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Cognitive neuroscience of cognitive retraining for addiction medicine: From mediating mechanisms to questions of efficacy

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Abstract

Cognitive retraining or cognitive bias modification (CBM) involves having subjects repeatedly perform a computerized task designed to reduce the impact of automatic processes that lead to harmful behavior. We first discuss the theory underlying CBM and provide a brief overview of important research progress in its application to addiction. We then focus on cognitive- and neural-mediating mechanisms. We consider recent criticism of both CBM and its theoretical foundations. Evaluations of CBM could benefit from considering theory-driven factors that may determine variations in efficacy, such as motivation. Concerning theory, while there is certainly room for fundamental advances in current models, we argue that the basic view of impulsive behavior and its control remains a useful and productive heuristic. Finally, we briefly discuss some interesting new directions for CBM research: enhancement of training via transcranial direct current stimulation, online training, and gamification, i.e., the use of gameplay elements to increase motivation.

Keywords

Cognitive bias modification, CBM, Mechanisms, Addiction, Bias, Implicit measures, Neuroimaging

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1 INTRODUCTION

Cognitive retraining or cognitive bias modification (CBM) concerns a broad class of interventions aimed at improving the balance between harmful “cognitive biases” and control over them. So, first, what are such biases? The general theoretical foundations of the concept of a cognitive bias are dual-process or dual-systems models (MacLeod and Rutherford, 1998; Stacy and Wiers, 2010; cf. Cisler and Koster, 2010; MacLeod et al., 2002; Mathews and MacLeod, 1986, 1994). Dual-process models distinguish two kinds of “processes,” using various terms: automatic versus controlled or strategic, bottom-up versus top-down, preconscious versus conscious, impulsive versus reflective, reflexive versus reflective, or system 1 versus system 2 (Gladwin and Figner, 2014; for reviews of dual-process models in general, see Deutsch and Strack, 2006; Evans, 2008; Gawronski and Bodenhausen, 2005; Gladwin et al., 2011; Smith and DeCoster, 2000; Strack and Deutsch, 2004; Wiers et al., 2013b; for reviews of dual-process models in addiction specifically, see Wiers et al., 2007). Intuitively, automatic processes are those thoughts and behaviors that seem to happen to us, without the sense of their being a consequence of conscious choice. For instance, our attention may be automatically drawn to an attractive person; we might gravitate toward a cool drink of beer; or we might feel unable to purchase and eat unhealthy snacks. Automatic and controlled processes can be less subjectively defined using the elegant abstraction of a cognitive process as a sequence of patterns of activation of memory representations (Schneider and Shiffrin, 1977). Such representations include associations, perceptual transformations, and motor responses. As one pattern evokes the next, these abstract activation patterns progress from one to the other, providing a route from, for instance, perception of a stimulus to execution of a response. In an automatic process, the progress through the activation sequence is fast but inflexible, stimulus-driven, unconscious, established via conditioning or training, and does not require effort. Automatic processes in addiction reflect fundamental conditioning processes (Gladwin and Wiers, 2012; Vollstädt-Klein et al., 2012), including mechanisms underlying positive and negative reinforcement of drug use (Koob and Volkow, 2010; Siegel et al., 1999; Solomon and Corbit, 1974); the attribution of incentive salience to addiction-related stimuli and the sensitization of the neural mechanisms of “wanting” (i.e., the tendency to exert effort for some reinforcer, as distinguished from simply hedonic “liking”), i.e., of driving behavior toward acquiring drugs (Berridge, 2007; Robinson and Berridge, 1993, 2001), and (to some extent relatedly) the formation of habits and compulsion (Everitt and Robbins, 2005; Robbins and Everitt, 1999).

Controlled processes, in contrast to automatic processes, are slow but flexible, goal-directed, associated with awareness, able to deal with novel situations, and depend on the limits of working memory capacity. Control allows for behavior that overcomes errors due to contingencies (such as long-term outcomes) that would tend to have weaker effects on learning processes than more immediate reinforcement. Due to the neurobiological features of drugs, addiction-related automatic processes will be relatively difficult to be successfully controlled.
Dual-systems models posit two systems that implement the two types of processes, of which the control system has the function of intervening when the automatic system fails, for example, when the response harms important long-term outcomes or when novel information must be dealt with. In social psychology and addiction research, models have been developed in which sets of various psychological constructs are assigned to the automatic or the controlled system (Strack and Deutsch, 2004; Wiers and Stacy, 2006; Wiers et al., 2007). For instance, in a dual-systems model for addiction (Wiers et al., 2007) controlled processing contained elements such as executive functions, emotion regulation, motivation to change or inhibit, negative expectancies; while automatic processing contained approach tendencies and the emotional appraisal of stimuli. Neural dual-systems models for the control and automatic systems have also been posited, in general (Lieberman, 2007), and for addiction (Bechara, 2005). Connectionist models may also provide a useful view of dual systems (Gilbert and Shallice, 2002; McClelland et al., 1995). In such models, the automatic part of the system consists of the weights between abstract nodes, e.g., representing stimulus types and responses. Additional top-down nodes are necessary to provide top-down biasing of network activation to allow accurate responses. Note that from this perspective a controlled process does not wholly occur within a separate control system, but involves the modulation of activation.

We note at this point that, if CBM is indeed at least partly based on dual-process models, then one could be concerned at the implications of recent strong criticism aimed at such models (e.g., Keren and Schul, 2009). We will argue below that such criticism is valuable but, first, should be taken as encouragement to formulate or maybe rediscover better dual-process models rather than to reject them, and second, that the points of criticism do not take away the heuristic value of the models for asking useful questions in relation to maladaptive behaviors such as addiction, in particular, in the sense of considering effects of working memory. However, the basic differentiation between automatic and controlled processes resonates with a very wide range of phenomena, in which behavior indeed seems to be influenced by some kind of fast, involuntary influence on performance (i.e., a cognitive bias) that subjects must try to control via effortful attention and inhibition.

Dual-process models are thus directly related to a central paradox in addiction: individuals persist in behavior they know has harmful consequences (Stacy and Wiers, 2010). Relatedly, such models provide a nuanced view of the disagreement between views of addiction as a moral problem (Dalrymple, 2008) versus a disease (Leshner, 1997): it can be true both that motivation, foresight, and the availability of alternative choices play a role in whether an individual can quit addictive behavior, and that there is also an involuntary drive toward self-harming behavior due to neural effects of addictive drugs. The degree to which an individual is addicted, as opposed to simply someone who chooses to use drugs and does not sufficiently care about the consequences, depends on the “balance of power” between automatic and controlled cognitive processes. Indeed, and this is an important test of the dual-process view of addiction, the impact of automatic processes on addiction-related behavior has been
shown to be moderated by individual differences in working memory or executive function capacity (Hofmann et al., 2008b; Houben and Wiers, 2009) or by experimental manipulations of working memory capacity (Houben et al., 2011b; Muraven et al., 2002; Ostafin et al., 2008). Similar results have been found in other domains, including snack-eating and aggression (Friese et al., 2008; Hofmann et al., 2008a; Wiers et al., 2009a).

2 COGNITIVE BIAS MODIFICATION

As CBM is aimed at adjusting maladaptive biases, it may complement standard treatment approaches focused more on explicit cognition, voluntary decision making and motivation, and approaches aimed at the immediate biological effects of drugs and withdrawal (e.g., medication). Note that relapse can occur long after withdrawal symptoms have stopped and despite strong personal interests in abstinence or controlled use. If persistent conditioning and automatic processes cause harmful behavior in such situations, methods aimed at this level of cognition may be necessary to improve outcome. Rather than using methods such as “talk therapy” (e.g., motivational enhancement or cognitive behavior therapy), medication, or surgery, CBM uses computerized training as its primary tool. Participants repeatedly perform a task that is designed to reverse undesirable biases or to strengthen control over them. Such tasks are generally modified versions of implicit measures used to assess cognitive biases related to automatic processes hypothesized to underlie addiction.

For example, attentional biases toward drug-related stimuli can be measured using variants of the dot-probe task. In this task, two pictorial cues are presented next to each other, and subsequently a probe appears at the location of one of the pictures, to which the subject must respond. If subjects tend to be relatively fast to respond to probes appearing at the position of certain types of pictures, this can be used as measure for an attentional bias toward that stimulus category. In alcohol addiction research, heavy social drinkers show a bias toward alcohol cues (Field and Cox, 2008; Field et al., 2004; Townshend and Duka, 2001). Further, there is evidence that alcohol-dependent subjects show an initial, fast bias toward alcoholic cues, followed by attentional disengagement when more time is provided between cues and probes (Noël et al., 2006; Townshend and Duka, 2007; Vollstädt-Klein et al., 2009), suggesting an interplay between automatic and controlled processes. To convert the alcohol dot-probe task into a training variant for Attentional Bias Modification, the probe would be made to predominantly appear at the nonalcohol cue’s location. Subjects would therefore be trained to avert their attention from alcohol cues, thus counteracting the tendency for the drug-relevant cue to attract attention. Studies have shown that even a brief single-session intervention can modify attentional biases in heavy drinkers, but this is insufficient to cause effects that generalize to untrained stimuli (Field et al., 2007; Schoenmakers et al., 2007). However, when multiple attentional CBM sessions were used, a generalized bias reversal
was found in alcohol-dependent patients, as well as a positive effect on time to relapse (Schoenmakers et al., 2010).

Various other training tasks have been developed and tested as CBM methods for addiction, e.g., alcohol Go/NoGo tasks (Houben et al., 2011a) and negative evaluative conditioning tasks (Houben et al., 2010). However, arguably the most noteworthy effects have been found in clinical trials using a specific type of CBM: Approach Bias Modification, which uses a training variant of the alcohol approach-avoidance task (AAT). In the AAT, subjects have to respond to stimuli with “pushing” and “pulling” responses (often using a joystick), which are disambiguated by zoom-in and zoom-out effects (the zoom-in effect upon a pull movement generates the feeling of approach, and the zoom-out effect upon a push movement the feeling of avoidance). In the alcohol AAT, pictures of alcoholic and nonalcoholic beverages must be pushed or pulled, and heavy drinkers (Wiers et al., 2009b) and alcohol-dependent patients (Ernst et al., 2014; Wiers et al., 2011, 2014) have been found to have an alcohol-approach bias. That is, they were faster to pull than to push alcohol stimuli, and this approach bias was stronger for alcohol stimuli than for nonalcohol stimuli. Moreover, in heavy drinkers the alcohol-approach bias was found to be modulated by the OPRM1 gene (Wiers et al., 2009b), which is related to alcohol cue reactivity (Van den Wildenberg et al., 2007; Filbey et al., 2008; Ray and Hutchison, 2004). In smokers, a smoking-cue approach bias was associated with tobacco craving and decreased after long-term abstinence (Wiers et al., 2013a). A cannabis AAT was found to predict escalation of cannabis use at 6-month follow-up in heavy users (Cousijn et al., 2011). We briefly note that different tasks can also be used to measure approach biases, such as the stimulus–response compatibility task, which may be a more reliable measure to assess alcohol-approach biases (Field et al., 2011). However, to the best of our knowledge, as yet only the AAT has strong evidence for use as CBM for approach bias modification.

In a preclinical study in hazardous drinkers (Wiers et al., 2010), it was found that manipulating the push–pull contingencies such that participants had to predominantly push away alcohol (90% vs. 10% of the trials), caused an alcohol-avoidance bias that generalized to untrained stimuli, relative to participants trained in the opposite direction. Further, those heavy-drinking participants who developed a bias due in the direction of their training condition showed corresponding drinking behavior in a taste test: heavy drinkers successfully trained to push alcohol drank less than heavy drinkers successfully trained to pull alcohol. In two subsequent large clinical trials, the AAT was tested in alcohol-dependent inpatients as an adjunct to treatment as usual. In both trials, approach bias modification was found to reduce relapse at a 1-year follow-up (Eberl et al., 2013; Wiers et al., 2011); we note that in the first study (Wiers et al., 2011), effects on outcome were at trend level, and became significant after controlling for gender. An interesting moderation effect was that the training was most effective for subjects with a strong initial approach bias (Eberl et al., 2013). This appears to agree with the rationale of CBM—if a subject does not have a certain bias in the first place, then that bias is unlikely to be related to the particular set of processes underlying their addiction, and retraining it might therefore be less effective.
3 MECHANISMS OF CBM

Given the accumulating evidence that CBM can be effective in the field of addiction, a theoretically and clinically essential question is what its mediating mechanisms are. That is, which intermediate cognitive and neural changes are caused by the training, and which of those changes actually affects real-life behavior? There are various theoretical possibilities: perhaps the undesired bias is reduced or reversed; perhaps a second bias is trained that exists in parallel with the original one; perhaps a more reflective process is trained, such that the original bias still exists but is swiftly overruled. For attentional CBM, some evidence points to this latter option (Schoenmakers et al., 2010): training caused a bias away from alcohol cues/toward soft drink cues on a dot-probe task, but only when sufficient time (500 vs. 200 ms) was provided between cues and probes. This suggests that the training affected a relatively slow process, as opposed to the fast initial bias. We briefly note that recent research strongly suggests that extinction in general is due to a second, “top-down” conditioned inhibitory response, rather than the removal of the original conditioned response (e.g., Bouton et al., 2006), which may have played a role in this finding.

For the clinical trials using the AAT training protocol (Eberl et al., 2013; Wiers et al., 2011), effects of CBM on relapse were mediated by the change in cognitive biases, as expected theoretically. In one study (Eberl et al., 2013), the change in approach bias itself was found to be a mediator. In the other study, an alcohol-approach association as measured by the implicit association test (IAT) was initially tested as a mediator. The IAT is a categorization task that provides a measure of automatic evaluative associations subjects have with target categories (Greenwald et al., 1998) that has been used to study disorder-relevant associations, for example, approach associations in addiction (Ostafin and Palfai, 2006; Palfai and Ostafin, 2003). In contradiction to the hypothesis, the change in alcohol-approach associations was not found to mediate effects of CBM. However, subsequent exploratory analyses tested the hypothesis that effects on the IAT may be stimulus specific in the case of alcohol associations. In these analyses, the development of an association between alcohol stimuli and avoidance was found to mediate CBM (Gladwin et al., 2015). These findings suggest that the clinical efficacy of CBM depends on its ability to affect cognitive biases, and more specifically to increase the relative strength of alcohol-avoidance associations and action tendencies, compared with alcohol-approach associations or tendencies.

The first two studies of effects of an alcohol approach-avoidance CBM training on neural cue reactivity were recently published (Wiers et al., 2015a, b). In drug cue reactivity paradigms, in which drug users passively view drug cues, it has been shown that BOLD levels in mesocorticolimbic brain areas are enhanced in drug users compared to nonaddicted individuals (Bühler and Mann, 2011; Heinz et al., 2009; Schacht et al., 2013). Key brain areas that are activated in drug users in cue reactivity paradigms are the nucleus accumbens (NAccs), medial prefrontal cortex (mPFC), basolateral amygdala, and dorsolateral prefrontal cortex (dLPFC). The NAccs, mPFC, and amygdala have been associated with bottom-up motivational aspects
of cue reactivity (Barrós-Loscertales et al., 2011; Hare et al., 2009; Heinz et al., 2009), reward processing and reinforcement learning (Heekeren et al., 2007; Kahnt et al., 2010; Koob and Volkow, 2010; Vink et al., 2013), subjective drug craving and relapse (Beck et al., 2012; Childress et al., 1999; Grüßer et al., 2004; Heinz et al., 2004; Sinha, 2012; Volkow et al., 2004). Moreover, the amygdala plays an important role in the emotional salience of drug stimuli and Pavlovian conditioned learning (Heinz et al., 2009; Schneider et al., 2001). In contrast, the dlPFC plays an important role in top-down control over motivational reactions to drug cues in addiction (Baler and Volkow, 2006; Bechara, 2005; Burger et al., 2011; Goldstein and Volkow, 2002, 2011; Jentsch and Taylor, 1999; Park et al., 2010; Sinha, 2012).

In an alcohol AAT CBM cue reactivity study, a pre- and posttraining alcohol cue reactivity fMRI measurement was performed in 32 recently detoxified alcohol-dependent patients (Wiers et al., 2015a). Patients were randomly assigned to a CBM group and a placebo group and performed six sessions of CBM/placebo training over 3 weeks. The posttraining measurement was done 3 weeks later. The results show that before training, alcohol cue-evoked activation occurred in the bilateral amygdala and in the right NAccs (the latter at trend level), which correlated with craving and arousal ratings of alcohol stimuli. After training, the CBM group showed greater reductions in cue-evoked activation in the amygdala and in behavioral arousal ratings of alcohol pictures, compared with the placebo training group. Decreases in right amygdala activity correlated with decreases in craving in the CBM but not the placebo training group. This suggests that CBM may affect the automatic attribution of incentive salience to alcohol cues.

Of these 32 patients, 26 patients also performed the AAT in the scanner pre- and posttraining (Wiers et al., 2015b). The relevant neuroimaging contrast for the alcohol-approach bias was the difference between approaching versus avoiding alcohol cues relative to soft drink cues: (alcohol pull > alcohol push) > (soft drink pull > soft drink push), which has been associated with stronger activations in the NAccs, medial prefrontal (Wiers et al., 2014) and orbitofrontal (Ernst et al., 2014) cortex in alcohol-dependent patients. After training, patients in the CBM group showed stronger reductions in mPFC activation compared with the placebo training group. Moreover, these reductions correlated with reductions in approach bias scores in the CBM group only. These findings provide evidence that alcohol approach-avoidance CBM affects alcohol cue-induced mesolimbic brain activity and neural mechanisms involved in the automatic alcohol-approach bias. This may be a key underlying mechanism of the therapeutic effectiveness of this training.
and meta-analyses have been published concerning CBM for anxiety (Hakamata et al., 2010; Linetzky et al., 2015; MacLeod and Mathews, 2012). However, there is also a highly critical commentary (Emmelkamp, 2012) and there is a recent meta-analysis concluding that the evidence for effectiveness of CBM is low in anxiety and that the literature suffers from publication bias (Cristea et al., 2015). We briefly reflect on the important question of what claims should be made concerning CBM, whether negative or positive. It is, first, important to realize that any meta-analysis, even if using a technique that is valid statistically, may make substantive choices that render its conclusions misleading or less relevant. For instance, what if important outcome measures or moderating variables the field is only now coming to understand are not accounted for? It may well be unfeasible to analyze the highly variable range of follow-up measurements and challenge-based measures given the goal of performing a meta-analysis at this point in time, but it is quite possible that clinical effects of CBM are less likely to be found immediately at posttest but involve longer-term interactions with treatment effects, or become most clear under circumstances involving stress or the complexity of daily life. Considering such possibilities must be part of an adequate evaluation of CBM. Further, it has been pointed out that failures to achieve clinical effects using CBM tend to be coupled with failures to actually affect the bias of interest (Clarke et al., 2014). In other words, studies in which a cognitive bias was successfully changed, generally found clinical effects, while studies that failed to change the cognitive bias, generally did not. For example, in a recent negative finding in a small study on attentional bias modification for cigarette smoking, retraining did not result in a change of bias, and no effects on quitting were found (Begh et al., 2015), while a larger study in which an attentional bias was reduced in the active condition did show effects on abstinence (Elfeddali, Vries, Bolman, Pronk, and Wiers, submitted). This pattern of results would actually seem to support the basic idea of CBM: namely, that actually changing biases is essential. We should not expect every method to successfully change biases, and that this is indeed not the case should not be surprising nor taken as evidence against CBM in general. From this perspective, meta-analyses appear to have a potential dark side: Taking a focus on meta-analysis to an extreme, they could discourage exploring interesting but uncertain possibilities, as “failures” could lead to premature negative generalizations. Nevertheless, the argument has merit that, if a theoretically as well as statistically adequate meta-analysis cannot provide strong evidence, this may entail “evidence of absence of evidence” (cf., Clarke et al., 2014), and this must be acknowledged when making claims about the efficacy of various kinds of CBM.

Another possibly essential factor that could modulate the effectiveness of CBM is motivation (Wiers et al., 2013b, 2015c). CBM only aims to affect the impact of automatic processes: it does not change what an individual wants. If a subject in a CBM study simply enjoys drinking and has little social incentive to stop (as will of course often be the case in student samples), then it is unlikely his or her drinking behavior will change. Another recent study in the field of cigarette smoking illustrates this point (Kerst and Waters, 2014): attentional bias modification successfully changed the attentional bias in heavy community smokers, compared to a control condition;
however, this did not result in any changes in behavior. Importantly, these smokers
did not want to quit, illustrating the idea that CBM might be most effective in people
who want to change an addictive behavior, but are hindered by impulsive processes
that keep on “pulling” them back to the behavior. CBM may best be conceived of as a
way to provide a “beat in time” at the point at which harmful impulsive behavior
might otherwise occur (Gladwin et al., 2011). It remains up to the further reflective
decision making of the individual to make use of that opportunity to move in a more
healthy direction, and such a direction must be available in the individual’s environ-
ment (that is, the claim that CBM may be useful does not diminish the role of social
factors). CBM is not aimed at this part of the puzzle. This is why, to have a chance at
finding strong effects in clinical studies or applications, it seems that CBM should
always be an adjunct to a different form of therapy aimed at motivation and healthy
choices (Wiers et al., 2013b).

Overall, the evidence for the efficacy of specifically approach-avoidance CBM in
addiction is strong and in any case positive (Wiers et al., 2013d), and the convergent
findings of cognitive and neural effects and mediators further bolster confidence in
approach-avoidance CBM as a supplementary treatment for addiction. The available
data appear promising for various other CBM approaches as well, but their clinical
efficacy is as yet uncertain. It must be acknowledged that publication bias in this field
of research has the potential to mislead (Cristea et al., 2015), a broad problem in ac-
ademia. At the very least, however, there is abundant reason to continue investing in
research, using both fundamental preclinical studies to explore novel hypotheses (as
we can by no means be sure we have already hit on optimal methods), as well as
larger-scale clinical trials using the most promising types and applications of
CBM. It seems essential that both kinds of studies use designs that can deal with
the effects of relevant moderating variables, in particular the existence of an initial
bias in the first place and the success of the particular training method in changing the
bias or establishing a bias at posttest.

5 DEVELOPMENTS IN DUAL-PROCESS MODELS

As described above, CBM is closely linked to the dual-process perspective in addic-
tion (Stacy and Wiers, 2010; Wiers et al., 2013b). It is therefore of interest, if not
concern, that the kind of dual-process models used in addiction research have been
strongly criticized, even in the sense of retarding the progress of science by providing
the illusion of theory without much content (Keren, 2013). It has been pointed out
that the evidence for dual systems is weak (Keren and Schul, 2009; Kruglanski,
2013; Kruglanski and Gigerenzer, 2011), certainly for strong models of separable
systems that can be distinguished based on a set of perfectly covarying dichotomous
features (Bargh, 1994). We have previously discussed the problem of the motiva-
tional homunculus that makes the kind of “cold” control system strictly separated
from emotion and motivation untenable (Gladwin and Figner, 2014; Gladwin
et al., 2011; Wiers et al., 2013b). However, we believe such criticism should lead
to rethinking dual processes and dual systems while retaining their most basic and important feature: the focus on interactions between involuntary influences on cognition and behavior and the ability to control them in line with voluntary choice. It may be possible to have our cake and eat it too: that is, to still have the fast and slow, impulsive and reflective processes that fit addiction so well at a phenomenal level, but without positing an unnecessary and theoretically dubious duality at the level of systems. For example, in our R3 model, the Reprocessing and Reinforcement model of Reflectivity (Gladwin and Figner, 2014; Gladwin et al., 2011), we define reflectivity versus automaticity as an emergent feature of a dynamic response-optimizing system, drawing on connectionist views of dual systems (Gilbert and Shallice, 2002; Schneider and Chein, 2003), work on reinforcement mechanisms (Bunge, 2004; Suri, 2002), and the concept of reprocessing (Cunningham et al., 2007). When confronted with a stimulus, available motor and cognitive responses given the current situation and the emotional evaluation of their predicted outcome will change over time, depending on the strength of available connections. Simply allowing such changes to progress over time will change the quality of the eventual response—in other words, reflective processing does not involve a special set of processes that take time, but is simply the state of taking more time to allow response selection to incorporate less immediately salient factors. In addiction, an individual cannot avoid the initial influence of the conditioned salience of drug cues, having the knowledge that using drugs will lead to a certain outcome, or being aware of the steps he or she could take to achieve that outcome. However, that individual may also have been retrained to have a secondary response that can inhibit the impulsive reaction, and have additional knowledge that can lead to a reevaluation of the initially positive outcome of drug use. The interplay between these elements of the system would lead to an initial impulsive approach toward drugs, followed by avoidance. As argued throughout this chapter, training targeted at changing biases may support the therapeutic goal of enhancing this controlled avoidance in the face of impulsive approach. Further research is needed to develop our understanding of the temporal dynamics of response activation (e.g., Gladwin et al., 2014; Noël et al., 2006) and the neural and computational mechanisms that allow the conditional binding of outcomes to actions, in order to further fill in essential details of such models. Of particular interest to future CBM methods for addiction is the interaction between making alternative responses more easily retrievable from memory, and strengthening the connections from tempting stimuli to response inhibition and delayed responding. Although we currently see motivation and long-term goals as the domain of different, complementary forms of therapy, the mechanisms of these aspects of healthy behavior may also be amenable to support via CBM.

6 ENHANCING EFFICACY AND EFFICIENCY OF CBM

Many interesting lines of research on “basic” lab-based CBM remain to be explored, but we mention here two novel ways in which CBM could be enhanced or made more effective.
First, an interesting possibility receiving increasing research interest is to enhance training by electrical stimulation or modulation of the brain. Transcranial direct current stimulation (tDCS) of the dPFC can temporarily enhance working memory (Fregni et al., 2005; Gladwin et al., 2012a; Ohn et al., 2008), although working memory consists of multiple components and probably only specific aspects are affected such as selective attention (Gladwin et al., 2012a,b). Interestingly, the same tDCS manipulation can also reduce craving for alcohol (Boggio et al., 2008; Den Uyl et al., 2014), food (Goldman et al., 2011), and cigarettes (Boggio et al., 2009). It is as yet unclear what these results precisely reflect in terms of cognitive-neural mechanisms, but positive stimulation of prefrontal regions would be expected to support executive functions necessary to inhibit craving. Since tDCS also influences neuronal plasticity (Nitsche et al., 2003; Paulus, 2003), tDCS could also have interactive effects with CBM. While the immediate effects of tDCS are temporary, its effects on concurrent training could be more persistent, either directly via plasticity or by aiding the subject in performing the training task at a higher level. We are currently exploring these possibilities, and briefly note that in a different field (posttraumatic stress disorder) clinical effects of working memory training have indeed been shown to be enhanced by tDCS (Saunders et al., 2015), and effects of response inhibition training (Ditye et al., 2012) and attentional training (Coffman et al., 2012) have been shown to be stronger in stimulated subjects.

Another intriguing possibility of computerized training such as CBM is having subjects perform sessions online. If effective, this would have significant advantages in terms of efficiency. It could also lower the threshold for certain patients to participate in this form of therapy. However, the evidence for the efficacy of online training is as yet weak: the first online-only CBM study in addiction also did not find the differential effects of training that were found in previous studies in a clinical setting (Wiers et al., 2015c), and the negative results in anxiety are largely in Internet trials, while clinical studies tend to be more positive (Linetzky et al., 2015). It seems important for this line of research to first motivate participants to change, either face to face or online (e.g., Van Deursen et al., 2013), and to increase motivation to do the training (Boffo et al., 2015). Of possible interest to the aim of increasing motivation, finally, CBM training lends itself to being “gamified,” that is, adapted to include gameplay elements. There are various ways in which this could make CBM less repetitive or more reinforcing, for instance, by incorporating CBM elements in the mechanisms of a computer game, or by connecting performance on CBM to rewards in a separate game (Boendermaker et al., 2015). As with tDCS and online CBM, such variants must be considered experimental, but seem clearly worth exploring.

7 CONCLUSION AND FUTURE DIRECTIONS

In summary (Table 1), cognitive retraining for addiction has a strong grounding in theory and there is accumulating evidence that at least in-clinic CBM for alcohol addiction can improve outcome, in particular alcohol-avoidance training.
Importantly, we envision CBM as an adjunct to other forms of therapy. Indeed, from a dual-process perspective, without complementary therapy that enhances motivation and strengthens alternative goals that are incompatible with continued heavy substance use, adjusting automatic processes by themselves is unlikely to be effective. Conversely, attempting to restructure patients’ higher level, conscious thoughts about drugs without providing bottom-up support via training could also be expected to often lead to disappointment, as they could fail due to impulsive, stimulus-driven conditioning. This may be one of the explanations of the high relapse rate in addiction—over 50% after 1 year, and 70% after 3 years (Cutler and Fishbain, 2005).

While this chapter concerned CBM for addiction, CBM has been extensively used as a method to treat anxiety. It seems likely that at least some overlap in neural and cognitive mechanisms is involved, such as a role for the amygdala in both anxiety (Britton et al., 2014) and alcohol dependence (Wiers et al., 2014). In that case, we may be able to take an important reductionist step in the treatment and understanding of diverse diagnoses. This may allow better understanding of the connections between anxiety and addiction, important in one global route to addiction, expressed in the relationship between coping drinking and genetic vulnerabilities (Wiers et al., 2013c).

In conclusion, theory and evidence suggest that computer-based cognitive retraining, or CBM, may be an important piece of the puzzle in treating addiction, but awareness is needed of the conditions under which it is likely to be effective. Research aimed at understanding its cognitive and neural mechanisms appears to be an important condition for further improving the efficacy of CBM for addiction in the future.

### Table 1 Overview of Major Points

| 1. | Addiction is related to cognitive biases, which can be defined in terms of dual-process models |
| 2. | Cognitive biases can be measured using implicit measures |
| 3. | Cognitive bias modification (CBM) is aimed at changing harmful biases |
| 4. | CBM for addiction has been shown to reduce relapse |
| 5. | This clinical effect is mediated by changes in cognitive biases and associated with changes in neural responses to cues and experimental manipulations |
| 6. | Current debate is focused on the efficacy of CBM: It is essential to consider moderating factors |
| 7. | There are potentially important developments in both theory and training applications |
| 8. | New dual-process models are being developed that address fundamental criticisms and suggest new avenues for research |
| 9. | New methods are being tested, such as brain stimulation, online training, and “gamification,” adding gameplay elements to CBM training to enhance engagement and motivation |

Note: Overview of the main points made in the current chapter. Dual-process models provide a theoretical context for cognitive bias modification (CBM). CBM involves adapting implicit measures to cause a training effect. CBM for addiction has shown convincing results: Both in terms of effects on relapse and in terms of first results finding mediating cognitive and neural mechanisms. There is ongoing critical debate on theory and efficacy which directly impacts CBM; this should lead to novel avenues of research to determine under which conditions CBM can or cannot be expected to be effective.
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