Chapter 17

Cognitive bias modification in the treatment of addiction

Reinout W. Wiers[1], Oulmann Zerhouni[2], Tess den Uyl[1] and Marilisa Boffo[1,3]

[1]Addiction Development and Psychopathology (ADAPT) Laboratory, Department of Psychology, University of Amsterdam, Amsterdam, The Netherlands; [2]UFR Sciences Psychologiques et Sciences de l'Éducation (SPSE), Université Paris Nanterre, Paris, France; [3]Department of Psychology, Education and Child Studies, Erasmus University Rotterdam, Rotterdam, The Netherlands

Introduction

Conceptually, cognitive training interventions can be divided into two broad classes: training of general abilities (e.g., working memory (WM), covered in Chapter 18) and training of automatically activated reactions (i.e., cognitive biases) to disorder-related stimuli, which fall under the general heading of cognitive bias modification (CBM, Wiers, 2018; Wiers et al., 2013). In CBM, different cognitive biases can be targeted, all in relation to motivationally salient environmental and internal cues relating to a substance or addictive activity: (a) selective attentional processes toward (salient) substance-related cues (attentional bias, AtB), (b) behavioral approach tendencies associated with the rewarding outcome of substance use (approach bias, ApB), and (c) memory associations (memory bias; see for a review Wiers et al., 2013). CBM interventions aim to modulate the relative strength of these biases, to allow for more adaptive behavior and emotion regulation. For example, memory bias can be targeted through a computerized procedure in which addiction cues are selectively inhibited, such as a modified go/no-go task, in which addiction cues are always coupled with a no-go response (Houben et al., 2011, 2012), making the affective evaluation of those stimuli more negative. Note that response inhibition can be trained both as a general ability (without addiction cues, such as WM training, see Wiers, 2018) and in relation to addiction cues (i.e., cue-specific response inhibition), which makes it is a form of CBM (see, Wiers, 2018) as discussed in Chapter 19.

Importantly, when synthesizing research in a clinically relevant domain such as CBM, it is crucial to distinguish at least between two types of qualitatively different studies: on the one hand, experimental proof-of-principle (PoP) studies (typically done in students not motivated to change) and on the other hand, behavior change studies, typically randomized controlled trials (RCTs), in clinical samples (Sheeran et al., 2017; Wiers et al., 2018a,b). Note that a recent metaanalysis cast doubt on the clinical usefulness of CBM for addiction, but it combined PoP studies in students with RCTs in clinical samples (Cristea et al., 2016). A recent review in which the "apples and oranges" were sorted (Wiers et al., 2018a,b) demonstrated that CBM has an add-on effect to regular treatment in clinical samples, which was also suggested by a recent Bayesian meta-analysis of patient-level data including only clinical studies (Boffo et al., 2019), although more evidence is needed to irrefutably establish CBM therapeutic effects.

The chapter is organized as follows: we first discuss the research in two branches of CBM that have been used in behavior change studies in clinical samples, AtB and ApB modification (AtBM and ApBM, respectively). We then discuss research aimed at a memory bias, with an emphasis on the role of awareness, which has so far mostly been used in preclinical experimental studies. We then discuss what is known of neurocognitive mechanisms underlying CBM. In the final section, we discuss ways forward, both regarding optimizing clinical applications, including combinations of CBM with neurostimulation, and by making training more motivating and personally relevant.

Attentional bias modification

CBM started with the seminal study of MacLeod et al. (2002), in the domain of anxiety, in which selective attention toward threatening cues was manipulated (i.e., AtB). Before this study, many studies had found correlations between AtB and anxiety. However, cross-sectional

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studies do not provide evidence for causal relationships, which require the adoption of an experimental approach (Spencer et al., 2005). The primary purpose of early PoP CBM studies was then to systematically manipulate disorder-relevant cognitive biases and test the effects on disorder-related symptoms. These were typically done in student volunteers without a disorder (e.g., students with medium levels of anxiety). Participants were randomly assigned to a condition in which their attention was trained toward or away from threatening stimuli. The latter group showed less anxiety during a subsequent stressful task compared with the first group. Note that to establish causality, psychological constructs can be manipulated in both directions: toward or away from disorder-relevant stimuli, which is not done in clinical trials for obvious ethical reasons (Wiers et al., 2018a). After establishing the causal role of AtB in disorder-relevant symptoms (in this case, sensitivity to stress), later studies also tested the effects of AtBM as a treatment intervention in clinical samples (e.g., Amir et al., 2009). Given these initial successes and the fact that AtBM, and more in general CBM, typically employs computerized interventions, large online trials were conducted. These largely resulted in nonsignificant findings, related to the fact that in most cases, the targeted bias was not changed when AtBM was delivered online (see Macleod and Clarke, 2015). Metaanalyses focusing on clinical samples (Heeren et al., 2015; Linetzky et al., 2015) concluded that there are reliable effects of AtBM on AtB and clinical symptoms in the anxiety domain. A recent individual participant data metaanalysis (including patient-level data from 13 clinical studies), confirmed this (Price et al., 2016), with training setting (clinical context or online) as a significant moderator (smaller effects for training online). Hence, from AtBM studies on anxiety, where CBM started, we can learn that it is crucial to distinguish PoP studies from clinical RCTs; that within RCTs, it is important to distinguish online trials from studies in a clinic; and that to establish effects on clinically relevant outcomes, it is important to first test whether the targeted bias is successfully manipulated.

In the field of addiction, a similar development can be observed. Many cross-sectional studies had demonstrated that an AtB toward substance-related cues was related to addictive behaviors (review and metaanalysis: Field and Cox, 2008; Rooke et al., 2008). First experimental studies investigated the causal status of AtB, by testing whether changing AtB in students resulted in short-lived changes in alcohol intake directly after the manipulation (Field et al., 2007; Field and Eastwood, 2005; Schoenmakers et al., 2007). Again, note that in some of these studies, one experimental group was trained toward alcohol to test whether this resulted in increased drinking in a bogus "taste test," compared with a group that was trained away from the alcohol stimuli (Field et al., 2007; Field and Eastwood, 2005), which was not done in a study with heavy drinking students (Schoenmakers et al., 2007), where continued assessment was used as a control condition. While these first studies found effects on the AtB for trained stimuli, no generalization was found to untrained stimuli (Field et al., 2007; Schoenmakers et al., 2007).

Similar to the anxiety domain, the second step was to move out of the lab and evaluate the effects of CBM in studies with a clinical goal (abstinence or reduction of use) in individuals aware of the behavior change goal of the intervention. These studies have been summarized in recent narrative reviews of all CBM studies in the alcohol (Wiers et al., 2018a) and tobacco use disorder (TUD) domains (Mühlig et al., 2017), and in a (Bayesian) metaanalysis of individual participant data from exclusively clinical studies evaluating CBM as a treatment intervention for alcohol use disorder (AUD) and TUD (Boffo et al., 2019).

Three clinical studies used multiple sessions of AtBM in AUD patients using training varieties of the visual probe task[1] (as in MacLeod and colleagues). The first small RCT included 43 patients, who received five sessions of AtBM training or sham training in addition to regular treatment (Schoenmakers et al., 2010). AtB for alcohol was reduced in the experimental condition (with generalization to untrained alcohol stimuli). Although there was no significant effect of AtBM on the primary outcome measures, there was an indication of clinical impact: patients in the experimental condition were discharged from treatment earlier than patients in the control condition and relapsed later. A second small RCT (86 participants randomized over four conditions) combined eight sessions of experimental or placebo AtBM training for alcohol and threatening cues in AUD patients with social anxiety (Clerkin et al., 2016). Alcohol AtB was reduced, as well as AUD outcomes across all conditions (no Time by Condition interaction).

Cox et al. (2015) combined AtBM training and motivational enhancement, in 148 university- and community-recruited individuals who wanted to reduce their drinking. The training paradigm employed was the Alcohol Attention Control Training Program (AACTP), which had shown promise in an earlier uncontrolled study in which problem

1. In this task, participants have to respond to a probe presented at the location of one of the two stimuli on the computer screen, such as a picture of a bottle of wine and a picture of a bottle of water. When used to assess AtB, the probe is presented equally often at the location previously occupied by both types of stimuli. Typically, participants respond faster when the probe appears at the location on which their attention was already focused (i.e., selective attention or AtB), e.g., in the case of drinkers, on the picture depicting the bottle of wine. When used for training, the task includes a built-in stimulus–response contingency systematically presenting the probe at the location of the neutral stimulus (i.e., the picture of the bottle of water), thus training participants to consistently shift attention away from substance-related cues and to attend to neutral cues instead.

drinkers reduced drinking compared with baseline (Fadardi and Cox, 2009). The AACTP uses training varieties of the emotional Stroop Task and employs increasing levels of difficulty to motivate participants. In a study by Cox et al. (2015), AACTP and motivational enhancement could both be present or absent (2 × 2 design). AACTP led to reduced drinking in the short term (3 but not 6 months after the intervention). Motivational enhancement reduced drinking 3 and 6 months after the intervention. The AACTP paradigm was also deployed in the first online CBM study in alcohol addiction (Wiers et al., 2015c) comparing the effects of AACTP with different varieties of ApBM (discussed below), including a sham control condition. A main effect of time was found, in the absence of an interaction with condition: hence, participants in all conditions reduced their drinking, which was also their goal (not abstinence).

A very recent large study (N = 1405 AUD inpatients, not yet included in the metaanlyses) examined two types of CBM as add-on to regular treatment: six sessions of AtBM or ApBM (discussed below) or the combination of the two (three sessions each; Rinck et al., 2018). A long-term effect was found for all three active CBM conditions, with 8.4% less relapse 1 year after treatment discharge compared with patients receiving sham training or no training. When looking at the effects on AtB (with much incomplete data; as the study was added to everyday practice, in the context of strict data privacy regulations prescribing that computers are "cleaned" every night, data on biases are missing from about half of the patients), the three active CBM groups showed no significant decrease in AtB, likely related to participants already showing an AtB *away* from alcohol at baseline. Further, changes in AtB did not mediate the clinical effect, which is likely related to the poor reliability of the visual probe task as an assessment instrument (Ataya et al., 2012) and to the absence of a strong AtB *toward* alcohol at baseline. Interestingly, although no effect was found on alcohol AtB, AtBM alone and in combination with ApBM showed a crossover effect on the other targeted bias, ApB for alcohol.

In the TUD domain, the evidence on the effect of AtBM as a behavior change intervention is still very limited. To date, only two studies evaluated multiple sessions of AtBM training on top of standard treatment (Begh et al., 2015; Lopes et al., 2014). In Begh et al. (2015), 118 adult smokers seeking help to quit completed five sessions of either AtBM or sham training on top of a smoking cessation program. Training effects were neither found on smoking-related AtB nor on craving, abstinence rates, or other clinical outcomes. Note that the sample showed on average no AtB toward smoking cues before treatment, which may have hindered the detection of effects for those with high level of AtB at baseline. In contrast, in Lopes et al. (2014), 67 adult smokers attending group CBT to quit smoking were randomized to receive either three sessions of AtBM, one AtBM session and 2 of sham training, or three sessions of sham training. Participants did show a strong smoking AtB bias at baseline, which significantly decreased in the short term (24 h and 1-month follow-up) in the group receiving three sessions of AtBM. However, no group by time interaction effects was found on any of the behavioral outcomes, which decreased across all groups. Note that the study suffered from 24% dropout after the 24 h posttest, greatly decreasing power to detect interaction effects over time (the groups had an n ~ 15 across the follow-ups).

In contrast to the only online study of AtBM for AUD (Wiers et al., 2015c), the first online study of AtBM for smoking cessation (N = 434 treatment-seeking smokers recruited online; Elfeddali et al., 2016) did find an increased abstinence rate only among heavy smokers (50% compared with 25% in the sham training control group). However, the effect on AtB reduction was not significant (probably again related to poor reliability of the visual probe task as an assessment instrument and to participants not showing a strong smoking AtB at baseline). The more positive finding in this online study could be related to the abstinence goal and motivation for treatment (before starting the training, participants were checked to have actually made a quit attempt on the indicated quit day).

The use of AtBM in other substance use disorders has been less explored, with one feasibility study examining the clinical effects of three sessions of AACTP in a sample of 48 male opiate abusers on methadone replacement therapy (Ziaee et al., 2016) and one in heavy cannabis users (Wolf et al., 2016). Ziaee et al. found that the AACTP group showed a greater reduction in AtB than the control group at posttest (but not at follow-up), temptations to use, and number of relapses from baseline to 3- and 6-month follow-up. Wolf et al. (2016), in contrast, did not find training effects in a small sample (N = 17).

In summary, AtBM shows promise as adjunct treatment intervention for AUD (Schoenmakers et al., 2010; Rinck et al., 2018), but a major limitation concerns the low reliability of the most often used assessment instrument, the visual probe task, which makes it hard to show effects on the bias and therefore to find mediation of the clinical effects by change in AtB. Although the evidence is currently very limited, there is also some promise to use AtBM to help people quit smoking, even when done in an online format only (Elfeddali et al., 2016), which has generally found less strong effects compared with training in a more controlled setting.

Approach bias modification

Based on emotion theory, in which an appraisal and action tendency are distinguished (Frijda, 1986), one can distinguish between an AtB for addiction-related stimuli and an associated action tendency, in the case of addiction

typically approach (Wiers et al., 2009, 2013). Different tasks have been developed to assess the approach bias, including varieties of the approach avoidance task (AAT, Rinck and Becker, 2007), which was originally developed as a relevant-feature task (i.e., in one block, the instruction was to pull the joystick in response to disorder-relevant stimuli, whereas in another block, the instruction was to push the joystick to disorder-relevant stimuli) but later used as an irrelevant-feature task, in which participants react to content-irrelevant feature of the stimulus, such as picture format (Wiers et al., 2009) or orientation (Cousijn, 2011). The disadvantage of using an irrelevant-feature version of a task is that the reliability is lower than for a relevant-feature task (Field et al., 2011), but the advantage is that the task can be changed from an assessment task to a modification instrument without changing the instructions (Wiers et al., 2010). In this first proof-of-concept study in moderately drinking students, participants were randomly assigned to a condition in which they started pulling in response to most of the alcohol pictures and pushing in response to most of the nonalcohol pictures ("approach alcohol condition") or to a condition with reversed contingencies ("avoid alcohol condition"). It was found that the bias changed in accordance with training condition, with effects on untrained stimuli (typically not found in AtBM), and on a relevant-feature task of implicit memory associations, the Implicit Association Test (IAT), in which alcohol and soft drink words were combined with approach or avoid words in different conditions (Ostafin and Palfai, 2006). In addition, an effect was found on alcohol consumption in a taste test, with heavier drinkers who had been successfully trained to avoid alcohol drinking less than heavier drinkers who had been successfully trained to approach alcohol. After this first successful proof-of-concept study, four studies tested ApBM as add-on to treatment for AUDs.

In the first study (N = 214), four sessions of ApBM resulted in reduced alcohol ApB, with generalization to alcohol-approach implicit associations in the IAT and 13% lower relapse rate a year after treatment discharge, compared with controls (Wiers et al., 2011). Mediation of the clinical effect by change in ApB was not found, although a later analysis using a different mathematical method to estimate the change in bias did find support for mediation by the change in alcohol-approach associations in the IAT (Gladwin et al., 2015). In the second large study (N = 509), 12 sessions of ApBM, compared with no training, resulted in 9% lower relapse rate at 1-year follow-up, and this effect was mediated by the change in ApB (Eberl et al., 2013). Moderation was also found, with a stronger effect on the change in bias in patients with a relatively strong alcohol ApB before training. A third study (N = 83) in Australia investigated the effect of four sessions of ApBM versus sham training administered during alcohol detoxification (Manning et al., 2019). At 2-week postdischarge, the ApBM group showed a 21% lower relapse rate than the sham training group (statistical trend for intention-to-treat [ITT] analysis and significant for per-protocol analysis). Training task performance improved in the ApBM group (i.e., increased accuracy in pushing away alcohol) but did not predict relapse rate. Finally, in the previously mentioned recent large study (N = 1405; Rinck et al., 2018), all three active CBM conditions showed better clinical outcomes (8.4% lower relapse rate) at 1-year follow-up than sham training or no training. Similar to the AtBM results, participants did not show an ApB toward alcohol at baseline. However, ApBM and the combination of ApBM and AtBM significantly modified the ApB into an avoidance bias. The effect was yet small and did not mediate the training effect on relapse, most likely because of measurement issues and loss of training data for half the sample. Finally, the first online study testing both AtBM and ApBM as a stand-alone intervention, already mentioned above (Wiers et al., 2015c), showed a significant decrease in drinking over time irrespective of condition.

In the smoking domain, the evidence for ApB is still very limited with only four clinical studies. Three studies examined the effects of four sessions of ApB against a sham training condition, two on top of CBT-based treatment for TUD (Kong et al., 2015; Machulska et al., 2016) and one as a stand-alone intervention (Baird et al., 2017). In Kong et al. (2015) and Machulska et al. (2016), 60 adolescent and 145 adult smokers, respectively, completed four sessions of ApBM or sham training on top of smoking cessation treatment (e.g., CBT or psychiatric treatment). In both studies, no changes in smoking ApB as a result of the ApBM intervention were observed, with no significant difference in smoking outcomes in Kong et al. (2015). However, in Machulska et al. (2016), the ApBM did result in a continued, larger decrease in self-reported amount of cigarettes at follow-up in the ApBM group, which was not mediated by changes in smoking ApB. In Baird et al. (2017), 52 treatment-seeking smokers were randomized to either stand-alone ApBM or sham training before a self-guided quit attempt and were assessed again a week later. Although there was no group difference in amount of days abstinent after the quit attempt, the ApBM group showed a significant reduction in smoking ApB. Further, a greater decrease in ApBM (but not baseline level of ApB) was associated with a larger decrease in amount of days abstinent (independently of condition).

The last study (N = 257 adult smokers recruited online) explored the short-term effects of one session of ApBM delivered online, compared with a waitlist control condition (Wittekind et al., 2015). Despite almost 30% dropout rate, both per-protocol and ITT analyses showed a significant decrease in self-reported smoking, craving, and symptoms of tobacco dependence in the ApB group at 4-week follow-up.

In summary, these findings indicate that ApBM shows a positive add-on effect in the treatment of AUD. This effect is small but similar to the effect of medication (number needed to treat of 12,[2] see Wiers et al., 2018b). When looking at the clinical efficacy of ApBM in TUD, evidence for positive effects is still scarce and inconsistent. Note that regarding other addictions, first PoP studies in cannabis users have been conducted (Jacobus et al., 2018; Sherman et al., 2018) but no RCTs yet in clinical samples. These findings are in line with the results of a Bayesian meta-analysis of patient-level data from 14 clinical CBM studies (Boffo et al., 2019), which showed small effects of CBM in general on cognitive bias and relapse rate but not on reduction of substance use (note that only studies published until May 2016 were included, hence not including the evidence provided by the more recent studies by Rinck et al., 2018; Baird et al., 2017; and Ziaee et al., 2016). Noteworthy, the effects of CBM on bias reduction were found to be stronger for AUD than for TUD, most likely related to the greater amount of studies in the alcohol domain and to the inconsistency of results in the few clinical TUD studies. However, both effects on bias reduction and relapse rate were associated with much uncertainty (i.e., extremely wide 95% Bayesian credible intervals), indicating the need for a larger body of evidence to draw firm conclusions about the clinical effectiveness of CBM interventions.

The latter result is of particular importance when summarizing the extant evidence of treatment effects: one of the advantages of the Bayesian approach is in fact the possibility of quantifying the likelihood that a hypothesis is true—otherwise not possible within the classical frequentist approach—therefore providing a realistic summary of the available evidence in favor or against a hypothesized effect. To date, the use of CBM as a behavior change interventions for addiction disorders appears to be still in its infancy, and a larger amount of clinical studies is necessary to fully establish the robustness and reproducibility of its clinical effectiveness (Boffo et al., 2019).

Memory bias modification—evaluative conditioning

Another approach to CBM is to focus on memory associations between substance-related concepts and (automatically activated) evaluations. Substance-related memory associations have now been studied for over 2 decades, starting with the pioneering work using open-ended memory associations by Szalay and Stacy and colleagues (Stacy, 1997; Stacy et al., 1994; Szalay et al., 1992), followed by first reaction time measures (Palfai and Wood, 2001; Wiers et al., 2002). Findings can be summarized as follows (see for review and metaanalysis: Roefs et al., 2011; Rooke et al., 2008; Stacy and Wiers, 2010): heavy drinkers tend to have stronger positive associations with alcohol than light drinkers, and stronger positive associations are related to heavier drinking. Similar results have been observed for smoking (e.g., McCarthy and Thompsen, 2006), and implicit associations with smoking have also been associated with craving for tobacco (Waters et al., 2007), as well as dependence and difficulty quitting smoking (Chassin et al., 2010). The relationship between associations and consumption is even stronger when individuals score low on executive functions, as now many studies have demonstrated (Friese et al., 2015; Grenard et al., 2008; Hofmann et al., 2008; Houben and Wiers, 2009; Thush et al., 2008). Substance associations are not necessarily formed through direct experience with substances, as they are also influenced by the social environment. For example, associations were found to predict alcohol consumption 1 year later in adolescents (Thush and Wiers, 2007) and found to be influenced by the degree of parental approval toward alcohol (Payne et al., 2016). Implicit associations have also been shown to explain substance use beyond direct measures (Rooke et al., 2008) and to prospectively predict substance use and problems (Lindgren et al., 2013, 2016; Stacy, 1997).

From these findings, the question arises on how associations can be modified to reduce substance use. As mentioned above, one paradigm used to this end has been selective inhibition, discussed in Chapter 19. Another well-established paradigm to alter evaluative memory associations is evaluative conditioning (EC), which has been defined as a change in the evaluation of the valence of a conditioned stimulus (CS, here a substance-related stimulus) after it has been paired with a positive or negative unconditioned stimulus (US, metaanalysis: Hofmann et al., 2010). Studies have shown that EC can change both indirect and direct measures of smoking evaluations and smoking (Măgurean et al., 2016), as well as alcohol evaluations and alcohol consumption (Houben et al., 2010a,b). However, the processes by which EC affects memory associations, and consequently behaviors, remain unclear. Traditionally, EC was thought to change associations by exerting its effect outside conscious awareness, in contrast to classical conditioning (De Houwer et al., 2001; Sweldens et al., 2014). More recently, the idea gained support that conscious detection of CS-US pairings may be necessary for EC. Methodological refinements in assessing contingency awareness revealed that EC effects were only observed in those participants with contingency awareness (Pleyers et al., 2007, 2009). However, other evidence suggests that, under certain conditions, EC may occur

2. This number indicates how many patients would have to be treated (based on statistical outcomes) to make a difference in the outcome. Hence a strong effect is reflected in a low NNT, e.g., NNT = 4 would indicate that four patients are needed (on average) to make the difference in one. For CBM as add-on (and medication) in alcohol use disorders, the NNT is around 12.

independently of contingency awareness (Rydell and McConnell, 2006; Walther and Nagengast, 2006). More recently, more sensitive methods have been proposed for assessing contingency awareness, which are more sensitive to implicit encoding (Hütter et al., 2012; see for an application to alcohol, Zerhouni et al., 2018). The current weight of the evidence suggests that awareness plays an important role in EC effects (review: Corneille and Stahl, 2018; but see Greenwald and De Houwer, 2017 for recent evidence in favor of unconscious conditioning). When applied to addiction, EC was also found to be more effective when it had features encouraging the implementation of propositional rather than associative processes (Zerhouni et al., 2018). Similarly, Măgurean et al. (2016) highlighted contingency awareness as a necessary condition for EC to have an effect on smoking-related measures. It has been proposed that the formation of propositional beliefs between the CS and the US (i.e., inferring a relation between stimuli) is critical in generating EC effects (De Houwer, 2018). This logic can be used to improve CBM (Van Dessel et al., 2018) and better link it to CBT (Kopetz et al., 2017; Wiers et al., 2016), further discussed below.

Neurocognitive effects of cognitive bias modification

As CBM interventions modulate cognitive processes, it is also important to learn what underlying neural processes are changed with CBM. These findings can help elucidate the underlying mechanisms of CBM and can be used to optimize interventions by targeted brain stimulation. Neural networks related to addiction, such as heightened cue reactivity and impulsivity, also play a role in cognitive biases. An AtB toward smoking or alcohol cues is associated with activation in limbic and reward-related areas (Janes et al., 2010; Luijten et al., 2011; Vollstädt-Klein et al., 2012). Dysfunctional prefrontal areas, such as lateral prefrontal cortex and anterior cingulate cortex (ACC), are associated with numerous problems in inhibitory and regulatory processes and also contribute to cognitive biases (Goldstein and Volkow, 2011). This was also shown with an AAT, where higher levels of dorsolateral prefrontal cortex (DLPFC) and ACC activation during approach predicted a decrease in problems with cannabis use (Cousijn et al., 2012).

The neurocognitive effects of CBM have recently been reviewed (Wiers and Wiers, 2017). Most studies have focused on CBM for anxiety and depressive behavior and indicate that CBM can influence activation and connectivity in relevant subcortical signaling structures and executive lateral and medial prefrontal areas. Two studies have specifically investigated the role of ApBM in samples of people with AUD during inpatient treatment (Wiers et al., 2015a,b). In the first study, effects of ApBM on neural cue reactivity was studied in 32 abstinent AUD patients, randomly assigned to receive 6 sessions of ApBM or sham training (Wiers et al., 2015b). After training, patients in the ApBM condition showed reduced cue reactivity to alcohol in the amygdala, which correlated with cue-induced craving, and reductions in neural cue reactivity correlated with reductions in craving in the ApBM group only. In a second study, effects of ApBM on neural correlates of the alcohol ApB were studied in 26 patients, who performed an fMRI-adapted version of the AAT before and after ApBM (Wiers et al., 2015a,b,c). Before training, both groups showed significant alcohol ApB-related activation in the medial PFC. After training, patients in the CBM group showed stronger reductions in medial PFC compared with the sham training group. These reductions in neural cue reactivity correlated with reductions in ApB scores in the CBM group only. These studies indicate that ApBM reduces the activation in brain areas that represent the motivational salience of alcohol cues.

Toward optimized clinical applications of cognitive bias modification in addiction

Given these neural effects of CBM, one potential way to improve effectiveness of CBM is by combining it with neuromodulation techniques, such as transcranial direct current stimulation (tDCS). There have only been a few studies exploring this new approach. In recent years, brain stimulation protocols without concurrent training have also been used to treat addiction (covered in Chapter 22). There are two types of techniques most frequently used: repetitive transcranial magnetic stimulation (rTMS) and tDCS. The working mechanism and underlying neural effects of these techniques are different; however, the objective in this research context is similar. Anodal tDCS or high-frequency rTMS is used to *enhance* cortical plasticity, and cathodal tDCS or low-frequency rTMS is used to *reduce* cortical plasticity in the targeted brain area. As cognitive biases of AUD patients have developed over many years and cognitive control processes are generally weak, improving the efficiency of the cortical processes involved in the modification of the bias could make it easier to retrain these cognitive biases. A first PoP study testing the combination of tDCS and CBM was done in the field of anxiety (Clarke et al., 2014). In a study with 77 healthy participants, they trained participants toward or away from threat in a single AtBM session, while receiving anodal or sham tDCS stimulation over the left DLPFC. They found that bias acquisition in the trained direction was enhanced by DLPFC stimulation. A first PoP study in healthy participants (heavy drinkers) did not find effects on bias enhancement after three sessions of ApBM combined with anodal left DLPFC tDCS (den Uyl et al., 2016).

Two clinical studies focused on stimulation of the left DLPFC in combination with AtBM and ApBM in alcohol-dependent inpatients (den Uyl et al., 2017, 2019). In the study combining tDCS with ApBM (den Uyl et al., 2017),

all 91 patients received four sessions of active CBM (after three positive trials now standard treatment), two groups received anodal tDCS, either during the training or separate from the training, and one group received sham tDCS. There was a small decrease in bias reduction in the second ApBM training session in the group who received tDCS concurrently, but no bias enhancing effects were found postassessment. In the study combining AtBM and CBM, in a two-by-two design with active/placebo tDCS and AtBM (den Uyl et al., 2019), no bias enhancing effects were found after assessment. A small effect—a larger avoidance bias in the active AtBM with anodal tDCS group—was found during training, but only when all four training sessions were combined. Hence, these findings suggest that there could be small benefits of this specific form of tDCS when added to CBM, but they do not translate into relevant clinical improvements afterward. However, anodal tDCS over the DLPFC irrespective of training did show indications of a beneficial effect on relapse.

Studies investigating optimization techniques would also benefit from better and more reliable assessment tasks, to be able to more confidently state whether enhancement effects are present or not. Other future directions would involve optimizing the combination of brain areas and training type. Brain stimulation without concurrent training already shows potential in treating addiction (Chapter 22 here; Dunlop et al., 2017). However, modulation of neural excitability is dependent of the current activation state (Hsu et al., 2016), thus it may be more beneficial to activate the neural pathways before neurostimulation. Note that this strategy may also be beneficial for CBM in general, as a recent PoP study indicated (Das et al., 2015). In contrast with the current studies on AtBM and ApBM, it may be that stimulation of the DLPFC may be more suitable to combine with cognitive control training (Chapter 18), as several studies have aimed to use neurostimulation techniques to improve training of general functions, such as WM training, mostly in healthy participants in relation to anxiety and depression (review: Elmasry et al., 2015). Current studies on CBM and brain stimulation have only focused on DLPFC stimulation, as this area is most frequently targeted in cognitive research and has shown beneficial effects on WM (Hill et al., 2016). However, other brain areas could also be targeted. Following the initial findings on neural effects of CBM discussed above, it may be useful to modulate activation in the mPFC, which has shown promise in the domain of changing affective associations in prejudice (Sellaro et al., 2015). It would also be relevant to first image the neural pathways that play a role in these biases and personalize combinations of treatments based on which areas show abnormal activation. An optimal optimization strategy has not been found, but there are many research directions still to be explored. Note that also other ways can be explored to enhance CBM training effects, such as combining it with pharmacological enhancers, but we are not aware of studies yet, testing this.

Second, one problem is that CBM is typically experienced as rather boring and useless (Beard et al., 2012). This might be countered in different (not mutually exclusive) ways. First, CBM can be gamified, but this runs the risk of only leading to a temporary increase in motivation to do the training, without affecting the necessary motivation to change the addictive behavior (see Boendermaker et al., 2015). However, when training is made more attractive in an unobtrusive way, for example, by contingent music reward (Lazarov et al., 2017), this may be helpful. Another promising avenue for clinical research is to personalize treatment elements from "treatment as usual" (CBT and/or motivational interviewing), such as personal goals to change (e.g., health, partner, live longer for grandchildren, etc.), and personally meaningful alternative means to deal with stress (e.g., jogging rather than smoking, Wiers et al., 2016). These elements can be included into CBM, as a recent PoP study in smoking demonstrated (Kopetz et al., 2017). Note that this makes CBM less "implicit" and more related to explicit goals, which might in fact be helpful as recent experimental work suggests (Van Dessel et al., 2018), and might lead to a more optimal mix of traditional treatment and CBM approaches.

References

Amir, N., Beard, C., Burns, M., Bomyea, J., 2009. Attention modification program in individuals with generalized anxiety disorder. J. Abnorm. Psychol. 118 (1), 28–33. https://doi.org/10.1037/a0012589.

Ataya, A.F., Adams, S., Mullings, E., Cooper, R.M., Attwood, A.S., Munafò, M.R., 2012. Internal reliability of measures of substance-related cognitive bias. Drug Alcohol Depend. 121 (1–2), 148–151. https://doi.org/10.1016/j.drugalcdep.2011.08.023. Elsevier Ireland Ltd.

Baird, S.O., Rinck, M., Rosenfield, D., Davis, M.L., Fisher, J.R., Becker, E.S., Powers, M.B., et al., 2017. Reducing approach bias to achieve smoking cessation: a pilot randomized placebo-controlled trial. Cogn. Ther. Res. 41 (4), 662–670. https://doi.org/10.1007/s10608-017-9835-z. Springer US.

Beard, C., Weisberg, R.B., Primack, J., 2012. Socially anxious primary care patients' attitudes toward cognitive bias modification (CBM): a qualitative study. Behav. Cognit. Psychother. 40 (5), 618–633. https://doi.org/10.1017/S1352465811000671.

Begh, R., Munafò, M.R., Shiffman, S., Ferguson, S.G., Nichols, L., Mohammed, M.A., Holder, R.L., et al., 2015. Lack of attentional retraining effects in cigarette smokers attempting cessation: a proof of concept double-blind randomised controlled trial. Drug Alcohol Depend. 149, 158–165. https://doi.org/10.1016/j.drugalcdep.2015.01.041. Elsevier Ireland Ltd.

Boendermaker, W.J., Prins, P.J.M., Wiers, R.W., 2015. Cognitive Bias Modification for adolescents with substance use problems - can serious games help? J. Behav. Ther. Exp. Psychiatry 49. https://doi.org/10.1016/j.jbtep.2015.03.008.

Boffo, M., Zerhouni, O., van Beek, R.J.J., Gronaua, Q.F., Marsman, M., Nikolaou, K., Wiers, R.W., 2019. Cognitive Bias Modification for behavior change in alcohol and smoking addiction: frequentist and Bayesian meta-analysis of individual participant data. Neuropsychol. Rev. https://doi.org/10.1007/s11065-018-9386-4. Online Fir.

Chassin, L., Presson, C.C., Sherman, S.J., Seo, D.-C., Macy, J.T., 2010. Implicit and explicit attitudes predict smoking cessation: moderating effects of experienced failure to control smoking and plans to quit. Psychol. Addict. Behav. 24 (4), 670. American Psychological Association.

Clarke, P.J.F., Browning, M., Hammond, G., Notebaert, L., MacLeod, C., 2014. The causal role of the dorsolateral prefrontal cortex in the modification of attentional bias: evidence from transcranial direct current stimulation. Biol. Psychiatry 76 (12), 946–952. https://doi.org/10.1016/j.biopsych.2014.03.003. Elsevier.

Clerkin, E.M., Magee, J.C., Wells, T.T., Beard, C., Barnett, N.P., 2016. Randomized controlled trial of attention bias modification in a racially diverse, socially anxious, alcohol dependent sample. Behav. Res. Ther. 87, 58–69. https://doi.org/10.1016/j.brat.2016.08.010. Elsevier Ltd.

Corneille, O., Stahl, C., 2018. Associative attitude learning: a closer look at evidence and how it relates to attitude models. Pers. Soc. Psychol. Rev. https://doi.org/10.1177/1088868318763261.

Cousijn, J., Goudriaan, A.E., Ridderinkhof, K.R., van den Brink, W., Veltman, D.J., Wiers, R.W., 2012. Approach-bias predicts development of cannabis problem severity in heavy cannabis users: results from a prospective FMRI study. PLoS One 7 (9), e42394. https://doi.org/10.1371/journal.pone.0042394.

Cousijn, J., 2011. Reaching Out Towards Cannabis : Approach - Bias in Heavy Cannabis Users Predicts Changes in Cannabis Use. https://doi.org/10.1111/j.1360-0443.2011.03475.x.

Cox, W.M., Fadardi, J.S., Hosier, S.G., Pothos, E.M., 2015. Differential effects and temporal course of attentional and motivational training on excessive drinking. Exp. Clin. Psychopharmacol. 23 (6), 445–454.

Cristea, I.A., Kok, R.N., Cuijpers, P., 2016. The efficiency of cognitive bias modification interventions for addictions: a meta-analysis. PLoS One 11 (9), e0162226. https://doi.org/10.1371/journal.pone.0162226.

Das, R.K., Lawn, W., Kamboj, S.K., 2015. Rewriting the valuation and salience of alcohol-related stimuli via memory reconsolidation. Transl. Psychiatry 5 (9), e645. Nature Publishing Group.

De Houwer, J., Thomas, S., Baeyens, F., 2001. Association learning of likes and dislikes: a review of 25 years of research on human evaluative conditioning. Psychol. Bull. 127 (6), 853–869. American Psychological Association.

De Houwer, J., 2018. Propositional models of evaluative conditioning. Soc. Psychol. Bull.

den Uyl, T.E., Gladwin, T.E., Wiers, R.W., 2016. Electrophysiological and behavioral effects of combined transcranial direct current stimulation and alcohol approach bias retraining in hazardous drinkers. Alcohol. Clin. Exp. Res. 40 (10) https://doi.org/10.1111/acer.13171.

den Uyl, T.E., Gladwin, T.E., Rinck, M., Lindenmeyer, J., Wiers, R.W., 2017. A clinical trial with combined transcranial direct current stimulation and alcohol approach bias retraining. Addict. Biol. 22 (6), 1632–1640. https://doi.org/10.1111/adb.12463.

den Uyl, T.E., Gladwin, T.E., Lindenmeyer, J., Wiers, R.W., 2019. A clinical trial with combined transcranial direct current stimulation and alcohol attentional retraining. Alcohol. Clin. Exp. Res. 42 (10), 1961–1969.

Dunlop, K., Hanlon, C.A., Downar, J., 2017. Noninvasive brain stimulation treatments for addiction and major depression. Ann. N.Y. Acad. Sci. 1394 (1), 31–54. https://doi.org/10.1111/nyas.12985.

Eberl, C., Wiers, R.W., Pawelczack, S., Rinck, M., Becker, E.S., 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.

Elfeddali, I., de Vries, H., Bolman, C., Pronk, T., Wiers, R.W., 2016. A randomized controlled trial of web-based attentional bias modification to help smokers quit. Health Psychol. 35 (8), 870–880. https://doi.org/10.1037/hea0000346.

Elmasry, J., Loo, C., Martin, D., 2015. A systematic review of transcranial electrical stimulation combined with cognitive training. Restor. Neurol. Neurosci. 33 (3), 263–278. https://doi.org/10.3233/RNN-140473.

Fadardi, J.S., Cox, W.M., 2009. Reversing the sequence: reducing alcohol consumption by overcoming alcohol attentional bias. Drug Alcohol Depend. 101 (3), 137–145. https://doi.org/10.1016/j.drugalcdep.2008.11.015.

Field, M., Cox, W.M., 2008. Attentional bias in addictive behaviors: a review of its development, causes, and consequences. Drug Alcohol Depend. 97 (1–2), 1–20. https://doi.org/10.1016/j.drugalcdep.2008.03.030.

Field, M., Eastwood, B., 2005. Experimental manipulation of attentional bias increases the motivation to drink alcohol. Psychopharmacology 183 (3), 350–357. https://doi.org/10.1007/s00213-005-0202-5.

Field, M., Duka, T., Eastwood, B., Child, R., Santarcangelo, M., Gayton, M., 2007. Experimental manipulation of attentional biases in heavy drinkers: do the effects generalise? Psychopharmacology 192 (4), 593–608. https://doi.org/10.1007/s00213-007-0760-9.

Field, M., Caren, R., Fernie, G., De Houwer, J., 2011. Alcohol approach tendencies in heavy drinkers: comparison of effects in a relevant stimulus-response compatibility task and an approach/avoidance Simon task. Psychol. Addict. Behav. 25 (4), 697–701. https://doi.org/10.1037/a0023285.

Friese, M., Gianotti, L.R.R., Knoch, D., 2015. The association between implicit alcohol attitudes and drinking behavior is moderated by baseline activation in the lateral prefrontal cortex. Health Psychol. 35 (8), 837–841. https://doi.org/10.1037/hea0000179.

Frijda, N.H., 1986. The Emotions. Cambridge University Press.

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. Alcohol. Clin. Exp. Res. 39 (1), 101–107. https://doi.org/10.1111/acer.12602.

Goldstein, R.Z., Volkow, N.D., November 2011. Dysfunction of the prefrontal cortex in addiction : neuroimaging findings and clinical implications. Nat. Rev. Neurosci. 12 https://doi.org/10.1038/nrn3119. Nature Publishing Group.

Greenwald, A.G., De Houwer, J., 2017. Unconscious conditioning: demonstration of existence and difference from conscious conditioning. J. Exp. Psychol. Gen. 146 (12), 1705–1721. https://doi.org/10.1037/xge0000371.

Grenard, J.L., Ames, S.L., Wiers, R.W., Thush, C., Sussman, S., Stacy, A.W., 2008. Working memory capacity moderates the predictive effects of drug-related associations on substance use. Psychol. Addict. Behav. 22 (3), 426–432. https://doi.org/10.1037/0893-164X.22.3.426.

Heeren, A., Mogoase, C., Philippot, P., McNally, R.J., 2015. Attention bias modification for social anxiety: a systematic review and meta-analysis. Clin. Psychol. Rev. 40, 76–90. https://doi.org/10.1016/j.cpr.2015.06.001.

Hill, A.T., Fitzgerald, P.B., Hoy, K.E., 2016. Effects of anodal transcranial direct current stimulation on working memory: a systematic review and meta-analysis of findings from healthy and neuropsychiatric populations. Brain Stimul. 9 (2), 197–208. https://doi.org/10.1016/j.brs.2015.10.006. Elsevier Inc.

Hofmann, W., Gschwendner, T., Friese, M., Wiers, R.W., Schmitt, M., 2008. Working memory capacity and self-regulatory behavior: toward an individual differences perspective on behavior determination by automatic versus controlled processes. J. Personal. Soc. Psychol. 95 (4), 962–977. https://doi.org/10.1037/a0012705.

Hofmann, W., De Houwer, J., Perugini, M., Baeyens, F., Crombez, G., 2010. Evaluative conditioning in humans: a meta-analysis. Psychol. Bull. 136 (3), 390. American Psychological Association.

Houben, K., Wiers, R.W., 2009. Response inhibition moderates the relationship between implicit associations and drinking behavior. Alcohol. Clin. Exp. Res. 33 (4), 626–633. https://doi.org/10.1111/j.1530-0277.2008.00877.x.

Houben, K., Havermans, R.C., Wiers, R.W., 2010a. Learning to dislike alcohol: conditioning negative implicit attitudes toward alcohol and its effect on drinking behavior. Psychopharmacology 211 (1), 79–86. https://doi.org/10.1007/s00213-010-1872-1.

Houben, K., Schoenmakers, T.M., Wiers, R.W., 2010b. I didn't feel like drinking but I don't know why: the effects of evaluative conditioning on alcohol-related attitudes, craving and behavior. Addict. Behav. 35 (12), 1161–1163. https://doi.org/10.1016/j.addbeh.2010.08.012. Elsevier Ltd.

Houben, K., Nederkoorn, C., Wiers, R.W., Jansen, A., 2011. Resisting temptation: decreasing alcohol-related affect and drinking behavior by training response inhibition. Drug Alcohol Depend. 116 (1–3), 132–136. https://doi.org/10.1016/j.drugalcdep.2010.12.011. Elsevier Ireland Ltd.

Houben, K., Havermans, R.C., 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 (7), 1280–1287. https://doi.org/10.1111/j.1360-0443.2012.03827.x.

Hsu, T.-Y., Juan, C.-H., Tseng, P., December 2016. Individual differences and state-dependent responses in transcranial direct current stimulation. Front. Hum. Neurosci. 10, 1–12. https://doi.org/10.3389/fnhum.2016.00643.

Hütter, M., Sweldens, S., Stahl, C., Unkelbach, C., Klauer, K.C., 2012. Dissociating contingency awareness and conditioned attitudes: evidence of contingency-unaware evaluative conditioning. J. Exp. Psychol. Gen. 141 (3), 539. American Psychological Association.

Jacobus, J., Taylor, C.T., Gray, K.M., Meredith, L.R., Porter, A.M., Li, I., Castro, N., et al., 2018. A multi-site proof-of-concept investigation of computerized approach-avoidance training in adolescent cannabis users. Drug Alcohol Depend. https://doi.org/10.1016/j.drugalcdep.2018.03.007. Elsevier Ireland Ltd.

Janes, A.C., Pizzagalli, D.A., Richardt, S., Frederick, B.D.B., Holmes, A.J., Sousa, J., Fava, M., et al., 2010. Neural substrates of attentional bias for smoking-related cues: an fMRI study. Neuropsychopharmacology 35 (12), 2339–2345. https://doi.org/10.1038/npp.2010.103. Nature Publishing Group.

Kong, G., Larsen, H., Cavallo, D.A., Becker, D., Cousijn, J., Salemink, E., Collot Descury-Koenigs, A.L., et al., 2015. Re-training automatic action tendencies to approach cigarettes among adolescent smokers: a pilot study. Am. J. Drug Alcohol Abuse 41 (5). https://doi.org/10.3109/00952990.2015.1049492.

Kopetz, C., MacPherson, L., Mitchell, A.D., Houston-Ludlam, A., Wiers, R.W., 2017. A novel training approach to activate alternative behaviors for smoking as part of a quit attempt. Exp. Clin. Psychopharmacol. 25 (1), 50–60. https://doi.org/10.1037/pha0000108.

Lazarov, A., Pine, D.S., Bar-Haim, Y., 2017. Gaze-contingent music reward therapy for social anxiety disorder: a randomized controlled trial. Am. J. Psychiatry 174 (7), 649–656. https://doi.org/10.1176/appi.ajp.2016.16080894.

Lindgren, K.P., Neighbors, C., Teachman, B.A., Wiers, R.W., Westgate, E., Greenwald, A.G., 2013. I drink therefore I am: validating alcohol-related implicit association tests. Psychol. Addict. Behav. 27 (1), 1–13. https://doi.org/10.1037/a0027640.

Lindgren, K.P., Neighbors, C., Teachman, B.A., Baldwin, S.A., Norris, J., Kaysen, D., Gasser, M.L., et al., 2016. Implicit alcohol associations, especially drinking identity, predict drinking over time. Health Psychol. 35 (8) https://doi.org/10.1037/hea0000396.

Linetzky, M., Pergamin-Hight, L., Pine, D.S., Bar-Haim, Y., 2015. Quantitative evaluation of the clinical efficacy of attention bias modification treatment for anxiety disorders. Depress. Anxiety 32 (6), 383–391. https://doi.org/10.1002/da.22344.

Lopes, F.M., Pires, A.V., Bizarro, L., 2014. Attentional bias modification in smokers trying to quit: a longitudinal study about the effects of number of sessions. J. Subst. Abus. Treat. 47 (1), 50–57. https://doi.org/10.1016/j.jsat.2014.03.002. Elsevier Inc.

Luijten, M., Veltman, D.J., van den Brink, W., Hester, R., Field, M., Smits, M., Franken, I.H.A., 2011. Neurobiological substrate of smoking-related attentional bias. NeuroImage 54 (3), 2374–2381. https://doi.org/10.1016/j.neuroimage.2010.09.064. Elsevier Inc.

Machulska, A., Zlomuzica, A., Rinck, M., Assion, H.J., Margraf, J., 2016. Approach bias modification in inpatient psychiatric smokers. J. Psychiatry Res. 76, 44–51. https://doi.org/10.1016/j.jpsychires.2015.11.015.

Macleod, C., Clarke, P.J.F., 2015. The attentional bias modification approach to anxiety intervention. Clin. Psychol. Sci. 3 (1), 58–78. https://doi.org/10.1177/2167702614560749.

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 (1), 107–123. https://doi.org/10.1037/0021-843X.111.1.107.

Măgurean, S., Constantin, T., Sava, F.A., 2016. The indirect effect of evaluative conditioning on smoking. J. Subst. Use 21 (2), 198–203. Taylor & Francis.

Manning, V., Staiger, P., Hall, K., Garfield, J., Flaks, G., Leung, D., Hughes, L., et al., 2019. Cognitive bias modification training during inpatient alcohol detoxification reduces early relapse: a randomized controlled trial. Alcohol. Clin. Exp. Res. 40 (9), 2011–2019. https://doi.org/10.1111/acer.13163.

McCarthy, D.M., Thompsen, D.M., 2006. Implicit and explicit measures of alcohol and smoking cognitions. Psychol. Addict. Behav. 20 (4), 436−444. https://doi.org/10.1037/0893-164X.20.4.436.

Mühlig, S., Paulick, J., Lindenmeyer, J., Rinck, M., Cina, R., Wiers, R.W., 2017. Applying the 'Cognitive Bias Modification' Concept to Smoking Cessation−A Systematic Review. SUCHT, Hogrefe, AG.

Ostafin, B.D., Palfai, T.P., 2006. Compelled to consume: the implicit association test and automatic alcohol motivation. Psychol. Addict. Behav. 20 (3), 322−327. https://doi.org/10.1037/0893-164X.20.3.322.

Palfai, T.P., Wood, M.D., 2001. Positive alcohol expectancies and drinking behavior: the influence of expectancy strength and memory accessibility. Psychol. Addict. Behav. 15, 60−67.

Payne, B.K., Lee, K.M., Giletta, M., Prinstein, M.J., 2016. Implicit attitudes predict drinking onset in adolescents: shaping by social norms. Health Psychol. 35 (8), 829−836. https://doi.org/10.1037/hea0000353.

Pleyers, G., Corneille, O., Luminet, O., Yzerbyt, V., 2007. Aware and (dis) liking: item-based analyses reveal that valence acquisition via evaluative conditioning emerges only when there is contingency awareness. J. Exp. Psychol. Learn. Mem. Cogn. 33 (1), 130. American Psychological Association.

Pleyers, G., Corneille, O., Yzerbyt, V., Luminet, O., 2009. Evaluative conditioning may incur attentional costs. J. Exp. Psychol. Anim. Behav. Process. 35 (2), 279. American Psychological Association.

Price, R.B., Wallace, M., Kuckertz, J.M., Amir, N., Graur, S., Cummings, L., Popa, P., et al., 2016. Pooled patient-level meta-analysis of children and adults completing a computer-based anxiety intervention targeting attentional bias. Clin. Psychol. Rev. 50, 37−49. https://doi.org/10.1016/j.cpr.2016.09.009. Elsevier Ltd.

Rinck, M., Becker, E.S., 2007. Approach and avoidance in fear of spiders. J. Behav. Ther. Exp. Psychiatry 38 (2), 105−120. https://doi.org/10.1016/j.jbtep.2006.10.001.

Rinck, M., Wiers, R.W., Becker, E.S., Lindenmeyer, J., 2018. Relapse prevention in abstinent alcoholics by cognitive bias modification: clinical effects of combining approach bias modification and attention bias modification. J. Consult. Clin. Psychol. 86 (12), 1005−1016.

Roefs, A., Huijding, J., Smulders, F.T.Y., MacLeod, C.M., de Jong, P.J., Wiers, R.W., Jansen, A.T.M., 2011. Implicit measures of association in psychopathology research. Psychol. Bull. 137 (1), 149−193. https://doi.org/10.1037/a0021729.

Rooke, S.E., Hine, D.W., Thorsteinsson, E.B., 2008. Implicit cognition and substance use: a meta-analysis. Addict. Behav. 33 (10), 1314−1328. https://doi.org/10.1016/j.addbeh.2008.06.009.

Rydell, R.J., McConnell, A.R., 2006. Understanding implicit and explicit attitude change: a systems of reasoning analysis. J. Personal. Soc. Psychol. 91 (6), 995. American Psychological Association.

Schoenmakers, T.M., Wiers, R.W., Jones, B.T., Bruce, G., Jansen, A.T.M., 2007. Attentional re-training decreases attentional bias in heavy drinkers without generalization. Addiction (Abingdon Engl.) 102 (3), 399−405. https://doi.org/10.1111/j.1360-0443.2006.01718.x.

Schoenmakers, T.M., de Bruin, M., Lux, I.F.M., Goertz, A.G., Van Kerkhof, D.H.A.T., Wiers, R.W., 2010. Clinical effectiveness of attentional bias modification training in abstinent alcoholic patients. Drug Alcohol Depend. 109 (1−3), 30−36. https://doi.org/10.1016/j.drugalcdep.2009.11.022.

Sellaro, R., Derks, B., Nitsche, M.A., Hommel, B., van den Wildenberg, W.P.M., van Dam, K., Colzato, L.S., 2015. Reducing prejudice through brain stimulation. Brain Stimul. 8 (5), 891−897. Elsevier.

Sheeran, P., Klein, W.M.P., Rothman, A.J., 2017. Health behavior change: moving from observation to intervention. Annu. Rev. Psychol. 68, 573−600. Annual Reviews.

Sherman, B.J., Baker, N.L., Squeglia, L.M., McRae-Clark, A.L., 2018. Approach bias modification for cannabis use disorder: a proof-of-principle study. J. Subst. Abus. Treat. 87, 16−22. https://doi.org/10.1016/j.jsat.2018.01.012. Elsevier Inc.

Spencer, S.J., Zanna, M.P., Fong, G.T., 2005. Establishing a causal chain: why experiments are often more effective than mediational analyses in examining psychological processes. J. Personal. Soc. Psychol. 89 (6), 845−851. https://doi.org/10.1037/0022-3514.89.6.845.

Stacy, A.W., Wiers, R.W., 2010. Implicit cognition and addiction: a tool for explaining paradoxical behavior. Annu. Rev. Clin. Psychol. 6, 551−575. https://doi.org/10.1146/annurev.clinpsy.121208.131444.

Stacy, A.W., Leigh, B.C., Weingardt, K.R., 1994. Memory Accessibility and Association of Alcohol Use and its Positive Outcomes. Experimental and Clinical Psychopharmacology.

Stacy, A.W., 1997. Memory activation and expectancy as prospective predictors of alcohol and marijuana use. J. Abnorm. Psychol. 106 (1), 61−73. https://doi.org/10.1037/0021-843X.106.1.61.

Sweldens, S., Corneille, O., Yzerbyt, V., 2014. The role of awareness in attitude formation through evaluative conditioning. Pers. Soc. Psychol. Rev. 18 (2), 187−209. https://doi.org/10.1177/1088868314527832.

Szalay, L., Bovasso, G., Vilov, S., Williams, R.E., 1992. Assessing treatment effects through changes in perceptions and cognitive organization. Am. J. Drug Alcohol Abuse 18 (4), 407−428. Taylor & Francis.

Thush, C., Wiers, R.W., 2007. Explicit and implicit alcohol-related cognitions and the prediction of future drinking in adolescents. Addict. Behav. 32 (7), 1367−1383. https://doi.org/10.1016/j.addbeh.2006.09.011.

Thush, C., Wiers, R.W., Ames, S.L., Grenard, J.L., Sussman, S., Stacy, A.W., 2008. Interactions between implicit and explicit cognition and working memory capacity in the prediction of alcohol use in at-risk adolescents. Drug Alcohol Depend. 94 (1−3), 116−124. https://doi.org/10.1016/j.drugalcdep.2007.10.019.

Van Dessel, P., Hughes, S.J., De Houwer, J., 2018. Consequence-based approach-avoidance training: a new and improved method for changing behavior. Psychol. Sci. 29 (12), 1899−1910.

Vollstädt-Klein, S., Loeber, S., Richter, A., Kirsch, M., Bach, P., Von Der Goltz, C., Hermann, D., et al., 2012. Validating incentive salience with functional magnetic resonance imaging: association between mesolimbic cue reactivity and attentional bias in alcohol-dependent patients. Addict. Biol. 17 (4), 807−816. https://doi.org/10.1111/j.1369-1600.2011.00352.x.

Walther, E., Nagengast, B., 2006. Evaluative conditioning and the awareness issue: assessing contingency awareness with the four-picture recognition test. J. Exp. Psychol. Anim. Behav. Process. 32 (4), 454. American Psychological Association.

Waters, A.J., Carter, B.L., Robinson, J.D., Wetter, D.W., Lam, C.Y., Cinciripini, P.M., 2007. Implicit attitudes to smoking are associated with craving and dependence. Drug Alcohol Depend. 91 (2−3), 178−186. Elsevier.

Wiers, C.E., Wiers, R.W., 2017. Imaging the neural effects of cognitive bias modification training. NeuroImage 151. https://doi.org/10.1016/j.neuroimage.2016.07.041.

Wiers, R.W., Eberl, C., Rinck, M., Becker, E., Lindenmeyer, J., 2011. Retraining automatic action tendencies changes alcoholic patients' approach bias for alcohol and improves treatment outcome. Psychological Science 22 (4), 490–497.

Wiers, R.W., Van Woerden, N., Smulders, F.T.Y., De Jong, P.J., 2002. Implicit and explicit alcohol-related cognitions in heavy and light drinkers. J. Abnorm. Psychol. 111 (4), 648–658. https://doi.org/10.1037//0021-843X.111.4.648.

Wiers, R.W., 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 (1), 101–106. https://doi.org/10.1111/j.1601-183X.2008.00454.x.

Wiers, R.W., Rinck, M., Kordts, R., Houben, K., Strack, F., 2010. Retraining automatic action-tendencies to approach alcohol in hazardous drinkers. Addiction (Abingdon Engl.) 105 (2), 279–287. https://doi.org/10.1111/j.1360-0443.2009.02775.x.

Wiers, R.W., Gladwin, T.E., Hofmann, W., Salemink, E., Ridderinkhof, K.R., 2013. Cognitive bias modification and cognitive control training in addiction and related psychopathology: mechanisms, clinical perspectives, and ways forward. Clin. Psychol. Sci. 1 (2), 192–212. https://doi.org/10.1177/2167702612466547.

Wiers, C.E., Ludwig, V.U., Gladwin, T.E., Park, S.Q., Heinz, A., Wiers, R.W., Rinck, M., et al., 2015a. Effects of cognitive bias modification training on neural signatures of alcohol approach tendencies in male alcohol-dependent patients. Addict. Biol. 20 (5), 990–999. https://doi.org/10.1111/adb.12221.

Wiers, C.E., Stelzel, C., Gladwin, T.E., Park, S.Q., Pawelczack, S., Gawron, C.K., Stuke, H., et al., 2015b. Effects of cognitive bias modification training on neural alcohol cue reactivity in alcohol dependence. Am. J. Psychiatry 172 (4), 335–343. https://doi.org/10.1176/appi.ajp.2014.13111495.

Wiers, R.W., Houben, K., Fadardi, J.S., van Beek, P., Rhemtulla, M., Cox, W.M., 2015c. Alcohol cognitive bias modification training for problem drinkers over the web. Addict. Behav. 40 https://doi.org/10.1016/j.addbeh.2014.08.010.

Wiers, R.W., Becker, D., Holland, R., Moggi, F., Lejuez, C.W., Yield, A., 2016. Cognitive motivational processes underlying addiction treatment. In: Kopetz, C.E., Lejuez, C.W. (Eds.), Addiction. Psychology Press, pp. 201–236.

Wiers, R.W., Boffo, M., Field, M., 2018a. What's in a trial? On the importance of distinguishing between experimental lab studies and randomized controlled trials: the case of cognitive bias modification and alcohol use disorders. J. Stud. Alcohol Drugs 79 (3), 333–343. https://doi.org/10.15288/jsad.2018.79.333.

Wiers, R.W., Boffo, M., Field, M., 2018b. Persistent mixing of apples and oranges, or carefully synthesizing and designing the next steps in research on cognitive bias modifi cation in addiction. J. Stud. Alcohol Drugs 79 (3), 348–349. https://doi.org/10.15288/jsad.2018.79.348.

Wiers, R.W., 2018. Cognitive training in addiction: does it have clinical potential? Biol. Psychiatry 3 (2). https://doi.org/10.1016/j.bpsc.2017.12.008.

Wittekind, C.E., Feist, A., Schneider, B.C., Moritz, S., Fritzsche, A., 2015. The approach-avoidance task as an online intervention in cigarette smoking: a pilot study. J. Behav. Ther. Exp. Psychiatry 46, 115–120. https://doi.org/10.1016/j.jbtep.2014.08.006. Elsevier Ltd.

Wolf, P.A., Salemink, E., Wiers, R.W., 2016. Attentional retraining and cognitive biases in a regular cannabis smoking student population. SUCHT 62 (6), 355–365. https://doi.org/10.1024/0939-5911/a000455.

Zerhouni, O., Bègue, L., Comiran, F., Wiers, R.W., 2018. Controlled and implicit processes in evaluative conditioning on implicit and explicit attitudes toward alcohol and intentions to drink. Addict. Behav. 76 https://doi.org/10.1016/j.addbeh.2017.08.026.

Ziaee, S.S., Fadardi, J.S., Cox, W.M., Yazdi, S.A.A., 2016. Effects of attention control training on drug abusers' attentional bias and treatment outcome. J. Consult. Clin. Psychol. 84 (10), 861. American Psychological Association.