UvA-DARE (Digital Academic Repository)

Mediation of cognitive bias modification for alcohol addiction via stimulus-specific alcohol avoidance association

Gladwin, T.E.; Rinck, M.; Eberl, C.; Becker, E.S.; Lindenmeyer, J.; Wiers, R.W.

DOI

[10.1111/acer.12602](https://doi.org/10.1111/acer.12602)

Publication date

2015

Document Version

Final published version

Published in

Alcoholism - Clinical and Experimental Research

License

Article 25fa Dutch Copyright Act

[Link to publication](#)

Citation for published version (APA):

Gladwin, T. E., Rinck, M., Eberl, C., Becker, E. S., Lindenmeyer, J., & Wiers, R. W. (2015). Mediation of cognitive bias modification for alcohol addiction via stimulus-specific alcohol avoidance association. *Alcoholism - Clinical and Experimental Research*, 39(1), 101-107. <https://doi.org/10.1111/acer.12602>

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (<https://dare.uva.nl>)

Mediation of Cognitive Bias Modification for Alcohol Addiction via Stimulus-Specific Alcohol Avoidance Association

Thomas E. Gladwin, Mike Rinck, Carolin Eberl, Eni S. Becker, Johannes Lindenmeyer, and Reinout W. Wiers

Background: Cognitive bias modification (CBM) studies have provided evidence that cognitive biases play a causal role in alcohol use disorders. In this study, data from a CBM experiment in alcoholic patients were re-analyzed. In the original study, no mediation by associations measured with an Implicit Association Test (IAT) was found. In this study, we explored the possibility that relevant alcohol-related automatic processes may be cue-specific.

Methods: Data from a previous clinical study in a sample of 214 alcohol-addicted patients were re-analyzed. Patients were assigned to a CBM intervention or control condition, performed an alcohol-approach IAT, and were followed up for relapse data a year after training. In this study, bias scores measured via the IAT were calculated and analyzed separately for different stimulus categories: Alcohol, Soft drink, Approach, and Avoid.

Results: Training reversed the alcohol-approach bias for all categories. This reversal of bias also predicted reduced relapse, but involved a complex stimulus category-dependent pattern in which an avoidance bias for Alcohol stimuli was most predictive of reduced relapse.

Conclusions: The results contribute to evidence that CBM indeed affects relapse probability via changes in automatic processes, although future study is needed to determine the precise nature of mediating processes. Automatic processes underlying alcohol-related associations may be stimulus-specific, which may be important for the methods of future studies involving implicit measures.

Key Words: Cognitive Bias Modification, Alcoholism, Mediation, Implicit Association Test.

Cognitive biases have been associated with alcohol use disorders (AUDs) and hazardous drinking (Stacy and Wiers, 2010), including abnormalities in approach tendencies, attention, response inhibition, and automatically activated memory associations. Studies with heavy-drinking students and alcoholic patients have shown that methods aimed at manipulating these biases, collectively termed cognitive bias modification (CBM), can influence drinking behavior (Fadardi and Cox, 2009; Field and Eastwood, 2005; Houben et al., 2010; Wiers et al., 2006) and improve treatment outcome in alcoholism (Schoenmakers et al., 2010; Wiers et al., 2011). Such results dovetail with the results of CBM studies in anxiety (e.g., Amir et al., 2009; MacLeod et al., 2002) and obesity (Houben et al., 2011).

These studies provide evidence that cognitive biases play a causal role in various forms of psychopathology. From the perspective of dual-process models of addiction (e.g., Bechara, 2005; Wiers et al., 2007), one pathway for such effects to be mediated is by changes in automatic processes.

Previous results suggest that at least some forms of CBM exert effects via automatic, especially evaluative or motivational processes. It has been shown that if responses to a stimulus with an initially positive valence must be consistently inhibited in a no-go training, they are rated as less attractive (Veling et al., 2008). This devaluation has furthermore been shown to occur without awareness by using implicit measurement (Veling and Aarts, 2009). This basic finding, of devaluation as a mechanism to reduce conflict due to a mismatch between valence and response inhibition, has been extended to alcohol stimuli (Houben et al., 2012): In a go/no-go training, associating beer stimuli with no-go responses led to less positive beer attitudes, which mediated an effect on a reduction in alcohol intake in the week after training.

The aim of this study was to further explore this issue via a re-analysis of data from a recent CBM study in alcoholic inpatients (Wiers et al., 2011). Patients received CBM training, sham training, or no training, in addition to treatment as usual. CBM consisted of approach action tendency re-training using the alcohol-Approach Avoidance Task (Wiers et al., 2009, 2010). Participants used a joystick to make a pulling or pushing movement in response to pictorial stimuli

From the Adapt Lab, Department of Psychology (TEG, RWW), University of Amsterdam, Amsterdam, the Netherlands; Behavioural Science Institute (BSI) (MR, ESB), Radboud University Nijmegen, Nijmegen, the Netherlands; and Salus Klinik (CE, JL), Lindow, Germany.

Received for publication May 23, 2014; accepted October 15, 2014.

Reprint requests: Thomas E. Gladwin, Department of Developmental Psychology, University of Amsterdam, 1018 WB Amsterdam, the Netherlands; Tel.: +31(0)618091496; Fax: +31-24-361-5594; E-mail: t.e.gladwin@uva.nl

This study concerns an extended analysis of previously published data (Wiers et al., 2011).

Copyright © 2015 by the Research Society on Alcoholism.

DOI: 10.1111/acer.12602

[Note 1]. The movement is coupled to a visual “zoom” effect: Pushing makes the picture smaller (avoidance), and pulling makes the picture larger (approach). In the CBM group, pictures of alcoholic drinks were always pushed, and pictures of soft drinks were always pulled. This training was found to affect the response bias on reaction time (calculated via a D-score algorithm), decrease craving, and decrease the likelihood of relapse at 1-year follow-up. In the sham training condition, alcohol and soft drink stimuli were pushed and pulled equally.

Further, the bias on an alcohol–approach Implicit Association Test (IAT) (Ostafin and Palfai, 2006; Palfai and Ostafin, 2003) was reversed by CBM, from an initial alcohol–approach bias to an alcohol–avoidance bias at post test. The IAT is a measure of associations of target concepts with an attribute, based on the finding that participants perform better when a target and its associated attribute are mapped to the same key (Greenwald et al., 1998). In Wiers and colleagues’ (2011) study, target stimuli were words representing alcoholic and nonalcoholic drinks, and attribute stimuli were approach and avoidance words. This variant of the IAT has been found to be associated with hazardous drinking in previous research (Ostafin and Palfai, 2006).

Evidence for mediating mechanisms is essential for understanding and improving CBM: What features of subjects’ post training state lead to improved outcome? Wiers and colleagues (2011) conducted analyses using IAT scores as a potential mediator between training and relapse, but found no effect. In that analysis, the IAT scores were calculated, as is usual, over all stimulus types. This may have obscured effects. Theories of alcohol addiction suggest that automatic processes underlying cognitive biases may arise from the abnormally strong incentive salience of alcohol cues (Robinson and Berridge, 1993). It could therefore be the case that the different stimulus categories of the IAT—Alcohol, Soft drink, Approach, and Avoid words—do not evoke the same automatic processes. Seeing an alcohol word may produce a tendency to provide the response associated with approach, while soft drink words have no such relationship with avoidance. Thus, the approach–avoidance association bias calculated per stimulus category could yet reveal mediation of training effects via associations as measured by the IAT. We note that, although this is not a standard approach for analyzing the IAT, previous studies have also considered or modeled potential differences between stimulus categories (e.g., Anselmi et al., 2011; Meissner and Rothermund, 2013). We explored this possibility in the current re-analysis of Wiers and colleagues’ (2011) original data and found that indeed, stimulus-specific biases were related to the outcome of training effects.

MATERIALS AND METHODS

Participants, Design, and Procedure

A full description of the study’s method is provided in Wiers and colleagues (2011); we repeat the essential information here for

convenience. The sample consisted of 214 alcohol-dependent inpatients (mean Alcohol Use Disorders Identification Test [AUDIT] score 24, mean duration of alcohol problems 12.5 years). All participants were informed of the general aims of the study and told that they could withdraw from the study without any implications for their treatment. All patients signed an informed consent form, and the study had the institutional review board’s approval. Participants were randomly assigned to receive CBM training, sham training, or no training. Half of the participants receiving CBM treatment performed a relevant feature version of the training task, and the other half performed an irrelevant feature version. In the relevant feature version, participants received instructions to respond on the basis of the alcohol-relatedness of the presented stimuli (e.g., “push alcohol”). In the irrelevant feature version, participants were instructed to respond on the basis of the picture format (e.g., “push images in landscape format”), with alcoholic stimuli being always presented in the format that was supposed to elicit an avoidance response. In the sham training, subjects responded to alcohol pictures with a push or pull equally often. As in the original study, the training conditions were treated as one condition, and the sham and no-training condition were treated as the other condition; this was done to simplify analyses and because no differences were found in the original study. Training was provided no sooner than 3 weeks after detoxification and took place on 4 consecutive days. In each session, participants performed 200 trials of the alcohol–Approach Avoidance Task for 15 minutes. All participants received treatment as usual after completion of the CBM intervention. Treatment consisted of individual and group sessions of cognitive behavioral therapy aimed at abstinence. Groups did not differ in the duration of their therapy, which was 3 months on average.

Approximately 1 week after training, participants performed a post test including an alcohol–approach IAT. The task was a standard IAT containing 7 blocks (Greenwald et al., 2003): practice target (24 trials), practice attribute (24 trials), practice combination (16 trials), test combination (32 trials), practice reversed target (24 trials), practice reversed combination (16 trials), and test reversed combination (32 trials). Alcohol words were (as the other word lists: the German words for) as follows: beer, wine, liquor, vodka, whiskey, and rum. Soft drink words were as follows: Coke, Fanta, orange juice, apple juice, water, and Pepsi. Approach words were as follows: reach out to, take, touch, grab, collect, and approach. Avoidance words were as follows: avoid, elude, push away, remove, flee, and disappear. In the combination blocks, alcohol-classification responses were mapped to the same key as approach responses (and soft drink with avoidance), or alcohol responses were mapped with avoidance responses (and soft drink with approach). The order of the 2 kinds of combination blocks and associated practice blocks was counterbalanced. Participants received the same version of the IAT in a pretest and the post test to minimize method variance (cf. Wiers et al., 2005). The IAT was presented as part of a series of other tests, not reported here, that had a fixed order: a craving measurement via picture ratings; the IAT; an assessment alcohol–Approach Avoidance Task.

Relapse was measured via a follow-up questionnaire 1 year after discharge. Success was defined as no relapse or a single lapse shorter than 3 days that was ended by the patient without further negative consequences. Eighty-six percent of the patients were reached at follow-up; of these, 50 of the 108 patients in the CBM group and 63 of the 106 patients in the Control group relapsed. An intention to treat analysis was followed, with nonreply taken as relapse, as in the original study.

Data Analysis

The IAT contained congruent and incongruent blocks. In congruent blocks, alcohol and approach words were mapped to 1 key and soft drink and avoid words to the other. In incongruent blocks,

Table 1. Mean Accuracy Rates in the Implicit Association Test Per Task Block, Stimulus Type, and Training Group

	Cognitive bias modification (CBM) (pretest)	CBM (post test)	Control (pretest)	Control (post test)
Simple blocks				
Alcohol	0.96 (0.085)	0.97 (0.081)	0.94 (0.11)	0.97 (0.077)
Nonalcohol	0.96 (0.081)	0.97 (0.073)	0.95 (0.10)	0.97 (0.068)
Approach	0.81 (0.21)	0.91 (0.14)	0.84 (0.21)	0.91 (0.17)
Avoid	0.84 (0.20)	0.91 (0.15)	0.86 (0.22)	0.91 (0.16)
Mixed blocks, alcohol–approach congruent				
Alcohol	0.95 (0.12)	0.95 (0.089)	0.95 (0.10)	0.97 (0.077)
Nonalcohol	0.96 (0.11)	0.92 (0.12)	0.96 (0.91)	0.97 (0.052)
Approach	0.84 (0.23)	0.82 (0.23)	0.82 (0.24)	0.88 (0.20)
Avoid	0.83 (0.21)	0.87 (0.19)	0.84 (0.23)	0.90 (0.18)
Mixed blocks, alcohol–approach incongruent				
Alcohol	0.89 (0.18)	0.96 (0.08)	0.91 (0.18)	0.93 (0.12)
Nonalcohol	0.90 (0.14)	0.97 (0.055)	0.90 (0.15)	0.91 (0.12)
Approach	0.78 (0.25)	0.88 (0.18)	0.77 (0.28)	0.84 (0.20)
Avoid	0.82 (0.22)	0.89 (0.16)	0.81 (0.24)	0.86 (0.20)

Standard deviations are printed in parentheses.

alcohol and avoid words were mapped to 1 key, and soft drink and approach words to the other. Biases were calculated as the accuracy in congruent blocks minus the accuracy in incongruent blocks. These biases were calculated separately for each stimulus category: Alcohol, Soft drink, Approach, and Avoid. For example, the bias for Alcohol stimuli (“Alcohol bias”) was the mean accuracy on trials with Alcohol stimuli in the congruent block, minus the accuracy on trials with Alcohol stimuli in the incongruent block. Relatively positive values thus indicate a stronger alcohol–approach association. These biases calculated at post test were used in mediation analyses.

Mediation (Baron and Kenny, 1986) was tested via joint significance tests (MacKinnon et al., 2002, 2007): Treatment must affect the mediator, and the mediator must predict relapse (MacKinnon and Fairchild, 2009; Shrout, 2002). Thus, a mediating relationship has to meet 2 criteria. First, CBM must significantly affect the bias. This was tested for each bias separately via ANOVAs. Second, a bias affected by CBM must also predict relapse. This was tested using a binomial logistic regression, with relapse as dependent variable and the 4 biases as independent variables. The same additional variables as in table 2 in Wiers and colleagues (2011) were also included as predictors: training condition, age, gender, duration of alcohol problems, number of detoxifications, alcohol problems as measured via the AUDIT (Saunders et al., 1993), duration of treatment, depression measured with the German translation of the Beck Depression Inventory (Hautzinger et al., 1994), and mental burden measured with the German translation of the Symptom Checklist-90-Revised (Franke, 1995). As the 4 biases are correlated, the analysis consisted of 2 steps to address interpretative difficulties due to multicollinearity. First, the significance was tested on the set of biases together using an F-test. Second, the contributions of specific biases were explored, by considering each bias separately and by using the hypothesis-driven contrast scores. First, Alcohol versus Other: the Alcohol bias minus the mean of the bias for the 3 other stimulus categories. Second, Alcohol versus Soft drink: the Alcohol bias minus the Soft drink bias. These contrasts thus aim to test the hypothesis that the automatic processes of interest can be measured using the IAT, but that they are evoked differentially by alcohol versus other cues.

RESULTS

Table 1 shows the IAT data at pretest. The first step of the mediation analysis determined which of the stimuli—

Table 2. ANOVA Results of Post training Biases on Accuracy

	Cognitive bias modification	Control	<i>F</i>	<i>p</i>	η_p^2
Alcohol	−0.015 (0.12)	0.037 (0.12)	8.10	0.005	0.043
Soft drink	−0.049 (0.13)	0.057 (0.12)	33.010	0.000	0.154
Approach	−0.058 (0.23)	0.040 (0.22)	10.24	0.002	0.053
Avoid	−0.023 (0.20)	0.035 (0.18)	4.60	0.033	0.025

Standard deviations are printed in parentheses. Alcohol, Soft drink, Approach, and Avoid bias refer to the biases for the respective stimulus categories at post test, measured as accuracy on congruent trials minus accuracy on incongruent trials, so that positive values indicate an alcohol–approach association.

Alcohol, Soft drink, Approach, and Avoid—had biases that were affected by CBM (Table 2). Training was found to shift biases toward alcohol-avoidance for all stimulus categories at post test, compared to Control (all $p < 0.05$).

The second step of the mediation analysis was determined which parameters were associated with relapse via binomial logistic regression. Correlations between all variables are provided in Table 3. Results of the regression are shown in Table 4. At postmeasurement, adding the set of biases led to a significantly improved prediction of outcome relative to training group and secondary predictors, $\chi^2(4) = 11.553$, $p = 0.021$. The effect of the bias for Alcohol stimuli in the model was significant, indicating a higher probability of success for subjects with an avoidance bias at post test, $B = -4.796$, $Wald(1) = 7.252$, $p = 0.007$. Unexpectedly, an effect was also found for Approach stimuli, in the reversed direction, $B = 2.236$, $Wald(1) = 4.518$, $p = 0.034$.

The 4 biases were subsequently tested separately from each other (but with the same set of other predictors as above), to aid interpretation of the coefficient-wise tests in the model including all 4 biases together. The effect for Alcohol stimuli in isolation nearly reached significance, $B = -2.680$, $Wald(1) = 3.394$, $p = 0.065$; no other effects were found ($ps > 0.1$), although we note for completeness that the effect for Approach stimuli remained in the same direction and

Table 3. Zero-Order Correlations Between All Variables in the Binomial Logistic Regression Analysis

Group	Gender	Age	Outcome	NDetox	DurProbl	AUDIT	DurTreat	BDI	SCL	Alc bias	Soft bias	App bias	Av bias
1	0.076	-0.094	0.119	-0.033	-0.056	0.026	-0.087	-0.011	0.024	-0.213*	-0.391**	-0.214*	-0.151*
Gender	1	0.179*	0.226**	-0.073	-0.040	-0.067	0.006	0.106	0.031	0.034	-0.101	-0.014	0.029
Age	0.094	1	0.126	-0.039	0.194**	-0.157*	-0.074	-0.079	-0.149*	0.127	0.111	0.178*	0.199**
Outcome	0.119	0.126	1	-0.111	0.073	-0.107	0.027	-0.016	0.032	-0.124	-0.002	0.139	0.034
NDetox	-0.033	-0.039	-0.111	1	0.094	0.074	-0.191**	0.159*	0.053	-0.036	-0.031	0.030	0.112
DurProbl	-0.056	0.194**	0.073	0.094	1	0.164*	-0.057	0.038	0.000	0.015	-0.062	0.060	0.039
AUDIT	0.026	-0.157*	-0.107	0.074	0.164*	1	0.139	0.140	0.209**	-0.050	-0.107	-0.083	-0.009
DurTreat	-0.087	0.074	0.027	-0.191**	-0.057	0.139	1	0.046	0.081	-0.002	0.044	-0.054	-0.118
BDI	-0.011	-0.079	-0.016	0.159*	0.038	0.140	0.046	1	0.701**	0.064	-0.003	0.021	-0.051
SCL	0.031	-0.149*	0.032	0.053	0.000	0.209**	0.081	0.064	1	0.016	-0.017	0.071	-0.123
Alc bias	0.024	0.127	-0.124	-0.036	0.015	-0.050	-0.002	0.064	0.016	1	0.435**	0.384**	0.276**
Soft bias	-0.213*	0.034	-0.002	-0.031	-0.062	-0.107	0.044	-0.003	-0.017	0.435**	1	0.319**	0.205**
App bias	-0.391**	-0.101	0.139	0.030	0.060	-0.083	-0.054	0.021	0.071	0.384**	0.319**	1	0.545**
Av bias	-0.214*	0.029	0.034	0.112	0.039	-0.009	-0.118	-0.051	-0.123	0.276**	0.205**	0.545**	1

Group = Training (1) versus Control (0). Gender = male (0) versus female (1). Age is in years. Outcome = success or single relapse (1) versus relapse (0). NDetox = number of detoxifications. DurProbl = duration of alcohol problems. AUDIT = Alcohol Use Disorders Identification Test. DurTreat = duration of treatment. BDI = depression as measured via the Beck Depression Inventory. SCL = mental burden as measured via the SCL-90-R. Alcohol, Soft drink, Approach, and Avoid bias refer to the biases for the respective stimulus categories at post test, measured as accuracy on congruent trials minus accuracy on incongruent trials. *Correlation is significant at the 0.05 level; **correlation is significant at the 0.01 level.

Table 4. Results of Binomial Logistic Regression Analyses Predicting Treatment Outcome Using Accuracy

	B	SE	Wald	df	Sig.	Exp(B)
Training	0.809	0.374	4.693	1	0.030	0.445
Gender	1.321	0.430	9.425	1	0.002	3.747
Age	0.029	0.023	1.537	1	0.215	1.029
NDetox	-0.036	0.030	1.457	1	0.227	0.965
DurProbl	0.036	0.020	3.257	1	0.071	1.036
AUDIT	-0.034	0.023	2.056	1	0.152	0.967
DurTreat	0.005	0.011	0.190	1	0.663	1.005
BDI	-0.013	0.025	0.294	1	0.588	0.987
SCL	0.018	0.022	0.657	1	0.417	1.018
Alcohol	-4.796	1.781	7.252	1	0.007	0.008
Soft drink	1.698	1.575	1.162	1	0.281	5.461
Approach	2.236	1.052	4.518	1	0.034	9.360
Avoid	-0.390	1.139	0.117	1	0.732	0.677
Constant	-2.936	1.870	2.465	1	0.116	0.053

Outcome is coded as success (1) or relapse (0). NDetox = number of detoxifications. DurProbl = duration of alcohol problems. DurTreat = duration of treatment. BDI = depression as measured via the Beck Depression Inventory. SCL = mental burden as measured via the SCL-90-R. Training = cognitive bias modification (coded as 1) versus Control (coded as 0). Alcohol, Soft drink, Approach, and Avoid refer to the biases for the respective stimulus categories at post test, measured as accuracy on congruent trials minus accuracy on incongruent trials. The positive value for alcohol thus means that higher accuracy on the alcohol-avoid than the alcohol-approach block predicts better outcome probability.

Fig. 1. Post test bias by group and outcome. Figure 1 shows the approach bias for Alcohol stimuli at post test: accuracy on Alcohol trials in the alcohol-approach/soft drink-avoid block, minus the accuracy on Alcohol trials in the alcohol-avoid/soft drink-approach block. The bars show the bias for the Training and Control groups (the right and left pairs) and relapse and success as outcome (the right and left bar within each pair). Error bars represent 1 standard error.

approached trend level ($p = 0.111$). As shown in Fig. 1, in the Training group only, a stronger alcohol-avoidance bias for Alcohol stimuli was related to a lower chance of relapse. Finally, the contrasts were tested, in models that included only 1 of the contrasts and the secondary predictors. The Alcohol versus Other contrast was a significant predictor of outcome, $B = -3.764$, $Wald(1) = 8.101$, $p = 0.004$, as was the Alcohol versus Soft drink contrast, $B = -2.848$, $Wald$

(1) = 4.741, $p = 0.029$. The results thus indicate that an avoidance bias found for alcohol-related cues, especially when corrected for the biases found for cues not involving alcohol, predicted reduced relapse rate.

We briefly note that while training also reversed the biases as measured via reaction time (Table 5), no effects were found in the second, outcome-related step of the mediation analyses (Table 6).

DISCUSSION

CBM improves treatment outcome in alcohol addiction, but much remains unknown about the mechanisms of the effects. In the current re-analysis of an earlier study, we attempted to address this issue using IAT data. This expected mediation via effects on alcohol–approach associations was not confirmed in the original report using standard IAT scores. However, using accuracy-based bias scores calculated separately for each stimulus category—Alcohol, Soft drink,

Approach, and Avoid—mediation was found. The relationship of bias scores to outcome was strongly dependent on stimulus category, explaining the previous lack of an overall mediating effect via the IAT (Wiers et al., 2011).

The bias found for Alcohol stimuli was related to training effect in the expected direction. Training reversed an initial alcohol–approach bias to an alcohol–avoid bias, and a stronger alcohol–avoid bias predicted lower relapse, especially when contrasted with bias for other stimulus categories. The above converges with a recent study, in which mediation was found via decreased alcohol–approach action tendencies, as measured by an Approach Avoidance Task (Eberl et al., 2013). Why the current association-based effect was found only for Alcohol stimuli could be due to cue-evoked automatic processes. Indeed, most theories would predict that specifically alcohol stimuli should evoke automatic approach associations (e.g., Berridge et al., 2009; Wiers et al., 2010). It is alcohol cues that have acquired incentive salience, not soft drink, approach, or avoidance stimuli. This mediation thus agrees with the expected pathway for training effects: Participants were trained to automatically avoid instead of approach alcohol-related stimuli, and the degree to which this was achieved predicted better clinical outcome. It appears to be protective for participants to acquire a relatively strong avoidance-response bias related to Alcohol stimuli.

This result is interesting in relationship to a recent study in which alcohol associations were measured using a Stimulus–Response Compatibility (SRC) task (Spruyt et al., 2013). In this study, abstaining alcohol-dependent participants who had stronger avoidance associations, as measured via an SRC task, was found to be more likely to relapse. These results might suggest that training subjects to avoid alcohol may in fact be harmful, raising the possibility that the beneficial effects of CBM could be due to a different mediating process. However, this is contradicted by the results described above and by the recent findings of Eberl and colleagues (2012), who found that the avoidance bias for Alcohol stimuli caused by CBM is associated with a reduced probability of relapse. This may be related to the fact that the SRC study by Spruyt and colleagues (2013) involved a measurement of associations, rather than an experimental manipulation of associations. The causal relationship in the former case is uncertain, as a stronger avoidance bias may reflect an unknown third variable effect. However, we note that we did find some evidence for an unexpected reversed relationship between Approach-related bias and outcome. If replicable, such counterintuitive results may prove important in future research.

The results suggest that accuracy but not reaction time scores were sensitive to the relevant underlying process. How could this be? In general, the 2 performance measures may detect different aspects of cognition. Error rates presumably reflect effects of automatic associations on impulsive responses (cf. Conrey et al., 2005): The subject executes the incorrect response before being able to prevent it. Reaction

Table 5. ANOVA Results of Post training Biases on Reaction Time

	Cognitive bias modification	Control	<i>F</i>	<i>p</i>	η_p^2
Alcohol	–87.94 (28.81)	99.65 (25.65)	23.66	0.000	0.11
Soft drink	–145.98 (26.86)	145.78 (21.93)	70.78	0.000	0.28
Approach	–93.07 (38.61)	149.55 (31.57)	23.67	0.000	0.11
Avoid	–83.30 (32.90)	170.01 (31.41)	31.02	0.000	0.14

Standard deviations are printed in parentheses. Alcohol, Soft drink, Approach, and Avoid bias refer to the biases for the respective stimulus categories at post test, measured as reaction time on incongruent trials minus reaction time on congruent trials, so that positive values indicate an alcohol–approach association.

Table 6. Results of Binomial Logistic Regression Analyses Predicting Treatment Outcome Using Reaction Time

	<i>B</i>	<i>SE</i>	Wald	<i>df</i>	<i>Sig.</i>	Exp(<i>B</i>)
Training	0.609	0.392	2.42	1	0.12	1.84
Gender	1.176	0.406	8.40	1	0.004	3.24
Age	0.033	0.022	2.20	1	0.14	1.03
NDetox	–0.034	0.030	1.29	1	0.26	0.97
DurProbl	0.034	0.019	3.12	1	0.077	1.035
AUDIT	–0.042	0.023	3.31	1	0.070	0.96
DurTreat	0.003	0.010	0.094	1	0.76	1.003
BDI	–0.023	0.024	0.94	1	0.33	0.98
SCL	0.029	0.021	1.83	1	0.18	1.029
Alcohol	0.001	0.001	0.63	1	0.43	1.001
Soft drink	–0.001	0.001	1.61	1	0.20	1.00
Approach	0.000	0.001	0.002	1	0.96	1.000
Avoid	0.001	0.001	0.87	1	0.35	1.001
Constant	–3.238	1.831	3.13	1	0.077	0.039

Outcome is coded as success (1) or relapse (0). NDetox = number of detoxifications. DurProbl = duration of alcohol problems. DurTreat = duration of treatment. BDI = depression as measured via the Beck Depression Inventory. SCL = mental burden as measured via the SCL-90-R. Training = cognitive bias modification (coded as 1) versus Control (coded as 0). Alcohol, Soft drink, Approach, and Avoid refer to the biases for the respective stimulus categories at post test, measured as reaction time on incongruent trials minus reaction time on congruent trials.

times could conceivably be affected by other processes: For instance, slowing due to interference would only be expected to occur when inhibition of an incorrect, impulsive response has been initiated and prevented, or when subjects apply a more reflective state of processing (Gladwin et al., 2011). Thus, biases measured on accuracy and reaction time may reflect different processes and hence have different relationships to other variables, or not be equally sensitive to the same processes. This suggests that it may be helpful for future studies to consider reaction time and accuracy scores of the IAT separately.

The current study is limited in its ability to assign specific cognitive processes to the observed bias scores. For our purposes, relatively positive or negative observed biases were sufficient to establish mediation, and given the effects of the training, these biases appear likely to reflect at least partly automatic approach-avoidance associations. The specificity of the primary mediation effect to Alcohol stimuli is in line with a role for the attribution of incentive salience to alcohol cues and the effect of training on associated automatic processes. We note that the separation of congruent–incongruent bias scores per stimulus category is not usual, but the current results suggest that this may reveal important sources of variation. We emphasize that the current analyses are not intended to support a generalized assumption that subsets of IAT trials can be used to measure dissociable associations for different target categories, as was shown to be problematic by Nosek and colleagues (2005). In the currently available CBM data, the separation by stimulus type is theoretically motivated by an incentive salience perspective, or more generally from the role of cue reactivity in addiction. This rationale does not necessarily assume that there are dissociable associations for each target category: Perhaps, for instance, only 1 association is involved in the task, but it is related in different ways to the various stimulus categories. Clearly, progress in relating observed bias scores to specific underlying cognitive processes is needed (Gladwin et al., 2011; Wiers et al., 2013; cf. Cunningham et al., 2007). Mathematical modeling may provide a useful tool to address these and other theoretical questions in the future (cf. Conrey et al., 2005; Hertel et al., 2011; Sherman et al., 2008, 2010). We anticipate that such models will be used to capture more fine-grained distinctions between cognitive processes and to find common processes measured by different tasks. Such refinements, including the currently used separation of stimulus categories, may help detect mediating processes by providing more precise measurements (MacLeod et al., 2009). We further note that it is as yet unknown whether the current results will generalize to other forms of CBM, such as those that manipulate spatial (Schoenmakers et al., 2010) or nonspatial (Fadardi and Cox, 2009) shifts of attention. Finally, future research is needed to determine effects of training on other potential mediators: other versions of the IAT such as the single-category IAT

(Houben et al., 2010; Karpinsky and Steinman, 2006), or other implicit measures in which it may be important to consider stimulus-specific effects.

In conclusion, we performed explorative analyses that appear to contribute to the evidence that the effect of CBM on relapse in alcoholism is mediated via automatic processes that can be measured by congruence effects expressed specifically on Alcohol trials of an IAT. The results may provide potentially important clues about the plausible causal pathways via which addiction develops and how CBM influences addiction. A further methodological conclusion is that it may be useful to study biases for separate stimulus categories when calculating implicit measures, in particular in disorders such as addiction where effects may be evoked only by certain types of stimuli.

ACKNOWLEDGMENTS

The authors would like to thank Thomas Pronk for the suggestion of helpful additional literature. RWW and TEG are supported by VICI award 453.08.01 from the Netherlands National Science Foundation (N.W.O.). TEG is supported by Grant EA1239 from the European Foundation for Alcohol Research.

REFERENCES

- Amir N, Beard C, Burns M, Bomyea J (2009) Attention modification program in individuals with generalized anxiety disorder. *J Abnorm Psychol* 118:28–33.
- Anselmi P, Viamello M, Robusto E (2011) Positive associations primacy in the IAT: a many-facet rasch measurement analysis. *Exp Psychol* 58:376–384.
- Baron RM, Kenny DA (1986) The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 51:1173–1182.
- Bechara A (2005) Decision making, impulse control and loss of willpower to resist drugs: a neurocognitive perspective. *Nat Neurosci* 8:1458–1463.
- Berridge KC, Robinson TE, Aldridge JW (2009) Dissecting components of reward: 'liking', 'wanting', and learning. *Curr Opin Pharmacol* 9:65–73.
- Conrey FR, Sherman JW, Gawronski B, Hugenberg K, Groom CJ (2005) Separating multiple processes in implicit social cognition: the quad model of implicit task performance. *J Pers Soc Psychol* 89:469–487.
- Cunningham WA, Zelazo P, Packer D, van Bavel JJ (2007) The iterative reprocessing model: a multilevel framework for attitudes and evaluation. *Soc Cogn* 25:736–760.
- Eberl C, Wiers RW, Pawelczack S, Rinck M, Becker ES, Lindenmeyer J (2013) Approach bias modification in alcohol dependence: do clinical effects replicate and for whom does it work best? *Dev Cogn Neurosci* 4:38–51.
- Fadardi JS, Cox WM (2009) Reversing the sequence: reducing alcohol consumption by overcoming alcohol attentional bias. *Drug Alcohol Depend* 101:137–145.
- Field M, Eastwood B (2005) Experimental manipulation of attentional bias increases the motivation to drink alcohol. *Psychopharmacology* 183:350–357.
- Franke G (1995) SCL-90-R Die Symptom-Checkliste von Derogatis-Deutsche Version: Manual. Hogrefe, Göttingen, Germany.
- Gladwin TE, Figner B, Crone EA, Wiers RW (2011) Addiction, adolescence, and the integration of control and motivation. *Dev Cogn Neurosci* 1:364–376.

- Greenwald AG, McGhee DE, Schwartz JL (1998) Measuring individual differences in implicit cognition: the implicit association test. *J Pers Soc Psychol* 74:1464–1480.
- Greenwald AG, Nosek BA, Banaji MR (2003) Understanding and using the Implicit Association Test: I. An improved scoring algorithm. *J Pers Soc Psychol* 85:197–216.
- Hautzinger M, Bailer M, Worall H, Keller F (1994) Beck-Depressions-Inventar (BDI). Huber, Bern, Germany.
- Hertel PT, Vasquez E, Benbow A, Hughes M (2011) Recollection is impaired by the modification of interpretation bias. *J Abnorm Psychol* 120:902–910.
- Houben K, Havermans RC, Nederkoorn C, Jansen A (2012) Beer à no-go: learning to stop responding to alcohol cues reduces alcohol intake via reduced affective associations rather than increased response inhibition. *Addiction* 107:1280–1287.
- Houben K, Havermans RC, Wiers RW (2010) Learning to dislike alcohol: conditioning negative implicit attitudes toward alcohol and its effect on drinking behavior. *Psychopharmacology* 211:79–86.
- Houben K, Nederkoorn C, Wiers RW, Jansen A (2011) Resisting temptation: decreasing alcohol-related affect and drinking behaviour by training response inhibition. *Drug Alcohol Depend* 116:132–136.
- Karpinsky A, Steinman RB (2006) The single category implicit association test as a measure of implicit social cognition. *J Pers Soc Psychol* 91:16–32.
- MacKinnon DP, Fairchild AJ (2009) Current directions in mediation analysis. *Curr Dir Psychol Sci* 18:16–20.
- MacKinnon DP, Fairchild AJ, Fritz MS (2007) Mediation analysis. *Annu Rev Psychol* 58:593–614.
- MacKinnon DP, Lockwood CM, Hoffman JM, West SG, Sheets V (2002) A comparison of methods to test mediation and other intervening variable effects. *Psychol Methods* 7:83–104.
- MacLeod C, Koster EH, Fox E (2009) Whither cognitive bias modification research? Commentary on the special section articles. *J Abnorm Psychol* 118:89–99.
- MacLeod C, Rutherford E, Campbell L, Ebsworthy G, Holker L (2002) Selective attention and emotional vulnerability: assessing the causal basis of their association through the experimental manipulation of attentional bias. *J Abnorm Psychol* 111:107–123.
- Meissner F, Rothermund K (2013) Estimating the contributions of associations and recoding in the Implicit Association Test: the ReAL model for the IAT. *J Pers Soc Psychol* 104:45–69.
- Nosek BA, Greenwald AG, Banaji MR (2005) Understanding and using the Implicit Association Test: II. Method variables and construct validity. *Pers Soc Psychol Bull* 31:166–180.
- Ostafin BD, Palfai TP (2006) Compelled to consume: the implicit association test and automatic alcohol motivation. *Psychol Addict Behav* 20:322–327.
- Palfai TP, Ostafin BD (2003) Alcohol-related motivational tendencies in hazardous drinkers: assessing implicit response tendencies using the modified-IAT. *Behav Res Ther* 41:1149–1162.
- Robinson TE, Berridge KC (1993) The neural basis of drug craving: an incentive-sensitization theory of addiction. *Brain Res* 18:247–291.
- Saunders JB, Aasland OG, Babor TF, de La Fuente JR, Grant M (1993) Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption—II. *Addiction* 88:791–804.
- Schoenmakers TM, de Bruin M, Lux IFM, Goertz AG, Van Kerkhof DHAT, Wiers RW (2010) Clinical effectiveness of attentional bias modification training in abstinent alcoholic patients. *Drug Alcohol Depend* 109:30–36.
- Sherman JW, Gawronski B, Gonsalkorale K, Hugenberg K, Allen TJ, Groom CJ (2008) The self-regulation of automatic associations and behavioral impulses. *Psychol Rev* 115:314–335.
- Sherman JW, Klauer KC, Allen TJ (2010) Mathematical modeling of implicit social cognition: the machine in the ghost, in *Handbook of Implicit Social Cognition: Measurement, Theory, and Applications* (Gawronski B, Payne BK eds), pp 156–175. Guilford Press, New York, NY.
- Shrout P (2002) Mediation in experimental and nonexperimental studies: new procedures and recommendations. *Psychol Methods* 7:422–445.
- Spruyt A, De Houwer J, Tibboel H, Verschuere B, Crombez G, Verbanck P, Hanak C, Brevers D, Noël X (2013) On the predictive validity of automatically activated approach/avoidance tendencies in abstaining alcohol-dependent patients. *Drug Alcohol Depend* 127:81–86.
- Stacy AW, Wiers RW (2010) Implicit cognition and addiction: a tool for explaining paradoxical behavior. *Annu Rev Clin Psychol* 6:551–575.
- Veling H, Aarts H (2009) Putting behavior on hold decreases reward value of need-instrumental objects outside of awareness. *J Exp Soc Psychol* 45:1020–1023.
- Veling H, Holland RW, van Knippenberg A (2008) When approach motivation and behavioral inhibition collide: behavior regulation through stimulus devaluation. *J Exp Soc Psychol* 44:1013–1019.
- Wiers RW, Bartholow BD, van Den Wildenberg E, Thush C, Engels RC, Sher KJ, Grenard J, Ames SL, Stacy AW (2007) Automatic and controlled processes and the development of addictive behaviors in adolescents: a review and a model. *Pharmacol Biochem Behav* 86:263–283.
- Wiers RW, Cox WM, Field M, Fadardi JS, Palfai TP, Schoenmakers TM, Stacy AW (2006) The search for new ways to change implicit alcohol-related cognitions in heavy drinkers. *Alcohol Clin Exp Res* 30:320–331.
- Wiers RW, Eberl C, Rinck M, Becker E, Lindenmeyer J (2011) Re-training automatic action tendencies changes alcoholic patients' approach bias for alcohol and improves treatment outcome. *Psychol Sci* 22:490–497.
- Wiers RW, Gladwin TE, Hofmann W, Salemink E, Ridderinkhof KR (2013) Cognitive bias modification and cognitive control training in addiction and related psychopathology: mechanisms, clinical perspectives and ways forward. *Clin Psychol Sci* 1: 192–212.
- Wiers RW, Rinck M, Dictus M, van den Wildenberg E (2009) Relatively strong automatic appetitive action-tendencies in male carriers of the OPRM1 G-allele. *Genes Brain Behav* 8:101–106.
- Wiers RW, Rinck M, Kordts R, Houben K, Strack F (2010) Retraining automatic action-tendencies to approach alcohol in hazardous drinkers. *Addiction* 105:279–287.
- Wiers RW, van de Luitgaarden J, van den Wildenberg E, Smulders FTY (2005) Challenging implicit and explicit alcohol-related cognitions in young heavy drinkers. *Addiction* 100:806–819.