Chapter 24

Cognitive Bias Modification as Add-On to the Treatment of Substance Use Disorders

Charlotte E. Wittekind[1]

Mike Rinck[2]

Reinout W. Wiers[3]

[1]Clinical Psychology and Psychotherapy, Department of Psychology, LMU Munich, Munich

[2]Behavioural Science Institute, Radboud University, Nijmegen, The Netherlands

[3]Addiction Development and Psychopathology (ADAPT-)lab, Dept of Psychology, University of Amsterdam & Centre for Urban Mental Health, University of Amsterdam

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INTRODUCTION

An extensive literature in the addiction field has demonstrated that substance misusers as well as people meeting criteria for substance use disorders (SUDs) often show cognitive biases for stimuli relating to their substance of abuse. At least three different types of biases have been distinguished: biases in attention (reviews: Field and Cox, 2008; Wiers et al., 2013; Field et al., 2016), memory associations (reviews: Rooke et al., 2008; Reich et al., 2010; Stacy and Wiers, 2010), and biases in action tendencies (reviews: Kakoschke et al., 2019; Loijen et al., 2020). Different techniques have been developed to manipulate these cognitive biases, collectively called cognitive bias modification (CBM). Note that there are other types of cognitive training – for example, working memory training, which has in some cases led to improvements in other cognitive processes (e.g., in future episodic thinking, Snider et al., 2018), but not in alcohol or drug use (see, Wanmaker et al., 2018; Anderson et al., 2021). Mindfulness could also be regarded as a variety of cognitive training and has shown promise in the treatment of addiction (e.g., Korecki et al., 2020; Garland et al., 2022; see also chapter 22, this volume), and there might be opportunities to combine these approaches (see Larsen et al., 2023). The focus in this chapter is on CBM in addiction, with an emphasis on effects in smoking cessation, after a brief review of effects in alcohol use disorder (AUD), which have recently been reviewed extensively elsewhere (Wiers et al., 2023).

COGNITIVE BIAS MODIFICATION (CBM): BRIEF BACKGROUND

While an extensive literature had shown correlations between cognitive biases and a variety of mental disorders, the nature of this relationship was unclear: were these biases following the development of a disorder, or did they play a causal role in its development?

To answer this question, researchers developed methods to experimentally manipulate cognitive biases in other areas of psychopathology (first in anxiety). Pioneering studies at the beginning of this century manipulated cognitive biases in healthy volunteers, to test if temporarily increasing the bias would result in an increase in symptomatology, and temporarily decreasing the bias in a decrease in symptomatology (Mathews and Mackintosh, 2000; MacLeod et al., 2002), which was indeed confirmed. Note that the goal of this type of experimental psychopathology or proof-of-principle studies is to establish causality; once this is confirmed, the next phase of intervention development can be initiated, in which the bias is targeted in patients with the goal to improve treatment outcomes (see Sheeran et al., 2017). In the domains of anxiety and depression, many clinical studies have been performed since (see, Price et al., 2016; Fodor et al., 2020).

META-ANALYSES OF CBM IN ADDICTION

So far, there have been two meta-analyses on CBM in addiction or SUDs. The first (Cristea et al., 2016) concluded that CBM resulted in an effect on the bias, but did not yield clinically relevant effects. The large majority of included studies were proof-of-principle studies in healthy volunteers that did not have a clinical goal, but were set up to test causality (participants were sometimes trained *toward* substance-related stimuli, which would not be done in patients). Therefore, conclusions regarding clinical effectiveness are likely to be invalid, as they were primarily based on proof-of-principle studies in healthy volunteers, a different phase of the experimental medicine approach to intervention development (Sheeran et al., 2017; Wiers et al., 2018).

A second (Bayesian) meta-analysis included only studies with a clinical goal (shared by researchers and participants): help people reduce or quit their substance use (Boffo et al., 2019). All included studies used varieties of CBM to help people

overcome excessive use of alcohol or tobacco. It was concluded that there is evidence that CBM has a small effect both on reducing the bias and on abstinence, but not on (reduced) use. The latter was likely related to the online studies in which participants set their own goal, which was almost always to reduce use, not to achieve abstinence, which led to non-specific reductions. In contrast, the evidence for an add-on effect to abstinence-oriented treatment of AUD was rather consistent (see below and, for a more extensive review, Wiers et al., 2023).

COGNITIVE BIAS MODIFICATION IN ALCOHOL USE DISORDERS

Soon after the first experimental studies in other areas of psychopathology, proof-of-principle studies were developed to target attentional biases for alcohol in heavy-drinking volunteers (e.g., Field et al., 2007; Schoenmakers et al., 2007), testing effects on the bias, generalizations to untrained stimuli and to other tests of the bias, which were generally not found. More promising was a first test of the malleability of an approach bias (action tendency manipulation), which did show signs of a generalized effects after a single manipulation (Wiers et al., 2010).

Following these studies, first randomized controlled trials (RCTs) in clinical samples were conducted, in which patients received CBM as add-on to treatment for AUD (attentional bias retraining, AtBM, Schoenmakers et al., 2010; approach bias retraining, ApBM, Wiers et al., 2011). Promising effects were found: a generalized effect on the bias in both studies and an indication of later relapse in the small study by Schoenmakers et al. (2010), and a 13% reduction in relapse rate one year after treatment discharge in the larger study by Wiers et al. (2011) (*N*=214). Since then, several replication studies were performed of ApBM as add-on to treatment for AUD, the first follow-up study found 9% less relapse one year later in a large sample (*N*=509), which was partly mediated by the change in approach bias. A recent study (Salemink et al.,

2022) found 10% less relapse one year later, with a larger effect for patients with comorbid anxiety or depression. A series of studies in Australia found positive effects for ApBM when added to detox treatment, first on short-term outcomes in a small sample (Manning et al., 2016), then in a larger trial (*N*=300) with significant effects up to three months after treatment discharge, but not at later assessments (Manning et al., 2021a; Manning et al., 2022).

While several large RCTs tested ApBM as add-on to AUD treatment, this was not the case for AtBM. One study used a gamified version and found no effects (Heitmann et al., 2021). The results are a bit difficult to interpret, as treatment for both AUD and cannabis use disorder (CUD) were included, and some had the goal to abstain, while others wanted to reduce use (which showed non-specific effects in the meta-analysis). The largest RCT of CBM in addiction so far (*N*=1405) tested the effect of both AtBM and ApBM as add-on to abstinence-oriented treatment (Rinck et al., 2018), and found reduced relapse rates for both (8.5%) after one year, compared with placebo-training or no training. Finally, one as-yet unpublished RCT in a clinical sample (*N*=247) did not find improved treatment outcomes for either CBM intervention (Spruyt et al., 2023).

When comparing the clinical RCTs, it is noteworthy that the positive trials after one year all used a 100% contingency training (after a brief initial assessment, participants consistently avoided alcohol and approached non-alcoholic drinks), while the RCT with significant effects up to three months (Manning et al., 2022) used a 95% contingency (occasional catch trials during the training in which alcohol was to be approached), and the one negative RCT (Spruyt et al., 2023) use an 87.5% contingency. Hence, CBM, especially ApBM, has a rather consistent add-on effect when added to abstinence-oriented treatment for AUD, with the best outcomes when a 100% contingency is used during training. The effect size is modest, but comparable to current

medication effects for AUD (Jonas et al., 2014). This has led to the clinical recommendation to add ApBM to abstinence-oriented treatment for AUD in several countries (Haber et al., 2021; Kiefer et al., 2021).

Note that while CBM has been found effective as add-on to abstinence-oriented treatment for AUD across many clinical RCTs, it has *not* been found to be effective in volunteers who wished to reduce their drinking (where typically a non-specific effect of time was found, indicating reduced drinking irrespective of experimental condition; e.g., R. W. Wiers et al., 2015; Jones et al., 2018) or in students with no wish to cut down their drinking (e.g., Lindgren et al., 2015).

Before summarizing the state of affairs for CBM in tobacco use disorder (TUD) in more detail, it is important to mention that in addition to the two prevalent varieties of CBM in AUD and TUD (i.e., AtBM and ApBM) other types of training have occasionally been used, such as selective inhibition training (based on a Go/NoGo task, in which pictures of one type of stimuli, e.g., alcohol, are always paired with a NoGo signal, e.g., Houben et al., 2011; for promising effects of an improved version as add-on to the treatment of AUD, see Stein et al., 2022).

ATTENTION BIAS MODIFICATION (ATBM) IN TOBACCO USE DISORDER (TUD)

Studies of AtBM in TUD are relatively rare. Most of them were recently reviewed by Heitmann and colleagues (2018) and by Mühlig and colleagues (2017). In addition, Boffo et al. (2019) included several of these studies in the aforementioned meta-analysis of participant-level data. Therefore, we refer the reader to these publications for a detailed description of relevant studies and more comprehensive overviews. Here, we only give a brief summary and evaluation of those AtBM studies that addressed TUD.

In all the relevant studies, the *dot probe task* was used in an attempt to modify an attentional bias for tobacco-related stimuli. In a typical design, the task is used in the neutral 50:50 version for a pre-training assessment of the bias, followed by an extended modified training version designed to train attention away from tobacco-related cues (by having the target stimuli always replace the non-tobacco alternative), and again followed by a neutral version for a post-training assessment. In addition, symptom-related measures include craving, number of cigarettes smoked, abstinence, or time until relapse, but these are not always measured both before and after AtBM.

When examining the few studies that include symptom-related measures and are not mere proof-of-principle studies, the overall results are disappointing. Often, there was no attention bias found at pre-training, and often the bias was not reduced more in the active training group than in a control group, but here the poor reliability of the dot probe task likely played a role (Ataya et al., 2012). More worryingly, the training did not affect smoking-related measures either (Begh et al., 2015; Field et al., 2009; Lopes et al., 2014; McHugh et al., 2010; Robinson et al., 2017. Slightly more promising results were reported by Elfeddali et al. (2016), who found a positive effect of AtBM on abstinence in the sub-group of heavy smokers. Although this concerned online training, an actual quit attempt was verified by telephone. Similarly, Kerst and Waters (2014) found that an extended 21-sessions AtBM training reduced craving, but only when compared to a non-intervention group, and without an effect on consumption. There does not seem to be a single study which fulfills all criteria needed for considering an AtBM application successful: a pre-existing attentional bias, a larger reduction of the bias and a larger effect on consumption-related variables in the active AtBM training group than in a control group, and a correlation between the amount of bias change and

the clinical effect size. Therefore, the available data do not supply sufficient evidence for the claim that AtBM would be a useful intervention for smokers.

APPROACH BIAS MODIFICATION (APBM) IN TOBACCO USE DISORDER (TUD)

Based on the promising findings of ApBM in AUDs described above, numerous studies investigated the efficacy of ApBM in smoking. Almost all of these studies used a training version of the *approach-avoidance task* (AAT; Rinck and Becker, 2007) to modify approach biases for smoking-related stimuli. During the AAT, smoking-related and non-smoking-related pictures are presented and need to be pushed (i.e., avoidance) and pulled (i.e., approach), typically by means of a joystick. During ApBM the majority (or all) smoking-related pictures (>80%) have to be pushed away. All training studies used task-irrelevant instructions – that is, the response direction depended on a non-affective dimension (e.g., tilt or color), not on the contents of the pictures. The vast majority of studies assessed whether ApBM reduced daily cigarette consumption (DCC); only few studies investigated its effects on (long-term) abstinence.

First evidence that ApBM might exert positive effects on smoking behavior was found in a study administering ApBM as a web-based stand-alone intervention (Wittekind et al., 2015). Two slightly different training versions were used (with vs without feedback after each trial). Four weeks after training, both training groups smoked significantly fewer cigarettes compared to baseline, but only ApBM without feedback led to a significantly greater reduction compared to the waiting list control group. Interpretability of the pilot study was restricted as no sham training was included, and neither long-term effects nor approach biases for smoking-related stimuli were assessed. These limitations were addressed in a web-based follow-up study (Wittekind et al., 2019a). ApBM did not consistently change approach biases for

smoking-related pictures, and all groups showed comparable reductions in DCC at six-month follow-up (FU). These results resemble those found in web-based studies in individuals with problematic drinking behavior (R. W. Wiers et al., 2015) and indicate that ApBM as a stand-alone intervention does not suffice to achieve clinically relevant, long-lasting change. Therefore, subsequent studies combined ApBM with a brief smoking cessation intervention (Machulska et al., 2016; Machulska et al., 2022). Again, ApBM did not significantly reduce approach biases for smoking-related pictures, but participants receiving ApBM (vs sham) showed a stronger reduction of DCC at the one-month FU. However, the effect of ApBM on DCC was not mediated by a bias change for smoking-related stimuli (Machulska et al., 2016). A later study (Machulska et al., 2022) compared the efficacy of ApBM to an inhibition training in a sample of smokers motivated to quit. Although ApBM was superior to the inhibition training in the short term, DCC, craving, and nicotine dependence were reduced in all groups at FU. As in prior studies (Machulska et al., 2016; Wittekind et al., 2019a), neither ApBM nor the inhibition training changed the targeted bias.

Given the overall disappointing findings summarized above, some avenues have been pursued to improve the efficacy of ApBM in smoking. As smoking lacks a natural contrast category, it has been investigated whether ApBM in which participants are trained to approach pictures of alternative positive behaviors is more effective than sham training in depressed smokers motivated to quit (Köpetz et al., 2017). This adapted ApBM was not superior to sham training in increasing the seven-day abstinence or in reducing smoking behavior. Another study combined pictures of alternative positive behaviors with a craving manipulation (Wen et al., 2021). Again, all groups showed significant reductions of approach biases and smoking-related variables across time.

Others strived to improve the efficacy of ApBM as add-on by means of novel training devices (Machulska et al., 2021; Machulska et al., 2023). In both studies, all participants received a single-session smoking cessation intervention and a self-help book, and they monitored their daily smoking behavior. Machulska et al. (2021) implemented ApBM (vs. sham) in a virtual reality environment, but again, smoking-related measures improved in both groups and ApBM did not successfully modify approach bias for cigarettes, nor attentional or associative biases. Machulska et al. (2023) administered a mobile-phone based ApBM and compared its efficacy to a sham training and a non-training control group. Effects on smoking-related variables were inconsistent. While ApBM led to a significantly stronger reduction of DCC compared to the non-training control group, both training groups were superior to the non-training group regarding nicotine dependence, and all groups significantly reduced craving and smoking attitudes, while increasing the desire to quit. No differential group effects emerged for tobacco bias change.

Given that smoking cessation is most important to avert the adverse health consequences of smoking (Jha, 2020), it is surprising that only few studies assessed whether ApBM can increase abstinence rates. In a pilot study in a sample of adolescents, ApBM (vs. sham training) was administered as add-on to a cognitive-behavioral smoking cessation intervention incorporating a quit attempt (Kong et al., 2015). Although participants receiving ApBM reported a higher seven-day point prevalence of abstinence (17.2% vs 3.2% in the sham training) post-intervention, effects had disappeared at the three-month follow-up. In a more recent study (Wittekind et al., 2019b) with adult smokers, all participants received a three-session smoking cessation intervention and were randomized to ApBM or sham training. ApBM was not superior to sham training on any clinical outcome, neither post-intervention nor at the

six-month FU. As the study did not include a non-training control condition, it remains unresolved whether both trainings are more effective than a smoking cessation intervention alone, or whether no beneficial effects emerge at all. This limitation is addressed in an ongoing large-scale clinical trial (Wittekind et al., 2022). Two studies provided more promising results (Baird et al., 2017; Smits et al., 2022). In the study by Baird and colleagues (2017), adult smokers received either four sessions of ApBM or sham training, and were instructed to quit smoking the day after the last training session. Only ApBM significantly reduced the approach bias for tobacco-related stimuli, with greater reductions related to longer abstinence; however, the number of abstinent days did not significantly differ between conditions. Smits and colleagues (2022) combined smoking cessation treatment (ST) including a quit attempt, with ApBM versus sham training. The ST+ApBM group achieved significantly higher prolonged abstinence at three-month FU compared to the ST+sham group (66% vs 47%). Moreover, ApBM showed the intended training effect so that avoidance biases increased over the course of ApBM. These effects are noteworthy as five (out of seven) trainings were conducted prior to the quit attempt, unlike most other studies.

In summary, the studies on ApBM in TUD show that ApBM neither changes smoking behavior in the long-term, nor does it exert positive effects on long-term abstinence, with an occasional exception (Smits et al., 2022). Attempts to improve training effects have only partly been successful and no effects of ApBM on bias change have been observed, echoing the findings of AtBM in smoking. However, in all studies a task-irrelevant feature ApBM was administered to assess approach biases pre- and post-intervention, which has been shown to be unreliable (Kahveci et al., 2023; Kersbergen et al., 2015). Consequently, the question whether no bias change occurs or whether it cannot be measured reliably remains unresolved.

DISCUSSION & CONCLUSIONS

There is a large variety in almost all methodological aspects of CBM research on addictions. In fact, there is no such thing as '*the* CBM intervention in addictions', not even '*the* AtBM in TUD', therefore it is difficult to draw general conclusions. Regarding ApBM and AtBM in TUD, however, it seems safe to conclude that the evidence for positive effects on consumption and abstinence is less convincing than for AUD. Numerous factors may be responsible for such a difference, including the physical and chemical differences between the two drugs. For instance, most successful alcohol-CBM training studies were conducted with currently abstinent patients, with the goal to remain abstinent. In contrast, most participants in TUD-CBM trainings were current smokers, and they participated with the goal to quit smoking, or to reduce consumption. Second, the neurotoxic effects of chronic AUD lead to neurological damage so that CBM training could be more effective in AUD than in smoking. Third, smoking, as suggested by some theoretical accounts (Tiffany, 1990; Everitt and Robbins, 2016), might have a stronger habitual component than AUD, which is underscored by the finding that nicotine receptors play a role in habit formation (Gould and Leach, 2014). While the compulsive habit account of addiction has not been supported by much evidence (Hogarth, 2020), smoking might be the addiction in which habits play the strongest role.

Finally, alcohol-CBM training has been able to use a 'natural' alternative stimulus category, namely non-alcoholic drinks that need to be approached or attended to instead of alcoholic drinks, and indeed neurocognitive studies have shown that the training not only reduces salience of alcohol stimuli, but also increases salience of non-alcoholic drinks (C. E. Wiers et al., 2015; Wiers and Wiers, 2017). In contrast, tobacco-related stimuli lack such a natural alternative stimulus category, and it is unclear what should

be approached or attended to instead of smoking-related objects. The currently used tobacco-control stimuli were primarily designed for assessment purposes (because of their visual similarity with the tobacco-related stimuli), not for training (because they do not constitute an alternative to the act of smoking). The latter issue has been addressed in recent studies, which included a motivationally relevant alternative (not necessarily visually matched, Köpetz et al., 2017; Wen et al., 2021), but results have not been strong. In a next step in this line of thinking, ABC training was proposed (Wiers et al., 2020). It introduced personalized alternative responses, and also an antecedent (e.g., coming home stressed) and consequences related both to the addictive behavior and to the alternative. For instance, go for a run rather than smoke, with positive vs negative effects on a personally relevant long-term outcome, such as long-term health. Promising initial results were found in a first proof-of-principle study (Dessel et al., 2023), but it remains to be tested in clinical AUD samples and in TUD.

Regarding promising avenues for CBM in TUD and other addictions (where a generally relevant alternative like non-alcoholic drinks is also lacking), we have some recommendations. First, as the positive findings in AUD all employed CBM as an add-on to abstinence-oriented treatment, this should be the primary focus for testing CBM for other addictions, but currently most studies focused on reduced use, which was *not* successful in alcohol (see Wiers et al., 2023). In fact, one of the few positive signals for CBM in smoking concerned an online study in which AtBM was employed in the context of a (verified) smoking cessation attempt, where a substantial effect was found in quitting success in heavy smokers (15+ cigarettes per day, Elfeddali et al., 2016). In contrast, a clinical RCT in which ApBM was added to smoking cessation treatment yielded disappointing result (Wittekind et al., 2019b). Second, as was noted in the review of CBM in TUD, effects on bias have been inconsistent, related to the poor

measurement of the biases involved (Ataya et al., 2012; Kahveci et al., 2023; Kersbergen et al., 2015). The good news is that much more reliable assessment instruments have recently been developed to assess attentional bias (Grafton et al., 2021), and tested successfully in the domain of addictive behaviors (internal consistency > .90, Wiechert et al., 2021). Developing more reliable measures to assess an approach bias would be beneficial as well. Finally, there is an impetus to move from computer assessment and training to mobile versions, which will create new possibilities but also challenges for reliable and valid assessment and training (e.g., Manning et al., 2021b).

In conclusion, CBM has been successful in one specific application, namely as add-on to the abstinence-oriented treatment for AUD, with many large clinical RCTs reporting reduced relapse rates compared to sham training or no training. However, in other contexts, CBM has been less successful for people who want to reduce rather than abstain use, or for people not motivated to change, such as student volunteers in alcohol studies. To what extent new personalized versions, such as ABC training (Wiers et al., 2020) will fare better is an open question now, but we have to conclude that so far, clinical applications of CBM outside the 'sweet spot' of adding it to abstinence-oriented treatment for AUD, have been largely disappointing.

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