Where is the bias?

Measuring and retraining cognitive biases in problem drinkers

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CHAPTER 1

General introduction
Alcohol use disorders (AUDs) are characterized by uncontrolled drinking and drinking in spite of adverse consequences (American Psychiatric Association, 2013), and pose a worldwide health, social and economic burden (Rehm et al., 2009; Whiteford et al., 2013). Providing effective and accessible interventions to individuals with AUDs is one of the ways in which this burden can be reduced; however, only a minority of individuals with AUDs receives treatment. In the Netherlands, for example, the 12-month prevalence of AUDs is estimated at 4.4% (478000 individuals aged 18-64 years), while only 7-8% of those with AUDs seek help in addiction treatment centers (de Graaf, ten Have, Tuithof, & van Dorsselaer, 2012; van Laar et al., 2017). This treatment gap is even larger when including problem drinkers, who do not necessarily meet the criteria for AUDs but whose alcohol use exceeds low-risk drinking guidelines1. Web-based interventions may help to decrease the treatment gap, by offering accessible and low-cost help for problem drinkers who are motivated to reduce their alcohol use.

Web-based interventions for problematic alcohol use are often computerized translations of common face-to-face interventions, such as cognitive behavioral therapy and motivational interviewing. Internet interventions have been proven effective in reducing alcohol use, though their effect size is small and leaves room for improvement (Riper et al., 2014). From the perspective of dual process theories of addiction (Wiers et al., 2007), one way to augment the effectiveness of alcohol interventions is to expand their

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1 There is no universally agreed upon definition of low-risk drinking. In this thesis, problem drinking is defined as more than 14 alcoholic drinks a week for women, and 21 for men (British Medical Association, 1995), as counted in Dutch standard units of 10 grams of alcohol. Note that many recent low-risk drinking guidelines are more stringent. For example, the Health Council of the Netherlands recommends drinking no more than one glass per day, for both men and women (Gezondheidsraad, 2015).
content from techniques focusing on motivation and other explicit cognitive processes, to techniques targeting more automatically activated cognitive processes.

**Theoretical background**
According to dual process models of addiction (Bechara, 2005; Deutsch & Strack, 2006; Wiers et al., 2007), the development and maintenance of problematic substance use is determined not only by the explicit motivation to limit one’s substance use, but also by automatic biases in the processing of substance related cues. For example, substance related cues may selectively capture attention (attentional bias), activate implicit memory associations (memory bias), and elicit an approach tendency (approach bias, Wiers et al., 2007). Incentive sensitization theory (Berridge & Robinson, 2003) posits that these biases result from a classical conditioning process, in which substance related cues (conditioned stimuli, e.g. the sight of alcohol) become associated with the rewarding effects of substance use (unconditioned stimulus). With repeated use, these conditioned stimuli acquire incentive salience, causing them to draw attention and trigger approach responses. Once formed, these automatic biases are hypothesized to stimulate substance use, but the extent to which they do so is thought to depend on a combination of motivation and executive functions (Wiers et al., 2007). In individuals with weak executive functions, substance use is believed to be affected relatively less by motivation, and more by the strength of automatic biases. Conversely, in individuals with stronger executive functions, automatic biases are deemed less influential, and substance use is determined more by the motivation to restrain. Therefore, interventions focusing on both explicit and automatic cognitive processes are
expected to be more effective than interventions focusing on either of the two alone.

**Measuring automatic processes**

In contrast to the explicit motivation to restrain, which is assessed with self-report measures, automatic processes are assessed with (computerized) implicit or indirect measures, which derive cognitive biases from participants’ task performance. For example, instead of asking participants directly how much their attention is grabbed by alcohol related cues, attentional bias is measured indirectly, by comparing participants reaction times (RTs) for alcohol related pictures or words to their RTs for pictures or names of non-alcoholic drinks or neutral stimuli (e.g. office supplies).

In line with dual process theories of addiction, meta-analyses have shown that implicit measures predict substance use (Rooke, Hine, & Thorsteinsson, 2008) and that they do so over and above explicit measures (Reich, Below, & Goldman, 2010). Moreover, most studies investigating the hypothesized interaction between automatic processes and executive functions have indeed found that strength of the association between automatic biases and alcohol is moderated by executive functions (Grenard et al., 2008; Houben & Wiers, 2009; Peeters et al., 2012; Peeters et al., 2013; Salemink & Wiers, 2014; Thush et al., 2008), but note that there are also studies that have not found this pattern of results (Pieters, Burk, Van der Vorst, Wiers, & Engels, 2012; van Hemel-Ruiter, de Jong, & Wiers, 2011; for a review, see Wiers, Boelema, Nikolaou, & Gladwin, 2015). Theoretically, inhibiting the influence of automatic biases on alcohol use is thought to require both strong executive functions and motivation; empirically, however, little is known about the role of motivation in this interplay. For example, does motivation to change
predict alcohol use to a larger degree in individuals with stronger than in those with weaker executive functions? And does motivation add to the prediction of alcohol use over the combination of automatic processes and executive functions? These questions will be addressed in Chapter 3 of this thesis.

**Changing automatic processes**

After establishing the association between automatic processes and alcohol use, researchers have begun investigating the effect of experimentally manipulating cognitive biases on drinking. The purpose of this line of research is twofold: the first is to study the causal effects of cognitive biases on alcohol use, and the second is to investigate whether decreasing cognitive biases can reduce problem drinking and prevent relapse. To these ends, the computerized implicit measures used to assess automatic processes have been adapted in such way that they are expected to change cognitive biases. This class of cognitive bias retraining procedures is collectively referred to as cognitive bias modification (CBM), and includes specific procedures to modify attentional bias, approach bias, and memory bias.

**Attentional bias modification**

Attentional bias can be assessed and modified with the visual probe task (as demonstrated both in the field of addiction: Field, M. & Eastwood, 2005; and in anxiety: MacLeod, Rutherford, Campbell, Ebosworthy, & Holker, 2002). In this task, a picture of an alcoholic drink and a picture of a non-alcohol drink are briefly (e.g. 500 ms) presented next to each other on a computer screen. When the pictures disappear, a probe (e.g. a small arrow) appears at the location that was previously occupied by either the alcohol or the non-alcohol related stimulus. Participants have to respond to a feature of the probe (e.g. indicate the direction of the arrow). In the assessment version of the task, the probe
appears equally often at the spatial location of the alcoholic and the non-alcoholic drink, and attentional bias for alcohol is indicated by smaller RTs for alcohol than for non-alcohol trials. In order to decrease attentional bias, the probe consistently appears at the location of the non-alcoholic drink (to create an attentional bias away from alcohol).

**Approach bias modification**

Approach bias is measured and retrained with the approach-avoidance task (Wiers, Rinck, Kordts, Houben, & Strack, 2010). In this task, participants are presented with a picture of an alcoholic or a non-alcoholic drink. Based on an irrelevant feature of the picture (e.g. a tilt to the left or right) participants have to either pull a joystick towards them, resulting in increased picture size, or push a joystick away from them, resulting in decreased picture size. An approach bias for alcohol is inferred by lower RTs for alcohol/pull than alcohol/push responses, and a relatively smaller difference in RTs between non-alcohol/push and non-alcohol/pull trials. To decrease approach bias, alcohol cues are consistently presented in push format, and non-alcohol cues in pull format.

**Memory bias modification**

In contrast to attentional and approach biases, biases in alcohol related memory associations have not been retrained with an adaptation of the task used to assess them, but rather with other tasks such as alcohol/no-go training (Houben, Nederkoorn, Wiers, & Jansen, 2011) and evaluative conditioning (e.g. Houben, Havermans, & Wiers, 2010). In alcohol/no-go training, participants are presented with a picture of an alcoholic or a non-alcoholic drink, combined with a go or no go cue (e.g. the letter p or f displayed in one of the four corners of the picture) that determines whether participants are required to respond (e.g.
by pressing the spacebar) or inhibit their response. Consistently pairing alcoholic drinks with no-go cues and non-alcoholic drinks with go cues is expected to create a response conflict, which is reduced by devaluing alcohol related cues (Veling, Holland, & van Knippenberg, 2008; but note that an alternative proposed working mechanism is that pairing alcoholic drinks with no-go cues creates alcohol-stop associations, see Verbruggen & Logan, 2008).

Reliably assessing change in cognitive biases
To test whether the above-mentioned CBM procedures succeed in manipulating cognitive biases, the strength of these biases should be assessed before and after bias retraining. A prerequisite for being able to detect changes in cognitive biases is that the measures used to assess them show adequate reliability; however, many implicit measures suffer from poor reliability (Ataya et al., 2012; Hedge, Powell, & Sumner, 2018; Schmukle, 2005). Given that this lack of reliability may be the result of low between-subject variability instead of high measurement error (Hedge et al., 2018), it has been argued that implicit measures with low reliability may still be suitable for use experimental research (Hedge et al., 2018; Schmukle, 2005). Of course, minimizing measurement error in implicit measures is still highly important in evaluating the effectiveness of CBM, as can be illustrated by the interpretation of null-findings of CBM on clinical outcomes. If CBM does not produce changes in alcohol use, this could either mean that cognitive biases do not have a causal effect on alcohol use, countering dual process theories; or it could mean that CBM procedures do not succeed in manipulating cognitive biases, thereby failing to test the prediction derived from dual process theories (Grafton et al., 2017; MacLeod & Clarke, 2015; Wiers, Boffo, & Field, 2018). However, these divergent interpretations of
the null-results cannot be distinguished if the implicit measures used to assess cognitive biases have insufficient reliability.

One of the factors that may influence the measurement error of implicit measures is the type of stimuli that are used. In the field of addiction, most tasks employed to measure and retrain cognitive biases use pictorial stimuli, that is, pictures of alcoholic versus non-alcoholic drinks\(^2\). In order to adequately assess to what extent participants’ task performance is influenced by the alcohol relatedness of the picture, the pictures used to measure cognitive biases should be a) comparable in all other respects, such as color and complexity; b) quickly identifiable as alcohol related or not; and c) able to cause variations in RTs. Furthermore, it appears preferable to use a wide variety of drink types and brands during CBM, in order to promote the generalization from the specific exemplars used during training to the broader category of alcohol related stimuli in daily life. So far, little research has been conducted on the quality of the pictures that have been used to measure and retrain cognitive biases. Chapter 4 of this thesis describes the results of a validation study of a large picture set that was created specifically for use in the cognitive bias assessment and modification tasks.

**The effectiveness of cognitive bias modification**

As mentioned above, research on CBM has aimed to examine both the causal relation between cognitive biases and alcohol use, and the clinical effectiveness of CBM as an alcohol intervention. In line with these diverging goals, the studies used to investigate them have also differed in sample type (heavy drinking

\(^2\) Note that pictures of neutral objects (e.g. office supplies) have also been used as a contrast category for pictures of alcoholic drinks, but for the ecological validity of cognitive bias assessment and training, pictures of non-alcoholic drinks are deemed preferable.
students who are not motivated to change their alcohol use, versus problem drinkers or abstinent alcoholic patients who want to change their alcohol use), setting (laboratory versus clinic), treatment context (no other treatment versus CBM as an add-on to motivational interventions or in-patient treatment), CBM doses (single versus multiple sessions of CBM), and expected effects (short-term effects on craving or alcohol use during a bogus taste test, versus long-term reductions in alcohol use or relapse). In addition, the proof-of-principle studies in healthy populations applied CBM both to reduce and to increase alcohol related biases, while the studies in clinical populations used CBM only to reduce these biases. In the latter category of studies, CBM was compared to placebo CBM (i.e. tasks in which participants were exposed to the same stimuli, but that were not intended to affect automatic biases, for example an extended version of the bias assessment tasks). Importantly, the differences between these two types of studies have been largely systematic, in the sense that only the studies investigating the clinical effects of CBM have been conducted in motivated samples and have examined the long-term effects of CBM compared to placebo CBM. Furthermore, the clinical effects of CBM have only been investigated after initial lab studies indicated that CBM could causally affect alcohol use (e.g. Field, M. & Eastwood, 2005; Field, M. et al., 2007; Houben, Havermans, Nederkoorn, & Jansen, 2012; Schoenmakers, Wiers, Jones, Bruce, & Jansen, 2007; Wiers et al., 2010). The design and hypotheses of the clinical CBM study described in Chapter 2 of this thesis were therefore based on the effects of studies examining the clinical effects of CBM, in samples that were motivated to change their alcohol use (note that recently, the distinction between these study types has been the subject of debate: Cristea, Kok, & Cuijpers, 2016; Cristea, Kok, & Cuijpers, 2018; Field, M., Jones, & Christiansen, 2016; Kamo, 2018; Wiers, 2016; Wiers et al., 2018).
When the current study was designed, most prior CBM studies in individuals who were motivated to change their alcohol use had investigated either attentional bias or approach bias modification as an add-on to in-patient treatment (Eberl et al., 2013; Schoenmakers et al., 2010; Wiers, Eberl, Rinck, Becker, & Lindenmeyer, 2011). These studies all found indications that CBM reduced the targeted cognitive bias, and decreased or delayed relapse. In addition, one of these studies showed that the effect of approach bias modification on relapse rate was mediated by the change in approach bias (Eberl et al., 2013). Based on the positive effects of CBM in individuals with AUDs, the effects of web-based attentional and approach bias modification were then studied in problem drinkers who were motivated to reduce their alcohol use (Wiers et al., 2015). This study found that neither of the CBM interventions led to a larger reduction in alcohol use compared to a placebo-CBM training. The contrast between these findings and the findings of studies on CBM as an add-on to treatment-as-usual suggested that changing automatic processes is only effective in reducing alcohol use when combined with an intervention aimed at changing explicit cognitive processes. This inspired the primary research question of Chapter 5, namely whether web-based CBM as an add-on to a brief motivational intervention (modules 1 and 2 of DrinkingLess, see Riper et al., 2008; Riper et al., 2009), would be effective in problem drinkers who were motivated to reduce their alcohol use.

After the start of the current study, the effects of attentional and approach bias modification over and above in-patient treatment were replicated (Manning et al., 2016; Rinck, Wiers, Becker, & Lindenmeyer, 2018). However, lab- and web-based studies did not find CBM to be effective in reducing alcohol use in problem drinkers beyond non-specific effects, neither
as a stand-alone treatment (Clerkin, Magee, Wells, Beard, & Barnett, 2016) nor
combined with a motivational intervention (Cox, Fadardi, Hosier, & Pothos,
2015; Jones, A. et al., in press). Since none of these studies demonstrated
changes in cognitive biases, it remained unclear whether the successful
modification of automatic processes would result in reductions in problem
drinking. Furthermore, none of the studies outside the addiction clinic
investigated whether combining different CBM interventions would augment
the effects compared to either intervention alone.

Aims of this thesis
The main aim of this thesis was to evaluate the effectiveness of web-based
attentional bias, memory bias, and approach bias modification in problem
drinkers as an add-on to a brief motivational intervention. Furthermore, it was
investigated whether alcohol use prior to the intervention was related to the
interaction between cognitive biases, executive functions and motivation to
change. In addition, the validity of the pictorial stimuli that were used for
cognitive biases assessment and modification was examined.

Overview of chapters
Chapter 2 describes the protocol of the main study of this thesis; a web-based
randomized controlled trial (RCT) in problem drinkers, on the effectiveness of
attentional bias, memory bias and approach bias modification as an add-on to
a brief personalized feedback intervention.

In Chapter 3, the results of the stimulus validation study are presented.
It was hypothesized that the pictures of alcoholic drinks would elicit a stronger
urge to drink in heavy than in light drinkers, and that this difference would be
smaller for pictures of non-alcoholic drinks. Students reported their mean
weekly alcohol use in the past year and rated their urge to drink a subset of
alcoholic and non-alcoholic beverages displayed on the pictures. Participants also completed a recognition task, to measure the speed with which the drinks could be recognized as alcoholic or non-alcoholic. The difference in urge to drink was compared between drink types and relatively heavy and light drinkers. Furthermore, the effect of social content on urge to drink and recognition speed was examined.

Chapter 4 focuses on the role of motivation in the relation between automatic associations, executive functions and alcohol use. It was expected that executive functions would moderate the association between automatic processes and alcohol use, and that this effect would be more pronounced in individuals with stronger motivation to change (Wiers et al., 2007). The baseline data of the web-based RCT on CBM were used, including participants’ alcohol use and motivation to change, as well as measures of automatic memory associations and executive functions.

In Chapter 5 the results of the RCT on web-based CBM are presented. The effectiveness of attentional bias, memory bias, and approach bias was investigated in a 2x2x2 design and it was hypothesized that each of the CBM interventions would result in reductions in the targeted cognitive bias and alcohol use, compared to the corresponding placebo CBM training (i.e. extended bias assessment tasks). Irrespective of CBM condition, all participants first completed a personalized feedback intervention (Riper et al., 2008; Riper et al., 2009), followed by 12 sessions of CBM. Cognitive biases were assessed before and after the CBM intervention, and alcohol use and the secondary outcome measures (i.e. binge drinking, drinking above the low-risk drinking guidelines, the use of other substances, alcohol related problems, craving, and
self-efficacy) were additionally assessed three and six months after the intervention.

Chapter 6, the general discussion, starts with a summary of the main results, followed by a discussion of a) the characteristics that make stimuli suitable for the assessment and retraining of cognitive biases; b) the importance of the reliable assessment of cognitive biases; and c) the conditions under which CBM is most likely to be effective. Next, the strengths and limitations of the above studies are addressed and the chapter ends with the general conclusions and clinical implications that can be drawn based on this thesis and concurrent research.