making alcohol one of the most widely used and most harmful substances.[2] Globally, 1 in 10 adults have experienced AUD during their lifetime.[3] Therefore, the development of scalable, low-cost AUD interventions is important. Standard AUD treatment includes outpatient counseling, peer support, and/or pharmacotherapy, but in severe AUD, associated physical complications often necessitate an initial inpatient withdrawal (ie, medically supported detoxification).[4] Approximately 85% of patients eventually relapse following withdrawal management,[5] with more than half consuming their first drink within 2 weeks.[6] Relapse is a major barrier to engagement in postwithdrawal treatment and often necessitates further costly inpatient admissions.

Current relapse prevention approaches include pharmacotherapy and psychotherapy. Medications such as naltrexone and acamprosate reduce relapse rates by 5% to 8% up to 1 year following treatment.[7] However, these medications prevent relapse in a minority of patients, have highly variable adherence rates, are contraindicated in patients with certain health conditions, cause adverse effects in some patients, and, most importantly, are prescribed to few patients.[7,8] Meta-analyses have suggested that psychosocial interventions, such as cognitive behavioral therapy and motivational interviewing, have significant, but small relapse prevention effects.[9,10] Recognizing the need for new approaches, researchers have begun developing neurocognitive interventions that target cognitive biases thought to play a role in the development and maintenance of addiction.[11] In people with AUD, exposure to cues (eg, images, smells, and physical and social contexts) associated with alcohol can rapidly activate mental representations of alcohol's rewarding effects, leading to cognitive biases, including approach bias (the automatic action tendency to approach alcohol-related cues).[11] Consequently, alcohol-related cues in the environment trigger automatic tendencies to approach and ultimately consume alcohol.

Research has suggested that cognitive bias modification (CBM), a novel computerized training intervention, can dampen alcohol approach bias and reduce likelihood of relapse. When delivered during residential rehabilitation treatment, just 4 to 12 CBM sessions lasting 15 minutes reduce alcohol relapse rates by 8% to 13% at 1-year follow-up.[12-14] Administering CBM during withdrawal treatment could help prevent early relapse during the critical period when patients transition from residential to community-based treatment. The likelihood of patients engaging in and benefiting from subsequent psychosocial interventions is higher if they remain abstinent during this transition. A pilot randomized clinical trial demonstrated the feasibility of delivering CBM during withdrawal treatment and found that 4 sessions significantly increased abstinence rates by 30% relative to a sham-training control condition at a 2-week follow-up, although intention-to-treat analysis was nonsignificant ($P = .07$).[6] Since the pilot trial had a small sample (N = 83), we now report findings from a subsequent well-powered, multisite trial to determine the efficacy of CBM in preventing early relapse following inpatient withdrawal. As described in the protocol,[15] the primary hypothesis was that patients who receive CBM would be significantly less likely to consume alcohol in the first 2 weeks following withdrawal treatment compared with patients in the sham-training control condition.

Key Points

Question Is computerized cognitive bias modification training during inpatient alcohol withdrawal treatment associated with the likelihood of relapse in the first 2 weeks after discharge?

Findings In a randomized clinical trial of 300 patients with alcohol use disorder receiving inpatient withdrawal treatment, cognitive bias modification significantly increased the proportion who maintained abstinence during the follow-up period (54.4% vs 42.5% with sham training) in intention-to-treat analysis and by 17% (63.8% vs 46.8%) in per-protocol analysis.

Meaning The findings of this trial show that cognitive bias modification during alcohol withdrawal helps prevent relapse during the high-risk early period following discharge from treatment; its implementation as an adjunctive intervention in this setting is recommended.

Methods

Study Design and Participants

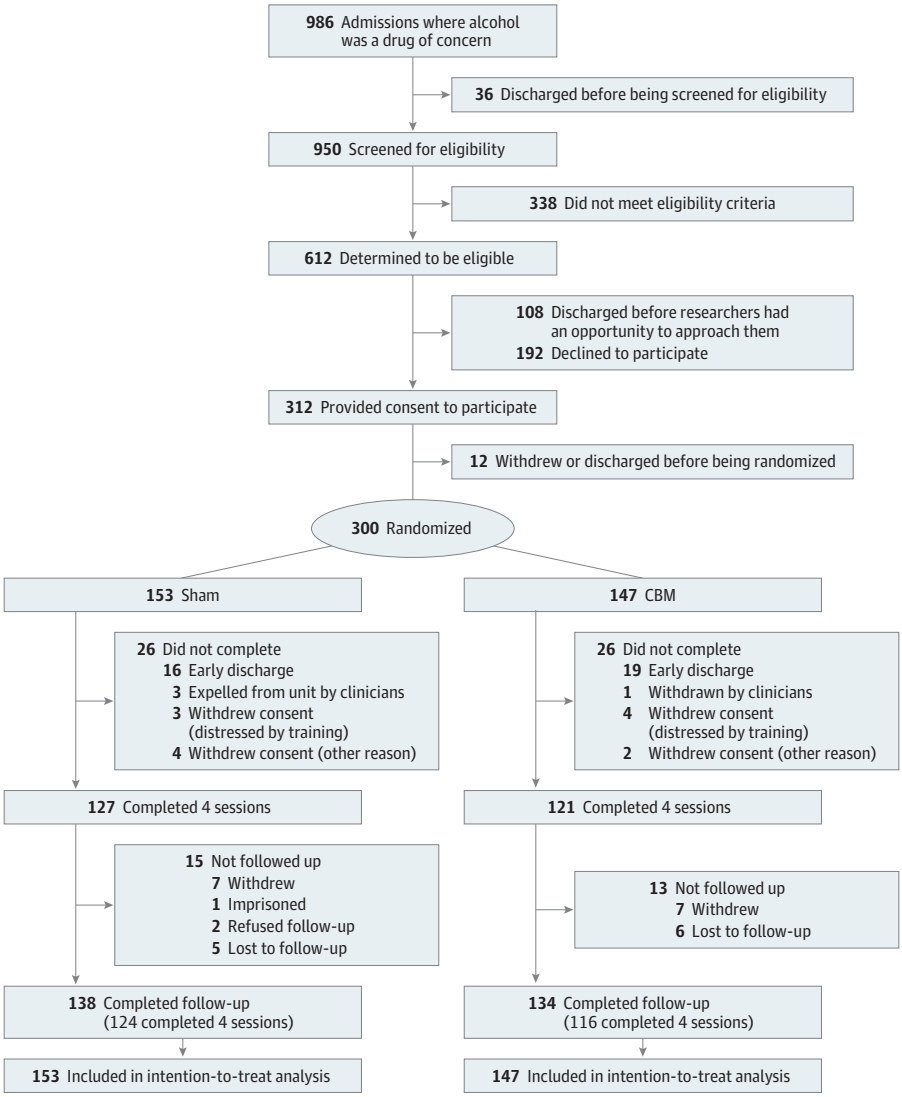
This was a randomized (1:1 allocation ratio), double-blind, sham-controlled, parallel-group clinical trial. Recruitment occurred at 4 alcohol and other drug residential withdrawal treatment units in the Melbourne metropolitan area in Australia. Three locations were public health services, and 1 was a nongovernment organization addiction treatment service that receives public funding. Participants provided written informed consent and received financial compensation. This study was approved by the St Vincent's Hospital Melbourne Human Research Ethics Committee and the Monash University Human Research Ethics Committee. The study protocol is available in Supplement 1. This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.

Three hundred patients admitted to inpatient withdrawal facilities were randomized between June 4, 2017, and July 14, 2019. Screening and recruitment information is shown in **Figure 1**. Inclusion criteria required that participants be aged 18 to 65 years; met *DSM-5*[16] criteria for current moderate or severe AUD; had at least weekly alcohol use during the month prior to admission; and intended to stay long enough to complete the 4-day training protocol. Inpatient withdrawal treatment typically lasted 1 week (mean [SD], 7.3 [2.6] days). Exclusion criteria were diagnosed history of neurologic illness, injury, intellectual disability, or concussion resulting in loss of consciousness longer than 30 minutes or deemed by clinical staff to be unable to provide informed consent or safely participate owing to acute mental or physical impairment.

Measures

A baseline researcher-administered questionnaire assessed demographic and clinical characteristics and confirmed eligi-

Figure 1. Screening, Recruitment, Randomization, Treatment Completion, and Follow-up Completion Data



CBM indicates cognitive bias modification.

bility (eMethods in Supplement 2). Researchers assessed AUD symptoms using the Structured Clinical Interview for *DSM-5* Disorders, Research Version (SCID-5 RV)[17] AUD module, which also verified eligibility. Participants self-administered the Severity of Alcohol Dependence Questionnaire (SADQ).[18]

The timeline followback (TLFB) interview method was used to quantify the number of days of alcohol use and estimated standard drinks consumed, as well as tobacco and other drug use.[19] At baseline, the TLFB assessed the 30 days preceding the inpatient withdrawal admission. At the 2-week follow-up, the TLFB covered the 14 days starting with the day of discharge.

An assessment version of the Alcohol Approach/Avoidance Task (AAT) was used to measure approach bias.[20] Internal consistency was low (Cronbach α = 0.35 for alcohol-related items and 0.34 for nonalcohol-related items). Further details of the AAT, including the internal consistency calculation method, are in the eMethods in Supplement 2.

Intervention

The CBM training task was a modified version of the assessment AAT. Participants were instructed to respond to images by pushing or pulling a joystick based on the orientation of the frame displayed around the picture (pushing landscape or pulling portrait), and the picture size decreased or increased accordingly. Following 8 practice trials (frames with no picture inside), 40 images of alcoholic beverages and 40 images of nonalcoholic beverages were presented 3 times each (ie, 240 total image presentations) in a random order. Ninety-five percent of landscape-oriented frames contained alcohol-related images and the remaining 5% contained nonalcohol-related images. Likewise, 95% of portrait-oriented frames contained nonalcohol-related images, and 5% contained alcohol-related images. Since participants were required to push away images with landscape-oriented frames and pull images with portrait-oriented frames, they pushed away nearly all alcohol-related images and pulled nearly all nonalcohol-related images,

implicitly training them to avoid alcohol. Additional task details are described in the eMethods in Supplement 2.

Sham training was identical to the CBM training except that each orientation (portrait or landscape) contained alcohol-related images 50% of the time and nonalcohol-related images 50% of the time. Moreover, participants were instructed to respond with lateral movements of the joystick according to picture orientation (left for landscape; right for portrait). The image moved in accordance with the joystick movement to the left or right edge of the computer screen but did not change size. The sham condition thereby controlled for participants' exposure to alcohol- and nonalcohol-related images, and for the demand to attend to and to manipulate the picture with a joystick based on orientation, without the approach/avoidance component hypothesized to underlie the therapeutic effect of CBM.

Procedures

Intake clinicians at the withdrawal treatment sites screened patients' eligibility at admission. Patients deemed eligible were approached by a researcher on the third day of their admission to explain the study and obtain informed consent. The researcher then administered the demographic questionnaire, SCID-5-RV, and TLFB. Participants self-administered the SADQ and completed the AAT.

Participants were automatically randomized when they began the first CBM session according to a randomization sequence preprogrammed into the training laptop by a statistician not involved in recruitment or data collection. Randomization of the participants was stratified by site, with a 1:1 allocation to treatment arms using permuted blocks of variable size. Participants were not told into which condition they were placed. Each training session lasted approximately 15 minutes. Further training sessions occurred on the following 3 days (ie, 4 consecutive days of training in total). Immediately before and after each session, participants were asked to rate the intensity of their alcohol craving on a visual analog scale scored from 0 (not at all) to 100 (extreme).

Following the final training session, participants repeated the AAT. At least 2 weeks after the participant's discharge, a researcher who was not involved in CBM training, and therefore blinded to the participant's condition, contacted them to conduct the follow-up TLFB. Following intention-to-treat principles, follow-ups were pursued with any participant who began training, regardless of whether they completed the 4-session training protocol, unless they withdrew consent.

Statistical Analysis

The primary outcome, abstinence (defined as no alcohol consumption during this 2-week period), was analyzed using Pearson χ^2. The sample size was based on an expected 20% difference between groups in abstinence rates (ie, 45% vs 65% based on pilot data[6]), with a sample of 256 allowing 90% power to detect a difference. We therefore aimed to recruit 300 participants to allow for 15% dropout. The primary analysis followed intention-to-treat principles, including all randomized participants regardless of completion of the training. Adopting a conservative approach to account for missing data, participants lost to follow-up were assumed to have consumed alcohol in this analysis. A supplementary per-protocol analysis included only participants who completed all 4 training sessions and the 2-week follow-up (ie, not imputing outcome for those lost to follow-up). Logistic regression, with baseline alcohol approach bias, group, and their interaction as predictors, was used to test whether baseline alcohol approach bias moderated the efficacy of CBM. Another logistic regression analysis, with change in alcohol approach bias between sessions 1 and 4 and group as predictors, was used to test whether change in approach bias may have mediated the efficacy of CBM. Analyses of the primary outcome variable used procedures (FREQ and LOGISTIC) in SAS, version 9.4 (SAS Institute Inc). Repeated measures analyses of approach bias scores used the REML directive in Genstat, release 19.1 (VSN International Ltd). For all analyses, the decision regarding whether to reject the null hypothesis was based on the 2-tailed *P* value, with $\alpha = .05$ as the threshold for significance.

Results

Sample Characteristics

Of the 950 patients screened for eligibility, 338 did not meet inclusion criteria, 108 were discharged before being approached, and 192 refused. Of the 312 patients who consented (referred sample), 12 withdrew before being randomized. Recruitment ceased after randomizing 300 participants based on the sample size calculation. In the final population of 300 randomized patients, 248 completed the intervention and 272 completed the follow-up. Numbers recruited at each site are presented in eTable 1 in Supplement 2. The participants included 173 men (57.7%), 126 women (42.0%), and 1 nonbinary individual (0.3%); mean (SD) age was 43.47 (10.43) years. **Table 1** presents other sociodemographic characteristics. **Table 2** summarizes participants' clinical characteristics. A total of 201 participants (67.0%) had previously undergone withdrawal treatment. They typically had severe AUD (mean of 10/11 *DSM-5* AUD criteria; mean SADQ score in the severe physical dependence range). Most drank daily or nearly daily, consuming a mean (SD) of 589.46 (344.92) standard drinks in the month before admission. Two hundred twenty-seven individuals (75.7%) had a comorbid psychiatric diagnosis. Despite their complexity, approximately 5 of 6 participants completed the 4 sessions of CBM, confirming our previous report[6] that CBM training is feasible in this population.

Primary Outcome

In the control condition, 42.5% (95% CI, 34.3%-50.6%) of participants abstained from alcohol, and 54.4% (95% CI, 46.0%-62.8%) of those in the CBM condition abstained, yielding an estimated difference in abstinence rates between groups of 11.9% (95% CI, 0.04%-23.8%; $P = .04$). In the per-protocol analysis, abstinence rates were 63.8% (95% CI, 54.4%-72.5%) in the CBM group and 46.8% (95% CI, 37.8%-55.9%) in the control group, yielding an estimated difference in abstinence rates between groups of 17.0% (95% CI, 3.8%-30.2%; $P = .008$).

Table 1. Demographic Characteristics of the Sample at Baseline

Characteristic	No. (%)		
	Whole sample (N = 300)	Control group (n = 153)	CBM group (n = 147)
Age, mean (SD), y	43.47 (10.43)	42.31 (10.67)	44.68 (10.07)
Sex			
Men	173 (57.7)	97 (63.4)	76 (51.7)
Women	126 (42.0)	55 (36.0)	71 (48.3)
Nonbinary	1 (0.3)	1 (0.6)	0
Born in Australia[a]	252 (84.0)	122 (79.7)	130 (88.4)
Aboriginal or Torres Strait Islander[a]	18 (6.0)	8 (5.2)	10 (6.8)
Years of completed education, mean (SD)	12.47 (2.56)	12.48 (2.70)	12.46 (2.42)
Currently employed	76 (25.3)	36 (23.5)	40 (27.2)
Current homelessness or unstable housing	42 (14.0)	26 (17.0)	16 (10.9)

Abbreviation: CBM, cognitive bias modification.

[a] Information on ethnicity other than Australian Indigenous status and country of birth was not collected.

Table 2. Clinical Characteristics of the Sample at Baseline

Characteristic	No. (%)		
	Whole sample (N = 300)	Control group (n = 153)	CBM group (n = 147)
Age at which alcohol use became problematic, mean (SD), y	26.29 (10.57)	26.33 (10.90)	26.25 (10.24)
Any previous acute withdrawal episodes	201 (67.0)	110 (71.9)	91 (61.9)
Current drugs of concern other than alcohol and tobacco	64 (21.3)	36 (23.5)	28 (19.1)
Current daily tobacco smoker	215 (71.7)	111 (72.5)	104 (70.7)
Substance use disorder in first-degree relatives	129 (43.0)	70 (45.8)	59 (40.1)
Current psychiatric diagnosis	227 (75.7)	114 (74.5)	113 (76.9)
No. of SCID AUD criteria met, mean (SD)	9.69 (1.44)	9.62 (1.44)	9.76 (1.44)
SADQ score, mean (SD)	32.19 (11.68)	31.99 (11.54)	32.40 (11.86)
No. of days of alcohol consumption in 30 d before admission, mean (SD)[a]	27.26 (4.97)	27.05 (5.19)	27.47 (4.74)
No. of standard drinks consumed in 30 d before admission, mean (SD)	589.46 (344.92)	588.38 (343.22)	590.60 (347.91)
Completed all 4 sessions of assigned intervention (CBM or sham training)	248 (82.7)	127 (83.0)	121 (82.3)

Abbreviations: AUD, alcohol use disorder; CBM, cognitive bias modification; SADQ, Severity of Alcohol Dependence Questionnaire; SCID, Structured Clinical Interview for *DSM-5*.

[a] In Australia, a standard drink is defined as 10 g of pure ethanol.

Approach Bias

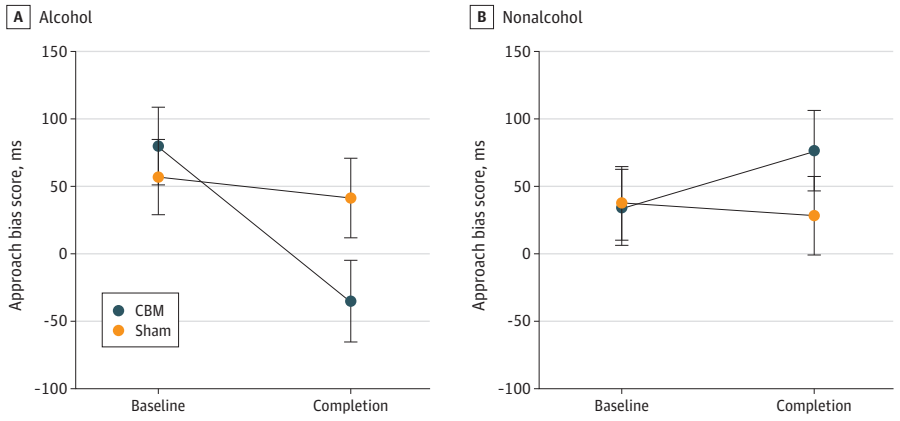
Approach bias was calculated separately for alcohol-related and nonalcohol-related images (eMethods in Supplement 2 provides details). Alcohol approach bias data were available for 277 participants (143 control and 134 CBM) at baseline and 248 participants (127 control and 121 CBM) after training. For nonalcohol-related pictures, these numbers were 281 (145 control, 136 CBM) at baseline and 247 (127 control, 120 CBM) at session 4. Neither baseline alcohol approach bias ($P = .55$) nor its interaction with group ($P = .60$) significantly predicted abstinence. The main effect of group remained significant when controlling for approach bias and the interaction term (odds ratio [OR], 1.626 at the mean of baseline alcohol approach bias; 95% CI, 1.009-2.618, $P = .04$).

Changes in approach bias scores are shown in **Figure 2.** For alcohol-related pictures, there was a significant interaction between group and time (interaction contrast: −99.4; 95% CI, −153.1 to −45.7; $P < .001$). There was no significant difference between groups at baseline (mean [SD]: CBM, 79.86 [165.43]; control, 56.90 [194.38]; $P = .13$), but alcohol approach bias was significantly lower in the CBM group than in the control group after training (CBM, −35.09 [169.03]; control, 41.35 [148.06]; $P < .001$). Between sessions 1 and 4, CBM participants' approach bias declined significantly (mean change: −115.0; 95% CI, −153.5 to −76.4; $P < .001$), reversing to become an avoidance bias, while controls continued to show a similar approach bias to baseline (mean change: −15.6; 95% CI, −53.0 to 21.8; $P = .21$).

For nonalcohol-related pictures, the interaction between group and time did not reach significance ($P = .055$). However, *t* tests conducted at each time point separately suggested that, while nonalcohol approach bias did not differ significantly between groups at baseline (mean [SD]: CBM, 33.98 [181.31]; control, 36.94 [188.69]; $P = .44$), it was larger in the CBM group after training (CBM, 76.06 [158.13]; control, 27.76 [138.59]; $P = .01$). Approach bias to nonalcohol-related images increased significantly between sessions 1 and 4 in the CBM group (mean change: 42.1; 95% CI, 4.7-79.5; $P = .01$) but not in controls (mean change: −9.2; 95% CI, −45.4 to 27.1; $P = .31$).

To test whether the change in alcohol approach bias mediated the effect of CBM on abstinence, we conducted logistic regression analysis with change score (session 4 score minus session 1 score) and group included as predictors of abstinence. Group was again a significant predictor (OR, 1.938; 95% CI, 1.130-3.322; $P = .02$) but not approach bias change score (OR, 1.000; 95% CI, 0.999-1.001; $P = .78$). Thus, we did not proceed to path analysis comparing the mediating path (group to change score to abstinence) to the direct path (group to abstinence).

Figure 2. Mean Approach Bias Scores for Alcohol-Related and Nonalcohol-Related Images



Bias scores for alcohol-related (A) and nonalcohol-related (B) images at baseline (before the first session) and completion (after the final session) of cognitive bias modification. Error bars show 95% CIs around the mean.

Analysis of single-item craving ratings taken before and after each training session are presented in the eResults in Supplement 2. We found that CBM did not acutely increase craving and slightly reduced craving between presession and postsession ratings relative to sham training (eTable 2 in Supplement 2). Analyses of participants' subjective ratings of how interesting the training task was and whether they felt it affected their craving and attention showed similar ratings between groups (eFigure in Supplement 2). Exploratory analyses testing whether treatment site (P = .47), sex (P = .84), age (P = .97), or SADQ score (P = .14) moderated the effect of CBM on the primary outcome are provided in the eResults in Supplement 2.

Discussion

To our knowledge, this was the first fully powered randomized clinical trial of CBM during inpatient alcohol withdrawal. Consistent with our feasibility pilot study findings, CBM significantly increased the likelihood of abstinence in the first 2 weeks following discharge relative to a sham-training control condition. The rate of abstinence was increased by 11.9% in the intention-to-treat analysis or by 17.0% if all 4 sessions were completed. Our replication of the pilot trial's findings regarding efficacy[6] is particularly important in light of the current replicability crisis, whereby many published findings fail to replicate owing to low statistical power and a lack of open science practices (eg, registration of protocols).[21] This finding adds further weight to the growing body of evidence supporting the clinical efficacy of CBM as an adjunctive treatment for AUD.[6,12-14]

Until now, the efficacy of CBM has been established only during postwithdrawal rehabilitation treatment,[12-14] yet most patients undergoing withdrawal do not proceed to longer-term residential rehabilitation.[22] This trial shows that, when delivered during withdrawal, CBM can prevent relapse during the highly vulnerable postdischarge phase, as patients transition from a protective inpatient environment to the community where they are bombarded with visual, auditory, and olfactory alcohol cues that trigger craving. The finding that more than half of the control group relapsed during the 2-week follow-up period illustrates the need to examine short-term effects of postwithdrawal relapse prevention interventions. It is necessary to prevent early relapse so that patients are more likely to engage in and reap greater benefit from ongoing psychosocial treatment and aftercare. This factor is particularly important because relapse often necessitates subsequent inpatient withdrawal treatment episodes, which are not only costly but potentially harmful in terms of exacerbating cognitive impairment.[23-25]

In line with previous trials,[12,14] we also observed a significantly greater reduction in alcohol approach bias (ie, the targeted mechanism) in the CBM group relative to controls. Cognitive bias modification, but not sham training, shifted the approach bias to an avoidance bias. However, pretraining approach bias did not moderate the effect of CBM on abstinence, nor did reduction in alcohol approach bias mediate the effect. Only 1 of the 3 large-scale alcohol CBM studies[12-14] has demonstrated moderation and mediation.[12] The question therefore remains as to whether change in approach bias is actually the mechanism by which CBM leads to abstinence. The low internal consistency of the approach bias measure may have impeded detection of mediation, and use of more reliable measures is recommended for future mediation tests. Regardless, the absence of mediation should not preclude the adoption and implementation of CBM given its demonstrated efficacy. There are numerous examples in which effective treatments are routinely provided despite their mechanisms of action not being fully understood (eg, lithium,[26] electroconvulsive therapy,[27] and acamprosate[8]).

Another observation that could inform the design of future CBM programs was the significant increase in approach bias toward nonalcohol-related cues among the CBM group, which suggests the possibility of strengthening approach bias toward stimuli through repeated approach movements. Thus, rather than using neutral cues (or even potentially harmful cues, such as sugary soft drinks) as approach stimuli, CBM could incorporate positive/healthy approach images that depict one's goals and motivations for behavior change (eg, family, employment, and hobbies) or positive alternatives to drink-

ing (eg, exercise). Contemporary behavioral and cognitive theories of addiction[28,29] suggest that reinforcing the value of these positive goals may help counter the effect of maladaptive cognitive biases on decision-making, possibly further enhancing the therapeutic benefits of CBM.

As noted by others, CBM is a promising adjunctive intervention that directly targets key cognitive mechanisms with minimal intensity in terms of time or cognitive demands on patients.[30] Its simple instructions mean CBM is easy to engage in during the early stages of AUD treatment, such as inpatient withdrawal, when cognitive recovery is yet to begin.[31,32] Our finding that craving did not increase and instead decreased after CBM sessions, and the low rate of withdrawal due to discomfort, allays concerns regarding the safety of exposing patients to alcohol stimuli at this stage of treatment. Nonetheless, we recommend monitoring acute craving during CBM training and providing support if a patient experiences discomfort. The low cost (requiring only a laptop and joystick, freely available software, and a few minutes of nonspecialist staff time per session) makes implementation of CBM feasible, including in low-income countries in which resources and treatment options are more limited.

Strengths and Limitations

This study's strengths include its double-blind design, sham-training control condition, low risk of methodologic and reporting bias, conservative estimation of abstinence rates, and measurement of approach bias. The main limitation of the trial was the reliance on self-reported alcohol use as the primary outcome. The vast geographic catchment of the 4 withdrawal units precluded in-person follow-up interviews and therefore the biological verification of abstinence. However, the TLFB interview method is considered valid for measuring recent use of alcohol and other drugs,[33-35] particularly when administered by a researcher who is independent from the clinical team and when confidentiality is ensured, as was the case in this trial. An additional limitation was that blinding (ie, awareness of condition assignment) was not assessed. However, the absence of group differences in subjective ratings of whether the task was interesting, reduced craving, or improved attention (eResults in Supplement 2) suggests that sham training offered a subjectively similar control condition to active CBM.

Conclusions

In light of its low cost, safety, brevity, and ease of implementation, we propose that CBM be routinely offered as an adjunctive approach during alcohol withdrawal treatment. Neurocognitive interventions are recommended for the postacute withdrawal phase in the alcohol treatment guidelines in Germany,[36] where CBM is delivered as treatment as usual in several residential rehabilitation facilities. Having demonstrated its efficacy during alcohol withdrawal, we encourage future research aimed at improving its efficacy. Such approaches include the personalizing of avoid (alcohol-related) and approach (positive) stimuli and gamification, which may increase engagement and adherence and enhance efficacy further.[37]

ARTICLE INFORMATION

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Author Contributions: Dr Reynolds had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Manning, Garfield, Staiger, Lubman, Lum, Reynolds, Hall, Lloyd-Jones, Wiers, Verdejo-Garcia.
Acquisition, analysis, or interpretation of data: Manning, Garfield, Lum, Reynolds, Bonomo, Lloyd-Jones, Piercy, Jacka, Verdejo-Garcia.
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