Can't take my eyes off of you

The role of cognitive biases, reward sensitivity and executive control in adolescent substance use and abuse

Madelon E. van Hemel - Ruiter

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ISBN printed book: 978-90-367-8261-6
ISBN e-book: 978-90-367-8262-3

This dissertation was supported by a grant of The Netherlands association for health research and development (ZonMw Risk Behavior and Dependence grant 60-60600-97-202) and by the University of Groningen Heymans Institute for Psychological Research. The infrastructure for the TRAILS studies is funded by the Netherlands Organization for Scientific Research NWO (Medical Research Council program grant GBMW 940-38-011; ZonMW Brainpower grant 100-001-004; ZonMw Risk Behavior and Dependence grants 60-60600-98-018, 60-60600-97-118; ZonMw Culture and Health grant 261-98-710; Social Sciences Council medium-sized investment grants GB-MaGW 480-01-006 and GB-MaGW 480-07-001; Social Sciences Council project grants GB-MaGW 457-03-018, GB-MaGW 452- 04-314, and GB-MaGW 452-06-004; NOW large-sized investment grant 175.010.2003.005) and is supported by participating universities (University Medical Center and University of Groningen; Erasmus University Medical Center Rotterdam; University of Utrecht; Radboud Medical Center Nijmegen), mental health care organisation (the Parnassia Bavo group), the Sophia Foundation for Medical Research; the Dutch Ministry of Justice (WODC); and the European Science Foundation (EuroSTRESS project FP-006).

Cover illustration: Matijs Ruiter
Printed by: Ridderprint BV

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Proefschrift

ter verkrijging van de graad van doctor aan de
Rijksuniversiteit Groningen
op gezag van de
rector magnificus prof. dr. E. Sterken
en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op

donderdag 10 december 2015 om 12.45 uur

door

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geboren op 27 juni 1978
te Leeuwarden

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Voor mijn prachtige, lieve kindjes

Go confidentially in the direction of your dreams! Live the life you've imagined.
Henry David Thoreau

CONTENTS

CHAPTER 1

General introduction

What makes young individuals at risk for developing problematic substance use, and which cognitive processes underlie the development from experimental or recreational to harmful substance use? These two questions have set the stage for the current project.

The main purpose of this dissertation is therefore to shed a light on the cognitive processes that are involved with the development and maintenance of adolescent alcohol and drug (mis)use. The introduction will first focus on the prevalence of addictive behaviors in adolescence. Then some theoretical background will be described about the cognitive processes that are involved in addictive behaviors, and the way in which these processes are suggested to be involved in the development and maintenance of adolescent substance use. Based on the available evidence, a model will be presented that will serve as a framework for the studies described in this dissertation. Finally, the outline of the dissertation will be introduced with a short introduction of the studies that will be described in the following chapters.

ADDICTIVE BEHAVIORS IN ADOLESCENCE

Substance abuse and addictive behaviors constitute a large problem in (young) adolescents with a huge impact at both the individual and the societal level. Epidemiologic studies both in the US and the Netherlands have demonstrated that the prevalence of alcohol and drug use and abuse increases with age during adolescence and peaks in young adulthood (Hibell et al., 2012; Johnston, O'Malley, Miech, Bachman, & Schulenberg, 2014; SAMHSA, 2014; Van Laar et al., 2014). Although in most parts of the Western world alcohol and illicit drug use in early adolescence has been declining since 2007, alcohol use levels in late adolescence remain alarming high (de Looze et al., 2014; Hibell et al., 2012; SAMSHA 2014; Van Laar et al., 2014; Verdurmen et al., 2012). In addition, although many differences are reported between countries, in average marijuana use among adolescents seems to be fairly stable since 2000. To illustrate this: recent epidemiological data indicates that 1% of Netherlands 12 year olds report having been drunk ever, a statistic that jumps to 45% for 16 year olds. Furthermore, 72% of the alcohol drinking secondary school students report heavy episodic drinking (i.e., consuming 5 or more drinks in a row) in the last month. Next, almost no 12-year olds indicate to have ever used cannabis in their lives, but 27% of the 16 year olds report lifetime cannabis use, of which 13% indicates to have used cannabis in the last month (de Looze et al., 2014).

In addiction, the large majority of adolescents enrolling addiction therapy are abusers of cannabis or alcohol. This yields for the U.S. (Johnston et al, 2014; SAMHSA, 2014) as well as for the Netherlands (Wisselink, Kuijpers & Mol, 2013). To illustrate, in the Netherlands, 51% of the adolescents (< 25 years) enrolling addiction therapy are abusers of cannabis, followed by 19% alcohol abusers.

COGNITIVE PROCESSES IN THE DEVELOPMENT AND MAINTENANCE OF ADDICTIVE BEHAVIORS

Dual-process models of addiction emphasize the importance of both relatively automatic appetitive or impulsive processes and relatively controlled or regulatory processes. These dual-process models hypothesize that addictive behaviors develop by an imbalance of both types of processes (e.g., Deutsch & Strack, 2006; Evans & Coventry, 2006; Stacy & Wiers, 2010; Wiers et al., 2007). The first class of processes concern automatically triggered appetitive processes, in which stimuli are valued in terms of their emotional and motivational significance, which automatically elicits heightened attention and triggers motivational orientation (approach or avoid). With repeated drug use, drug stimuli may acquire conditioned incentive properties, and as a consequence, they are able to grab the attention and to elicit approach behaviors (Robinson & Berridge, 1993, 2000, 2003). These implicit processes are believed to occur spontaneously and fast, and they are difficult to control. Further, the second class of processes (or "system") concern regulatory executive processes, which are proposed to operate in a more controlled way. These processes are associated with conscious thoughts, emotion regulation, and propositionally expected outcomes, and this system is usually not fully matured before young adulthood (e.g., Wiers et al., 2007). These regulatory processes are suggested to inhibit more automatic, impulsive thinking and behavior (e.g., Barrett, Tugade, & Engle, 2004; Strack & Deutsch, 2004). However, self-regulation is assumed to depend not only on whether an individual is able to inhibit automatic processes, but also on individual's motivation (Wiers et al., 2007). Hence, the automatic appetitive processes will guide substance-use behavior, unless the individual is motivated and has the ability to regulate this behavior (Fazio & Towles-Schwen, 1999). As a consequence of the imbalance between both systems, addicted individuals can have the explicit wish to stay away from the alcohol and drugs, but their eyes are attracted strongly to the signs of the alcohol, their body starts to crave for the drugs and their hand seems to grab the substance by itself. That is, automatically triggered appetitive processes guide their behavior towards the addictive substance, and their regulating system is not strong enough to inhibit these action tendencies. These automatically triggered cognitive processes, such as paying attention to, and approaching drug cues are called cognitive biases. One of those, attentional bias, is the degree to which substance-related stimuli capture the attention of individuals who use or abuse these addictive substances. Another cognitive bias is an approach bias, which is the degree to which substance-related stimuli provoke an automatic tendency to approach the substance in individuals who use or abuse these addictive substances.

Attentional bias in substance use and addiction

As previously mentioned, repeated substance use may lead to substance cues developing incentive salience, with concomitant ability to attract attention and motivated approach behavior (Robinson & Berridge, 2003). Thus, heavy substance users are thought to have a bias to selectively attend to substance-related stimuli (e.g., a glass of beer or the smell of cannabis) at the expense of other stimuli. There is considerable evidence that non-clinical users of alcohol, cannabis, and heroin (see for review, Field & Cox, 2008) as well as clinical populations of adult alcohol abusers (see for review, Sinclair, Nausheen, Garner & Baldwin, 2010) are characterized by substance-related attentional bias. Further, the strength of the attentional bias has shown to be an important predictor of escalation of substance use and risk of relapse (Cox et al., 2002, 2007; Marhe, Waters, van de Wetering & Franken, 2013; Marissen et al., 2006; Streeter et al., 2008; Waters, Marhe & Franken, 2012; but see Christiansen, Schoenmakers & Field, 2015, for a critical evaluation of the evidence).

A variety of paradigms have been used to measure substance-related attentional bias. Of those, the visual probe task is used to measure how participants' visuo-spatial attention is allocated to substance-related stimuli (MacLeod, Mathews & Tata, 1986). During a substance-variety of this task a substance-related stimulus (e.g., word or picture), and a matched control picture are presented on a computer screen side by side. After disappearance of the stimuli, a visual probe appears at the location of one of the previous stimuli. Participants get the instruction to respond to the probe rapidly, and their response time to probes that replace substance-related stimuli is compared with their response time to probes that replace control stimuli. Spatial attention is composed of at least two operative components that might be relevant in the present context: attentional engagement (i.e., facilitated attention towards a cue) and attentional disengagement (i.e., difficulty to disengage attention from a cue; Posner, Inhoff, Friedrich, & Cohen, 1987). It is assumed that with different stimulus presentation times (i.e., stimulus onset asynchrony, SOA) different aspects of spatial attention can be assessed (see e.g., Field & Cox, 2008). It is suggested that an SOA between 50 ms and 200 ms does not allow shifting of attention, and thus, an attentional bias that is detected with this SOA is interpreted as initial orienting, or engagement of attention. Further, an SOA of 500 ms (or rather 1000 ms) or longer allows multiple shifts and is usually interpreted as maintained attention, or delayed disengagement (see for review Field & Cox, 2008). Previous studies have found that heavy users of addictive substances showed an attentional bias for substance stimuli that were presented for 2000 ms (Bradley, Mogg, Wright & Field, 2003; Bradley, Field, Mogg & De Houwer, 2004; Field, Mogg, Zetteler & Bradley, 2004), with the exception of one study (2000 ms: Field, Eastwood, Bradley & Mogg, 2006). Using shorter SOA's (i.e., 200 ms, 500 ms) results on this issue were mixed, with studies that did (200 ms: Bradley at al., 2004; 500 ms: Field et al., 2004; Townshend & Duka, 2001), and did not find an attentional bias (200 ms: Field et al, 2004, 2006; 500 ms: Bradley et al., 2003). These findings might indicate that attentional biases in substance use are more characterized by maintenance and/or difficulty in disengagement of attention towards substance-related stimuli than rapid initial allocation towards those stimuli.

Approach bias in substance use and addiction

Given an increased incentive salience of alcohol and drug cues, heavy substance users might also show a tendency to automatically approach cues that have been associated with alcohol and drug use, like the glass of beer or the smell of cannabis mentioned before (Stacy & Wiers, 2010; Wiers et al., 2007; Wiers, Rinck, Dictus & van den Wildenberg, 2009). This approach bias might lead to an increase in alcohol or drugs use. A series of studies have successively demonstrated automatic approach tendencies in adult and late-adolescent heavy drinkers (Field, Kiernan, Eastwood, & Child, 2008; Field, Mogg, & Bradley, 2005; Palfai & Ostafin, 2003; Wiers, et al., 2009), in cigarette smokers (Bradley, et al., 2004; Field, et al., 2005; Mogg, Bradley, Field & De Houwer, 2003) and cannabis users (Cousijn, Goudriaan & Wiers, 2011; Field, Eastwood, Bradley & Mogg, 2006).

A variety of paradigms have been used to measure substance-related approach bias. One category of tasks is the affective Simon task (Simon task; De Houwer, Crombez, Baeyens, & Hermans, 2001). In these tasks, substance-related or neutral pictures are presented on a computer screen. Participants have to react on this with an approach or avoidance response. That is, they have to move a manikin towards or away from the picture (Simon task; see e.g., De Houwer et al., 2001, exp 4), or move a joystick towards or away from the screen (approach avoidance task, AAT; as in Rinck & Becker, 2007; Wiers et al., 2009). Importantly, in these tasks the substance-relatedness is not relevant for the task (De Houwer, 2003). That is, participants have to categorize pictures on the basis of the orientation (i.e., portrait or landscape; Huijding & de Jong, 2005) instead of the content of the picture. The underlying idea is that the automatic evaluation of the picture contents, elicits relatively automatic (in the sense of non-intentional) action tendencies and may thus lead to facilitation or interference with the required response. Accordingly, a picture with an attractive contents is assumed to automatically elicit an approach tendency and thus to result in faster responding when the response requirement is to approach the picture and slower responding when the response requirement is to avoid the picture. Previous studies have demonstrated an approach bias towards substance stimuli in heavy and light users of alcohol (with heavy drinkers showing stronger approach bias than lighter drinkers), cigarette smokers and cannabis users (see for review, Watson, de Wit, Hommel & Wiers, 2012). However, one study that included both the manikin and the joystick version failed to find a correlation between the two approach bias scores (Krieglmeyer & Deutsch, 2010). Taken together, these findings indicate that there is a reliable relationship between substance use and approach bias, although the two paradigms might measure different aspects of approach bias.

Regulatory processes in substance use and addiction

In the relationship between cognitive biases and substance (mis)use, the ability to inhibit these automatic impulses is suggested to play a crucial role. That is, it is proposed that the ability to control behavior influences whether the impulse to use alcohol or drugs will be followed or regulated. This ability of controlled processes to moderate the impact of spontaneous appetitive reactions on behavior is thus proposed to depend on the strength of executive functions. Recent studies have successfully demonstrated the moderating effect of executive control on the relation between automatic processes and alcohol use in late adolescents and adults (Farris, Ostafin, & Palfai, 2010; Friese, Bargas-Avila, Hoffman & Wiers, 2010; Grenard et al., 2008; Houben & Wiers, 2009; Thush et al., 2008; Willem, Vasey, Beckers, Claes & Bijttebier, 2013). More specifically, it was shown that especially (or only) in low executive control individuals there was a relationship between cognitive biases and alcohol use. In this way suboptimal executive control function can be considered a vulnerability factor for the development of addictive behaviors.

Automatic and regulatory processes in (young) adolescent substance use and addiction

Whereas there is ample evidence that heavy substance users and addictive persons are characterized by substance-related cognitive biases, not so much is known about the role of automatic appetitive bias in early and middle-adolescent substance use. Only a few studies have examined cognitive biases in pre-adult samples, and almost all those have focused on alcohol use. These studies have demonstrated an attentional bias for alcohol cues in adolescents with alcohol-dependent parents (15-20 years: Zetteler, Stollery, Weinstein & Lingford-Hughes, 2006), in heavy drinking adolescents (16-18 years: Field, Christiansen, Cole & Goudie, 2007), and an attentional bias related to alcohol use in young adolescents with a genetic predisposition (12-16 years: Pieters, et al., 2011), but not in normative samples of adolescents (15-21 years: Willem et al., 2013; 12-16 years: Pieters, Burk, Van der Vorst, Engels & Wiers, 2014). However, a recent longitudinal study in a normative sample of young adolescents showed that alcohol attentional bias predicted adolescent alcohol use later on (12-18 years: Janssen, Larsen, Vollebergh & Wiers, 2015). Only one study investigated the role of attentional bias in adolescent cannabis users, demonstrating an attentional bias for cannabis cues in adolescent heavy cannabis users, which was strongest in cannabis dependent adolescents (18-30 years: Cousijn, et al., 2013).

Next, it was found that a stronger alcohol approach bias was related to alcohol in male adolescents (15-21 years: Willem et al., 2013), in male adolescents with permissive parents (12-16 years: Pieters, Burk, Van der Vorst, Wiers & Engels, 2012) and to concurrent alcohol use (13.6 years: Peeters, et al., 2012) and future alcohol use in at-risk adolescents (13.6 years: Peeters et al., 2013), but it was not predictive for future alcohol use in a normative sample of adolescents (12-18 years: Janssen et al., 2015). One recent cannabis study demonstrated a cannabis approach bias in adolescent heavy cannabis users, which was also predictive for cannabis use 6 months later (18-25 years: Cousijn et al., 2011).

Previous research also showed inconsistencies with respect to the influence of executive functions, with some studies showing that indeed the predictive validity of automatically triggered appetitive processes (e.g., attentional bias) toward alcohol was restricted to adolescents with relatively weak executive functions (Grenard et al., 2008; Houben & Wiers, 2009; Peeters et al., 2012, 2013; Thush et al., 2008), and some studies that did not find such a moderating role of executive functioning on automatic processes (Cousijn et al., 2013; Pieters et al., 2012, 2014).

In conclusion, the extent to which appetitive biases and controlled processes are related to common (young) adolescent substance use and the extent to which they precede substance use, abuse, and addiction, or result from experience with alcohol and drug is still unclear (cf., de Jong, Kindt & Roefs, 2006; Field and Eastwood, 2005; Wiers, De Jong, Havermans & Jelicic, 2004; Wiers, Houben, Smulders, Conrod & Jones, 2006, see also Wiers, Boelema, Nicolaou & Pronk, 2015, for review).

REWARD-RELATED PROCESSES IN ADOLESCENT SUBSTANCE USE

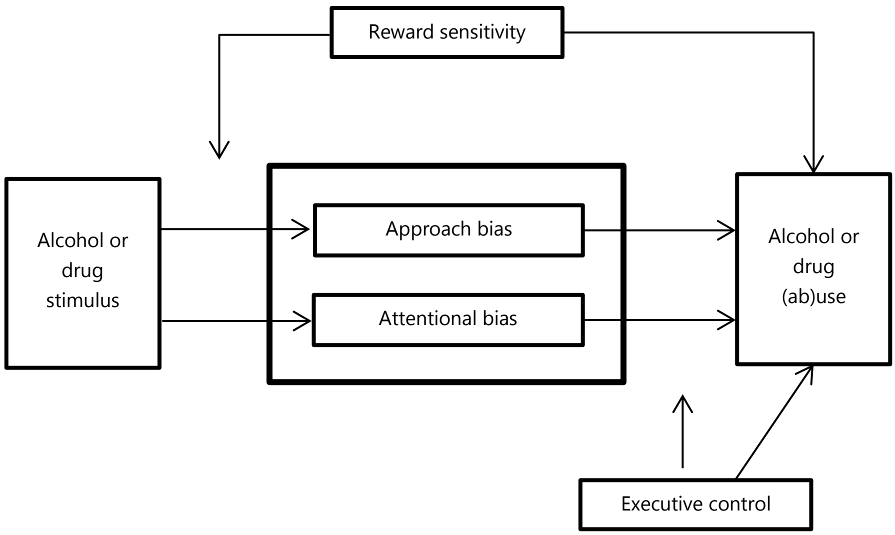
As previously mentioned, it has been hypothesized that substance-related cognitive biases develop by the process of classical conditioning. That is, by repeated experience of the rewarding effects of drug-taking, drug-related cues become associated with these rewarding effects and consequently acquire the ability to grab the user's attention, and elicit approach tendencies (e.g., Franken, 2003; Robinson & Berridge, 1993, 2001, 2003). Following this perspective, adolescents with high reward sensitivity may be especially at risk for developing cognitive biases for substance cues. Germane to this, it has been argued that individuals' responding to cues in the environment depends on their trait reward sensitivity (RS) and punishment sensitivity (PS; Gray, 1970, 1982). In the development of early adolescent substance use this would imply that the initial responses to substance-related cues would vary as a function of adolescents' reward and punishment sensitivity, whereas the repeated experience of the effects of substance use would subsequently shape the development of heightened attention and approach tendencies towards substance stimuli. In line with this view, previous research has found a consistent link between adolescent substance use and high RS (Knyazev, 2004; Lopez-Vegara et al., 2012; O'Connor & Colder, 2005; Pardo, Aguilar, Molinuevo & Torrubia, 2007). However, none of the few published studies that examined attentional and approach biases for substance cues in adolescents included measures of RS (or PS).

Thus, it remains to be tested whether indeed cognitive biases would be most pronounced in high RS adolescents and whether the previously found relationship between RS and alcohol use might indeed be (partly) mediated by cognitive bias for substance cues. The hypothesized role of RS in the prediction of substance use is depicted in Figure 1.1.

OUTLINE OF THIS DISSERTATION

Although there is ample evidence that adult heavy substance users are characterized by cognitive biases for substance-related stimuli, and that the strength of these biases are associated with substance use and relapse-risk, little is known about the role of automatic appetitive biases in the initiation stages of adolescent substance use, and in the development of substance use problems. The interplay between relatively automatic and relatively controlled processes in the development of adolescent substance use problems is largely unknown. We do not know how reward-related processes might be involved in the development of more substance specific cognitive biases. The current dissertation will present five studies investigating the hypothesized interplay of cognitive biases, executive control and reward sensitivity in the explanation of adolescent substance use (see Figure 1.1).

Figure 1.1
Hypothesized interplay of approach bias and attention bias, reward sensitivity and executive control in adolescent substance use



These studies used both cross-sectional and prospective designs in different samples of common (young) adolescents and in a clinical sample of adolescents diagnosed with substance dependency. These studies examined whether (i) reward sensitivity is related to current and prospective adolescent substance use, (ii) attentional and approach biases are related to young adolescent alcohol use, (iii) adolescents diagnosed with substance abuse or dependency are characterized by an attentional bias for substance related stimuli, and (iv) this substance-related attentional bias mediates the relationship between reward sensitivity and adolescent substance use. Furthermore, following the available evidence on the moderating role of executive controlled processes, the studies investigated whether (v) the association between cognitive biases and substance use would be especially (or only) pronounced in (young) adolescents with weak executive functions.

Chapter 2 starts off with a correlational study investigating the role of reward-related processes in adolescent substance use. In this study we used a Spatial Orienting Task to measure attentional bias for appetitive (rewarding) cues. Following the starting point that reward-related attentional bias might underlie the development of substance use and substance-related attentional bias, we investigated whether adolescents with stronger reward-related attentional biases would report a higher use of alcohol, tobacco and cannabis. We hypothesized that a stronger attentional bias towards cues of reward and non-punishment would be related to heavier adolescent substance use.

Chapter 3 subsequently focuses on the predictive role of these reward-related attentional biases and the study presented investigated whether attentional bias for reward and non-punishment would be predictive for adolescent substance use three years later, and for the increase in substance use over three years.

In Chapter 4 we investigated whether young adolescent alcohol use would be related to automatic alcohol approach tendencies, using two different versions of the Affective Simon Task (AST; de Houwer, 2004). We further investigated the role of subjective appetitive evaluations in adolescent alcohol use, and the moderating influence of working memory capacity. We hypothesized that stronger alcohol approach tendencies and more positive alcohol evaluations would be related to heavier adolescent substance use, and that this relationship would be moderated by working memory capacity.

In Chapter 5 we took a comparable approach investigating the role of automatic attentional bias in young adolescent alcohol use, and the possible moderating influence of executive control. We further investigated whether alcohol attentional bias would mediate the relationship between reward sensitivity and alcohol use. The studies in this section are one of the first examining cognitive biases related to substance use in an unselected young adolescent sample.

Chapter 6 presents a study that investigated whether adolescents diagnosed with substance dependence or addiction would be characterized by a substance-related attentional bias, compared to a control group. Further, in this study we investigated whether especially in patients with weak executive control substance-related attentional bias would be more strongly related to substance use. We subsequently focused on the influence of treatment as usual on the substance-related attentional bias and investigated whether this attentional bias would diminish after six months of therapy, and whether there would be a stronger decline in patients with relatively strong executive control.

CHAPTER 2

Reward-related attentional biases and adolescent substance use

Published as:
Van Hemel-Ruiter, M. E., de Jong, P. J., Oldehinkel, A. J., & Ostafin, B. D. (2013).
Reward-related attentional biases and adolescent substance use: The TRAILS study.
Psychology of Addictive Behaviors, 27(1), 142-150.

ABSTRACT

Current cognitive-motivational theories of addiction propose that prioritizing appetitive, reward-related information (attentional bias) plays a vital role in the development and maintenance of substance abuse. This study focused on reward-related attentional processes that might be involved in young-adolescent substance use. Participants were young adolescents (N = 682, mean age = 16.14), who completed a motivated game in the format of a spatial orienting task as a behavioral index of appetitive-related attentional processes and a questionnaire to index substance (alcohol, tobacco, and cannabis) use. Correlational analysis showed a positive relationship between substance use and enhanced attentional engagement, with cues that predicted potential reward and non-punishment. These results are consistent with the view that adolescents who show a generally enhanced appetitive bias might be at increased risk for developing heavier substance use.

INTRODUCTION

Current cognitive-motivational theories of addiction propose that prioritizing appetitive, reward-related information (attentional bias) plays a vital role in the development and maintenance of substance abuse (Field & Cox, 2008; Franken, 2003; Wiers et al., 2007). The selective processing of reward-related information may facilitate detection of substances with desirable (rewarding) consequences. After repeated experiences of the rewarding effects of drug taking, people may end up in a self-reinforcing "attentional bias–craving cycle": attentional bias for drug cues may facilitate the generation of craving, whereas craving may enhance further attentional bias for drug cues, and so forth (e.g., Franken, 2003; Robinson & Berridge, 1993, 2001). In line with this, previous research has found that attentional bias for general reward cues was positively related to alcohol use in students (Colder & O'Connor, 2002) and that people who use or misuse various addictive substances were characterized by an attentional bias for personally relevant substance cues (Field & Cox, 2008; Franken, 2003; Lubman, Peters, Mogg, Bradley, & Deakin, 2000). In addition, high levels of self-reported general reward sensitivity were found to be associated with strong reactivity to alcohol cues among heavy drinkers (Kambouropoulos & Staiger, 2001).

To investigate whether a generally enhanced attentional bias for appetitive information may be involved in early substance (ab)use, the present study was designed to test the relationship between appetitive-related attentional processes and substance use. The use of addictive substances often starts during early adolescence (e.g., Monshouwer et al., 2008), and because it has been shown that the early use of addictive substances is a reliable predictor of later dependence and abuse (Li, Hewitt, & Grant, 2007), the present study focused on early adolescents.

Spatial attention is composed of at least two operative components that might be relevant in the present context: attentional engagement (i.e., facilitated attention toward a cue) and attentional disengagement (i.e., difficulty to disengage attention from a cue; Posner, Inhoff, Friedrich & Cohen, 1987). Both enhanced engagement and enhanced difficulty to disengage attention from reward-relevant cues may independently contribute to the development of substance use and misuse (cf., Koster, Crombez, Verschuere, & De Houwer, 2004). Therefore, we preferred an attentional bias task that can index both types of reward related biases allowing investigating the relative importance of both components of attentional bias. Accordingly, we used a modified Spatial Orienting Task (SOT), as originally designed by Derryberry and Reed (1994, for more details, see Method section). This task was developed to explore to what extent people direct and hold their attention to places where a potential reward is expected, and/or to places where prevention of punishment (i.e., non-punishment) is expected. In terms of Gray's Reinforcement Sensitivity Theory, the Behavioral Approach System (BAS) is responsible for organizing behavior in response to appetitive stimuli, which signals both unconditioned reward and the relief from punishment (non-punishment; Gray, 1970, 1982). There is ample evidence that substance abuse disorders are related to high self-reported BAS-sensitivity, which motivates behaviors that are intended to attain rewards (or non-punishment), with little attention for the possibilities of negative consequences (i.e., nonreward or punishment; see for review, Bijttebier, Beck, Claes, & Vandereycken, 2009). Attentional biases as indexed by the SOT have been linked to reward- and punishment-related processes, suggesting that this task is useful for assessing biases in processing positive and negative incentives (Colder & O'Connor, 2002; Derryberry & Reed, 2002; Pratt, 2008). Therefore, the SOT provides the welcome opportunity to investigate attentional responses to both expected reward and non-punishment, and thus, to examine to what extent individual differences in both of these aspects of BAS are involved in substance use.

During the present SOT, participants respond to a simple target appearing on the left or the right side of a fixation cross by pressing a single response button. Their score after responding depends on their speed in detecting the target. The target is preceded by a peripheral cue that acts as a signal and appears left or right of the fixation cross. That is, the cue (i.e., a blue arrow pointing upward or a red arrow pointing downward) predicts whether a target at that location would result in a probable positive or negative outcome. Specifically, a blue arrow predicts higher chance at a positive outcome (either reward or non-punishment), if the target appears at the location cued by the blue arrow, whereas a red arrow predicts higher chance at a negative outcome (either nonreward or punishment), if the target appears on the location cued by the red arrow (for more detail, see Method section). It is important to note that this task consists of two different games: a positive game in which a positive outcome is a 10 point gain, and a negative outcome a null-gain, on the one hand, and a negative game in which a positive outcome is a null-loss, and a negative outcome a 10-point loss, on the other. Thus, the positive games (blocks of trials) result in a positive (or null) score and the negative games in a negative (or null) score. It is proposed that the cues in the positive games elicit states related to potential reward (i.e., blue arrow cues) and frustrative nonreward (i.e., red arrow cues), and the cues in the negative games signal potential safety/non-punishment (i.e., blue arrow cues) and punishment (i.e., red arrow cues). Because the cues are designed to be predictive for the outcomes, a person's motivation for reward or non-punishment are inferred from attention toward or away from the presented cues. Thus, this task allows influence of more strategic or voluntary control. The posterior attentional system is assumed to be a relatively reactive (involuntary) system that focuses the attentional "spotlight" to a particular location. During subsequent stages of attentional processing, the anterior system gets into action, which is generally viewed as an executive system that serves the more voluntary functions and regulates the posterior orienting system (for more details, see Derryberry & Reed, 2002). To examine the relative importance of more automatic and more voluntarily attentional processes in the alleged relationship between attention bias for reward and substance use, we included two different cue presentation times (250 ms and 500 ms) in the present SOT, which were successfully used to demonstrate differences in attentional biases for threat and safety in anxious people (Derryberry & Reed, 2002). It is important to note that using two different presentation times allowed testing whether the hypothesized relationship between substance use and attentional biases for appetitive stimuli would be especially pronounced under conditions that allow, or under conditions that preclude, a regulatory influence on participants' appetitive bias. Thus, the present approach enabled us to examine whether substance use is predominantly associated with relatively strong involuntary (automatic) attentional processes, with relatively strong regulatory (effortful) processes, or both.

In short, the present study investigated the relationship between appetitive attentional processes and adolescent substance use. According to cognitive motivational models of addiction, heightened attentional bias to appetitive cues will be related to high levels of substance use. We therefore hypothesized that an attentional bias toward cues of reward and non-punishment would be associated with high levels of substance use. We expected this bias to emerge as (a) an enhanced engagement toward and (b) a reduced disengagement from cues of reward and non-punishment. Furthermore, we explored whether this relationship is especially strong when there was little or when there was much time to voluntarily control attentional processes. The current study used a behavioral measure to examine the role of BAS sensitivity in substance use, complementing previous work that (a) investigated BAS sensitivity in addiction with self-report measures and (b) examined attentional biases toward specific addiction-relevant items (e.g., beer, wine, cigarettes). Furthermore, this study focused on young adolescents instead of adults. Therefore, this study provides a unique opportunity to behaviorally test the role of appetitive attentional bias in the initiation stage of substance use and may give clues for preventing the development of substance use problems.

METHOD

Participants and Recruitment

Participants were a subsample of Tracking Adolescents' Individual Lives Survey (TRAILS), a large prospective population study of Dutch adolescents with bi- or triennial measurements from age 11 to at least age 25. This cohort of 2,230 adolescents (baseline: mean age = 11.09 years, *SD* = 0.56, 50.8% female, response rate = 76%) was recruited via primary schools in five northern municipalities (including urban and rural areas) and constituted 64% of all children born between October 1989 and September 1990 (first three municipalities) or October 1990 and September 1991 (last two municipalities) in these areas (for more details, see Huisman et al., 2008; de Winter et al., 2005). The present study reports data from the third (T3) assessment wave that ran from September 2005 to December 2007, in which 1,816 (81% of initial sample) adolescents participated. Because all participants were recruited from the same school grade, the age range was relatively narrow (i.e., mean age = 16.3, range = 14.7–18.7). For reasons of feasibility and costs, a focus cohort of 744 adolescents was invited to perform a series of laboratory tasks on top of the usual assessments, of whom 715 (96%) agreed to participate. Adolescents with a high risk of mental health problems had a greater chance of being selected for the experimental session. High risk was defined based on temperament (high frustration and fearfulness, low effortful control), lifetime parental psychopathology (depression, anxiety, addiction, antisocial behavior, psychoses), and living in a single-parent family. In total, 66% of the focus cohort had at least one of these risk factors. The remaining 34% were randomly selected from the low-risk TRAILS participants. Hence, the focus cohort still represented the whole range of problems seen in a normal population of adolescents, which made it possible to represent the distribution in the total TRAILS sample by means of sampling weights (for more detailed information on the selection procedure and response rates within each stratum, see Appendix 2A). The present study included only participants who completed both the Spatial Orienting Task and the Substance Use Questionnaire (SUQ). Two participants were excluded because of incomplete SOT data and one participant for making over 25% errors on the SOT. Twenty-seven participants were excluded for having more than three missing SUQ item scores, and three because of extreme outlier scores (N = 682).[1] Descriptive statistics of the final sample (weighted estimates) are presented in Table 2.1.[2]

Table 2.1
Sample Characteristics (N = 683 [a])

Variable	Mean (SD) or percentage
Female Gender	51.3%
Age	16.14 (0.60)
Servings of alcohol/week over previous month [b]	6.00 (7.24)
Cigarettes/day over previous month	2.22 (4.71)
Frequency of cannabis use over previous month	0.75 (2.47)
Lifetime Abstainer of alcohol, tobacco and drugs	9.9%

Note. SD = standard deviation; [a] The sample size reported reflects the weighted sample size; [b] One serving of alcohol contains approximately 11 ml of pure alcohol.

Procedure

Laboratory behavioral assessment. As an index of attentional bias for appetitive stimuli we used the SOT (Derryberry & Reed, 2002). The SOT was the first computer task of a larger set of experimental tests. The experimental protocol was approved by the Central Committee on Research Involving Human Subjects (CCMO). The test assistants received extensive training to optimize standardization of the experimental session. Participants were tested on weekdays, in a sound-attenuating room with blinded windows at selected locations in the participants' town of residence.

Spatial Orienting Task. The task was presented on a Philips Brilliance 190 P monitor controlled by an Intel Pentium 4 CPU computer using E-prime software version 1.1 (Psychology Software Tools Inc, Pittsburgh, Pennsylvania). Participants were seated 50 cm away from the screen, and responses were collected on the computer's keyboard.

[1] Because the missing participants were only a 5% of the total group, there are no strong indications that these few differences could have influenced the data. To be sure, we imputed the data set, and reanalyzed the data, which resulted in the same conclusions.

[2] As a result of the exclusion of 33 participants, who carried different weights, the use of this weighting procedure resulted in a deviant final weighted sample size of 683.

Table 2.2

Description of scores in the positive and negative games

Game	Target trials		Catch trials	
	RT<cut-off (fast enough)	RT>=cut-off (too slow)	No response (accurate)	Response (inaccurate)
Positive	+ 10 points	0 points	0 points	- 10 points
Negative	0 points	- 10 points	0 points	- 10 points

Note. RT = reaction time.

Table 2.3

Overview of trial types; anticipated outcomes of targets following easy or hard cues and the calculation of exact cut-off times (in ms) for response time-interval

SOT – trials

Cue	Delay	Odds	Target	Signal	Relative time to respond	Exact cut-off time to respond	Anticipated outcome
Easy (blue)	250ms	2/3	Cued	Easy	Much	mRT+0.55SD+12 ms	75% chance of a positive outcome
		1/3	Uncued	Hard	Little	mRT-0.55SD+12ms	75% chance of a negative outcome
Easy (blue)	500ms	2/3	Cued	Easy	Much	mRT+0.55SD-12ms	75% chance of a positive outcome
		1/3	Uncued	Hard	Little	mRT-0.55SD-12ms	75% chance of a negative outcome
Hard (red)	250ms	2/3	Cued	Hard	Little	mRT-0.55SD+12ms	75% chance of a negative outcome
		1/3	Uncued	Easy	Much	mRT+0.55SD+12ms	75% chance of a positive outcome
Hard (red)	500ms	2/3	Cued	Hard	Little	mRT-0.55SD-12ms	75% chance of a negative outcome
		1/3	Uncued	Easy	Much	mRT+0.55SD-12ms	75% chance of a positive outcome

Note. SOT = Spatial Orienting Task; m = median; RT = reaction time; SD = standard deviation.

Task description. In collaboration with Derryberry and Reed, we programmed an SOT that was virtually identical to their original task (SOT; Derryberry & Reed, 2002). The task consisted of four positive and four negative blocks of trials (games), which alternated in sets of two, starting with two positive games (see Tables 2.2 and 2.3 and Appendix 2B). On positive blocks, participants gained 10 points for fast responses, and did not gain points for slow responses (definitions of fast and slow are given below). Thus, positive blocks allow for the assessment of approach toward reward. On negative blocks, participants lost 10 points for slow responses and did not lose points for fast responses. Thus, negative blocks allow for the assessment of approach toward non-punishment. Regardless of the block, 10 points were lost for inaccurate responses. The score was reset to zero at the start of each game. Participants were informed that those with the highest scores in the positive games would win an attractive prize (e.g., a balloon ride), while extremely low scores in the negative games could result in having to do the task again, until performance would be good enough.

Stimuli. Throughout each game, two vertical black bars were displayed against a white background, which marked the location of the cues and targets (for a schematic overview of trial structure, see Appendix 2C). Participants were instructed to fixate on the score, which was presented in black at the screen's center. The score was updated after each response (see below) and remained on the screen throughout the trial. Each trial began with turning the fixation score off for 200 ms and then back on for 250 ms. Next, a cue arrow replaced one of the two vertical black bars. After a delay of 250 or 500 ms, a target appeared. The target was a small vertical gray rectangle centered within the cue arrow (cued target) or within the vertical black bar on the opposite side of the fixation score (uncued target; see Appendix 2D). Participants were told that a blue up-arrow (easy cue) signaled that a target appearing in that location (cued) would be “easy” (i.e., own mean reaction time (RT) + 0.55 SD to react) and result in a sufficiently fast response about 75% of the time, whereas a target in the uncued bar's position would be “hard” (i.e., own mean RT – 0.55 SD to react); that is, resulting in a too slow response about 75% of the time. A red down-arrow (hard cue) indicated that a cued target would be “hard” (the response would be too slow 75% of the time) and an uncued target “easy” (the response would be sufficiently fast 75% of the time). In addition, they were informed that the cue would also indicate the probable location of the target, with 2/3 of the targets appearing in the cued location, and that occasionally no target would appear (catch trials). Participants were instructed to press the ‘b’ key as soon as they detected the target. Pressing the key before the target appeared or when no target appeared resulted in a loss of 10 points. Each block consisted of 32 cued, 16 uncued, and 8 catch trials, in random order. A total of 500 ms after the response (or 1 s following the delay interval on catch trials), the cue arrow and target were removed by reinstating the two black bars, and a feedback signal was presented below the central score. Feedback consisted of the same arrows as used for the cues. A blue up-arrow indicated a fast response or (accurate) nonresponse on catch trials. A red down-arrow signaled a slow response or (inappropriate) response on catch trials. After a delay of 250 ms, the score was updated (if changed). After a randomly selected inter-trial interval of 500 or 1000 ms, the next trial began by removing the feedback signal and blanking the score for 200 ms.

Feedback computation. At the end of each game, the participant's median RT and standard deviation were computed to calculate cutoffs for fast and slow responses on the next game of the same type (positive or negative; see also Tables 2.2 and 2.3). Consistent with the previous work of Derryberry and Reed, for easy targets, the response was labeled as fast if the RT was less than the median plus 0.55 times the SD. For hard targets, a response was treated as fast if the RT was less than the median minus 0.55 times the SD. If RTs equaled or exceeded these cutoffs, they were treated as slow. Because RTs tend to be about 25 ms slower after short delays, 12 ms were added to the cut-off for short-delay trials and subtracted for long-delay targets (see Appendix 2E; for more detailed task description, see also Derryberry & Reed, 2002). Because the response window was adapted online on the basis of the participant's individual performance, there were no participants with extremely low scores.

Self-reported substance use. Measures of alcohol, tobacco, and cannabis use were part of a larger self-report survey, which was completed at school, supervised by test assistants (see Huizink, Ferdinand, Ormel, & Verhulst, 2006). Noncannabis illicit drug use (e.g., amphetamines, cocaine, XTC) was left out of the analyses because only 21 participants (4%) indicated having used these drugs. Substance use was calculated on quantity and frequency items of alcohol use (nine items), tobacco use (four items), and cannabis use (three items, see Appendix 2F). Because of their different scaling, standardized scores were used to calculate measures for alcohol (Cronbach's alpha = .85), tobacco (Cronbach's alpha = .84), and cannabis use (Cronbach's alpha = .90). Finally, as an index of general substance use, we used the means of these alcohol, tobacco and cannabis measures to calculate a substance use measure (Cronbach's alpha = .70). This measure was skewed and to normalize the distribution a square root transformation was carried out.

Data Reduction and Analysis

The SOT RT data were analyzed following Derryberry and Reed (2002). First, RTs below 125 ms (probable anticipations) and above 1,000 ms (probable distractions) were removed. The mean percentage of outliers was 5%. Mean RT for each condition was calculated after removing outlier trials.

Participants generally respond faster to cues that appear in regions of a visual display to which they are attending than to cues in regions to which they are not attending (Posner et al., 1987). Therefore, attentional engagement toward expected reward (positive games) or non-punishment (negative games) is inferred when participants respond faster to cued targets preceded by easy (blue) cues than to those preceded by hard (red) cues. Difficulty to disengage attention from expected reward (positive games) or non-punishment (negative games) is inferred when participants respond slower to uncued targets preceded by easy (blue) cues than to those preceded by hard (red) cues (e.g., Koster et al., 2004).

Table 2.4
Calculation of approach toward reward scores

Type of game	Positive games: approach toward reward			
Type of trial	Short-delay trials (250 ms)		Long-delay trials (500 ms)	
Attentional bias scores	Engagement towards expected gain	Difficulty to disengage from expected gain	Engagement towards expected gain	Difficulty to disengage from expected gain
Formula's	RT cued red trials minus RT cued blue trials	RT uncued blue trials minus RT uncued red trials	RT cued red trials minus RT cued blue trials	RT uncued blue trials minus RT uncued red trials

Note. RT = reaction time.

Table 2.5
Calculation of approach toward non-punishment scores

Type of game	Negative games: approach toward non-punishment			
Type of trial	Short-delay trials (250 ms)		Long-delay trials (500 ms)	
Attentional bias scores	Engagement towards expected non-loss	Difficulty to disengage from expected non-loss	Engagement towards expected non-loss	Difficulty to disengage from expected non-loss
Formula's	RT cued red trials minus RT cued blue trials	RT uncued blue trials minus RT uncued red trials	RT cued red trials minus RT cued blue trials	RT uncued blue trials minus RT uncued red trials

Note. RT = reaction time.

Accordingly, we computed the engagement and disengagement scores (see Tables 2.4 and 2.5). Hence, attentional bias for reward was represented in the positive games as both (a) a relatively faster engagement toward cues of expected gain (blue arrow acting as correct cue for target; cued blue trials) than cues of expected nongain (red arrows acting as correct cue for target; cued red trials) and (b) slower disengagement from expected gain (blue arrow acting as incorrect cue for target; uncued blue trials) than expected nongain (red arrows acting as incorrect cue for target; uncued red trials). Analogously, attentional bias for non-punishment was represented in the negative games, by both (a) a relatively faster engagement toward cues of expected nonloss (blue arrows acting as correct cue for target; cued blue trials) than cues of expected loss (red arrows acting as correct cue for target; cued red trials) and (b) slower disengagement from expected nonloss (blue arrow acting as incorrect cue for target; uncued blue trials) than expected loss (red arrows acting as incorrect cue for target; uncued red trials). All scores were separately calculated for short-delay and long-delay trials (i.e., when there was less or more time to voluntary control the attention).

Table 2.6

Mean score reaction times (M in ms) and standard deviations (SD) of SOT scores (N = 683 [a])

Type of game	Short Delay				Long Delay			
	Cued		Uncued		Cued		Uncued	
	Easy	Hard	Easy	Hard	Easy	Hard	Easy	Hard
	M(SD)	M(SD)	M(SD)	M(SD)	M(SD)	M(SD)	M(SD)	M(SD)
Positive	335(42)	366(47)	467(89)	469(88)	341(57)	378(66)	382(75)	376(73)
Negative	328(46)	356(52)	453(88)	456(92)	331(58)	365(68)	379(81)	373(76)

Note. SOT = Spatial Orienting Task; [a] The sample size reported reflects the weighted sample size.

RESULTS

Reaction time data

RT data are shown in Table 2.6. First, we examined whether general task performance was in line with the design of the task. Therefore, we carried out a series of paired samples t tests comparing participants' performance during uncued versus cued trials for all relevant types of trials (Table 2.7). These tests showed an overall engagement effect (i.e., participants were generally faster at cued easy trials than at cued hard trials; mean difference cued hard-cued easy = 32 ms, t = 31.46, $p < .001$, Cohen's d = 1.25), and a disengagement effect only for long-delay trials (i.e., in 500 ms games, participants were faster at uncued hard trials than at uncued easy trials, mean difference = 6 ms, t = 4.05, $p < .001$, Cohen's d = 0.16). Attesting to the validity of the present approach, participants generally showed a preference for directing their attention toward cues of reward or non-punishment (easy [blue] cues) compared with cues of frustrative nonreward or punishment (hard [red] cues) and that this effect occurred both when the conditions supported automatic (250-ms delay condition) and voluntary (500-ms delay condition) attentional processes. In addition, participants demonstrated more difficulty in disengaging attention from cues of reward or non-punishment (easy [blue] cues) compared with cues of frustrative nonreward or punishment (hard [red] cues), but only when they had more time to voluntarily control their attention (500-ms delay condition).

Table 2.7

Paired-samples t-tests testing the differences in reaction times between hard and easy trials of the Spatial Orienting Task (SOT), separated between type of trials (cued vs. uncued, short-delay vs. long-delay and positive vs. negative game); as measures for engagement and disengagement effects (N = 683 [a])

Type of trial			Mean	t	Cohens *d*	Df
Positive games	S-D	Attentional engagement to reward (ch – ce)	30.65	24.97**	0.97	682
		Difficulty to disengage from reward (ue – uh)	-2.70	-1.13	-0.04	682
	L-D	Attentional engagement to reward (ch – ce)	36.23	19.36**	0.75	682
		Difficulty to disengage from reward (ue – uh)	5.76	2.85**	0.11	682
Negative games	S-D	Attentional engagement to non-punishment (ch – ce)	27.91	20.92**	0.81	682
		Difficulty to disengage from non-punishment (ue – uh)	-2.53	-1.01	-0.04	682
	L-D	Attentional engagement to non-punishment (ch – ce)	33.91	17.24**	0.67	682
		Difficulty to disengage from non-punishment (ue – uh)	6.81	3.00**	0.12	682

Note. S-D = short-delay; L-D = long-delay; ce = cued easy; ch = cued hard; ue = uncued easy; uh = uncued hard; [a] The sample size reported reflects the weighted sample size; ** p < 0.01 (two tailed).

Reward-Related and Punishment-Related Attentional Biases and Substance Use

To investigate the relationship between substance use and attentional biases, we first performed a bivariate correlational analysis. Table 2.8 shows that substance use correlates with age and with engagement toward both reward and non-punishment for both short-delay and long-delay trials. There were no significant correlations between substance use and gender, or the disengagement from either reward or non-punishment scores.

Table 2.8
Bivariate correlations of attentional bias scores and substance use (N = 683 [a])

		1	2	3	4	5	6	7	8	9	10	11
1	Substance use [b]	-										
2	Gender	.06	-									
3	Age	.12**	-.03	-								
4	Attentional engagement toward reward (S-D)	.08*	.02	-.05	-							
5	Difficulty disengaging from reward (S-D)	-.02	-.08*	-.01	-.05	-						
6	Attentional engagement toward non-punishment (S-D)	.11**	.01	-.02	.29**	-.05	-					
7	Difficulty disengaging from non-punishment (S-D)	.02	.06	.01	.02	.04	-.08*	-				
8	Attentional engagement toward reward (L-D)	.12**	.01	-.01	.22**	-.01	.12**	-.06	-			
9	Difficulty disengaging from reward (L-D)	-.03	-.01	-.01	-.05	.01	-.08*	-.00	.01	-		
10	Attentional engagement toward non-punishment (L-D)	.09*	.00	-.05	.22**	.04	.20**	.05	.20**	-.05	-	
11	Difficulty disengaging from non-punishment (L-D)	-.05	-.01	-.03	.00	.02	-.06	-.00	-.07	.05	-.03	-

Note. S-D = short-delay; L-D = long-delay; [a] The sample size reported reflects the weighted sample size; [b] Substance use was square root transformed before analysis; * $p < 0.05$; ** $p < 0.01$.

Bivariate Correlations of Attentional Bias Scores and Substance Use

We carried out a hierarchical regression analysis to test the unique contribution of each of the attentional engagement scores in predicting substance use. Step 1 included age, and Step 2 included attentional engagement to reward (both short and long-delay blocks) and attentional engagement to non-punishment (both short and long-delay blocks. Gender and disengagement variables were left out of analysis, as there were no indications that these variables contributed to the prediction of substance use. The alpha level was set to 0.05. This full model explained 4% (R^2 adjusted = 0.04), $F(5, 677) = 6.09$, $p < .001$, of all variance. The model showed that age, attentional engagement toward non-punishment (short delay), and attentional engagement toward reward (long delay) all predicted unique variance of substance use (Table 2.9).[3]

Table 2.9

Hierarchical regression model for variables explaining substance use [a] (N = 683 [b])

Variable		B	t	R^2 Change
Step 1				
	(Constant)		55.36**	
	Age	0.12	3.19**	0.02
Step 2				
	(Constant)		55.29**	
	Age	0.13	3.41*	
	Attentional engagement toward reward (short-delay)	0.03	0.67	
	Attentional engagement toward non-punishment (short-delay)	0.09	2.20*	
	Attentional engagement toward reward (long-delay)	0.09	2.31*	
	Attentional engagement toward non-punishment (long-delay)	0.05	1.40	0.03

Note. R^2 final model = 0.04**; Adjusted R^2 = 0.04; [a] substance use was square root transformed before analysis; [b] the sample size reported reflects the weighted sample size; * p < 0.05; ** p < 0.01.

DISCUSSION

The present study was designed to explore whether attentional biases for general appetitive cues (of reward and non-punishment) might be related to substance use in early adolescence. This study tested the relationship between the strength of attentional biases and substance use behavior in a large representative cohort of young adolescents. The main results can be summarized as follows: First,

[3] Regression analysis was repeated for the square root transformations of alcohol use, tobacco use and cannabis use separately, which showed that there was an effect for attentional engagement toward reward (long delay) in the prediction of alcohol (p = .03), and cannabis use (p = .05), but not for tobacco use. Attentional engagement toward non-punishment (short-delay) predicted tobacco use (p = .02), but not alcohol or cannabis use. Note that the variable of cannabis use was highly skewed (i.e., >2).

substance use was related to attentional bias for appetitive cues. Hierarchical analyses indicated that of the four measures of attentional biases which demonstrated bivariate correlations with substance use, attentional engagement toward non-punishment in the 250-ms delay condition and attentional engagement toward reward in the 500-ms delay condition both predicted unique variance of substance use. Second, independent of their substance use score, adolescents showed an enhanced engagement toward both reward and non-punishment in both short-delay and long-delay trials. Furthermore, they showed a difficulty to disengage their attention from reward and non-punishment during long-delay trials.

The finding that, overall, adolescents showed an attentional bias for reward and non-punishment is in line with previous reports indicating that adolescence is characterized by an enhanced sensitivity to appetitive stimuli (e.g., Spear & Varlinskaya, 2010; Van Leijenhorst et al., 2010) and attested to the validity of the task. Most important in the present context, the use of this particular behavioral paradigm provided additional clues regarding the nature of substance-related attentional biases concerning reward and non-punishment. The results suggest that the crucial substance-related attentional biases involve enhanced engagement with cues of reward and non-punishment rather than with problems disengaging from cues of reward and non-punishment. That is, attention is attracted and held more strongly to cues predicting reward compared with cues predicting frustrative nonreward, and to cues predicting non-punishment compared with cues predicting punishment. This correlational pattern was apparent for both short-delay trials, which reflect the relatively automatic processes, and long-delay trials, in which there is more opportunity to voluntary control attention. Regression analyses indicated that relatively strong automatic engagement toward non-punishment and relatively strong voluntary engagement toward reward have unique value in the explanation of substance use. Thus, the predictive value of the various engagement scores are not entirely redundant and the more automatic and the more controlled attentional engagement scores showed at least partly complementary predictive value. A possible explanation for this pattern could be that a strong automatic engagement toward non-punishment relative to engagement toward punishment reflects weak automatic fear of negative consequences (e.g., fear of getting a hang-over), and a strong voluntary engagement toward reward represents a heightened voluntary drive to receive rewards (e.g., attaining pleasant feelings after drug use). Obviously, before making any strong conclusions, these results have to be replicated and tested subsequently.

The general pattern of results is consistent with research showing strong self-reported BAS sensitivity (i.e., sensitivity to stimuli that signal reward and non-punishment) to be associated with substance use (see for review, Bijttebier et al., 2009). Moreover, these results replicate and add to the central findings of other researchers, that high BAS sensitivity is associated to adolescent and adult substance use (e.g., Franken, 2002; Genovese & Wallace, 2007; Johnson, Turner & Iwata, 2003; Knyazev, 2004). Furthermore, finding this relationship in a young adolescent sample lends support to the idea that this appetitive bias might be an important factor in the initiation of adolescent substance use. That is, this facilitated attention toward appetitive cues may lead to a more detailed and sustained processing of the positive effects of substance use, and may increase the likelihood that the association between cues and positive (desired) effects of substance use will be stored in memory. This may lead to an increase in arousal and an enhanced attentional bias for substance cues, which both may lower the threshold for eliciting craving and approach tendencies, which may eventually lead to an increase in use. Accordingly, (young) adolescents who show heightened attentional bias toward appetitive stimuli might therefore be at risk for initiating substance use at a younger age and subsequently for developing substance use problems.

However, it is important to note that the cross-sectional design of our study does not allow any firm conclusion regarding the direction of the relationship between attentional bias and substance use. Therefore, it is important to test the proposed interrelationship in a longitudinal design. This would give the opportunity to investigate not only whether there is a correlation between attentional bias and adolescent substance use, but also whether attentional bias precedes abuse, and thus has predictive value for future substance abuse. Furthermore, combining this SOT with a measure that assesses substance-related attentional bias (e.g., a Visual Probe Task) might provide supplementary information about the proposed relationship between the more general reward-related attentional processes and the more stimulus-specific attentional bias for personally relevant substances.

Finally, some comments are in order regarding the limitations of the present study. Perhaps most important, it should be acknowledged that the effect-size of our study was rather small (i.e., R^2 = 0.04). Nevertheless, given the relatively small range in substance use in the present sample, together with the methodological limitations of the type of behavioral measure we used (i.e., RT measures such as the

SOT provide only a rough indicator of attentional processes), small effects are noteworthy. The importance of even small effects is underscored by the considerable risk for negative health and social consequences that are associated with substance use behavior. As a further limitation, commonly used measures of substance use problems such as the Rutgers Alcohol Problem Index (RAPI; White & Labouvie, 1989) were not included in TRAILS, although this type of information would have been of supplemental value for the current study. Finally, because of the unbalanced, fixed order of the positive and negative games, it is not possible to draw any conclusion regarding absolute effects. However, because the order was the same for all participants, no problems seem to arise inferring the relative effects of this study.

To conclude, this study was the first to show that heavier-using adolescents were characterized by a generally enhanced attentional engagement toward cues of reward and non-punishment. The pattern of findings is consistent with the hypothesis that such a generally enhanced attentional bias for appetitive cues may set adolescents at risk for developing excessive substance use. An important next step would be to corroborate these findings in a longitudinal design.

APPENDIX 2A

Number of participants in the low and high risk profile groups in the total TRAILS population (i.e., pop.) and in the focus cohort of participants who performed laboratory tasks (i.e., focus)

		Boys	Girls	Total
		N	N	N
Low risk (not A, B or C)	pop.	462	477	939
	focus	119	123	242
Temp. (A)	pop.	165	138	303
	focus	53	56	109
Parental psychopathology (B)	pop.	142	175	317
	focus	51	52	103
Single-parent family (C)	pop.	79	96	175
	focus	28	38	66
AB	pop.	72	66	138
	focus	33	32	65
AC	pop.	41	25	66
	focus	13	10	23
BC	pop.	76	99	175
	focus	31	33	64
ABC	pop.	57	53	110
	focus	23	20	43
Total	pop.	1094	1129	2223
	focus	351	364	715

Note. The selection criteria for high-risk profile group were as follows:

High-risk temperament: EATQ (Early Adolescent Temperament Questionnaire) Frustration ≥ 90^{th} percentile or EATQ Fear ≥ 90^{th} percentile or EATQ Effortful Control ≤ 10^{th} percentile. N_A = 617 (27.8%), 282 girls, 335 boys.

Parental psychopathology: at least one parent with severe psychopathology. N_B = 740 (33.3%), 393 girls, 347 boys.

High environmental risk: at least one of both biological parents is not part of the family. N_C = 526 (23.7%), 273 girls, 253 boys.

APPENDIX 2B

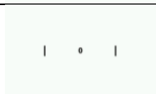
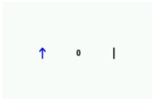
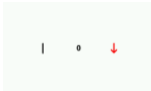
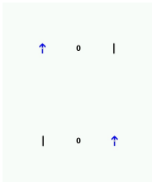
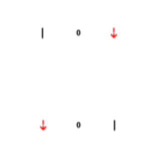
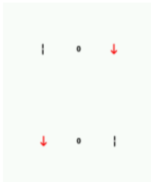
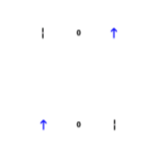
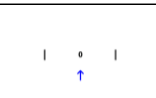
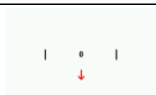
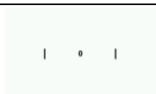
Overview of the Spatial Orienting Task procedure

Spatial Orienting Task					
		N trials			
Block	Game	Cued	Uncued	Catch	Cut-off RTs
1	Practice pos. game	6	6	2	Fixed 350ms
2	Practice neg. game	6	6	2	Fixed 350ms
3	Positive game	32	16	8	Based on RT block 1
4	Positive game	32	16	8	Based on RT block 3
5	Negative game	32	16	8	Based on RT block 2
6	Negative game	32	16	8	Based on RT block 5
7	Positive game	32	16	8	Based on RT block 4
8	Positive game	32	16	8	Based on RT block 7
9	Negative game	32	16	8	Based on RT block 6
10	Negative game	32	16	8	Based on RT block 9

Note. RT = reaction time; pos. = positive; neg. = negative.

APPENDIX 2C

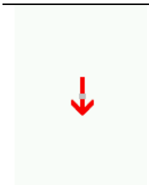
Schematic overview of trial structure

Duration	Trial structure	Composition of sequential screens within one trial		
200ms	2 vertical black bars (size 0.16 x 0.64 cm) – mark location of cues and targets			
250ms	Fixation score in between 2 bars (size 0.6 x 0.9 cm per digit)			
250ms (short-delay trial) or 500ms (long-delay trial)	Cue arrow (size 0.5 x 1.3 cm, shaft width 0.16 cm) replaces one of the bars	Easy cue - high chance at positive outcome 	Hard cue – high chance at negative outcome 	
500 ms after response or 1s when no response	Target (small vertical gray rectangle, 0.08 x 0.24 cm) - press 'b' as fast as possible if you see target (see fig. S1), no target: don't press any button	2/3 of targets cued – (target easy or hard) PRESS B Easy condition – much time to react (i.e., own median RT + 0.55 SD)  Hard condition – little time to react (i.e., own median RT – 0.55 SD) 	1/3 of targets uncued – (target easy or hard)  	1/7 of trials no target DON'T PRESS
500ms	Reinstated black bars + feedback signal			
250 ms	Updated total score			

Note: RT = reaction time.

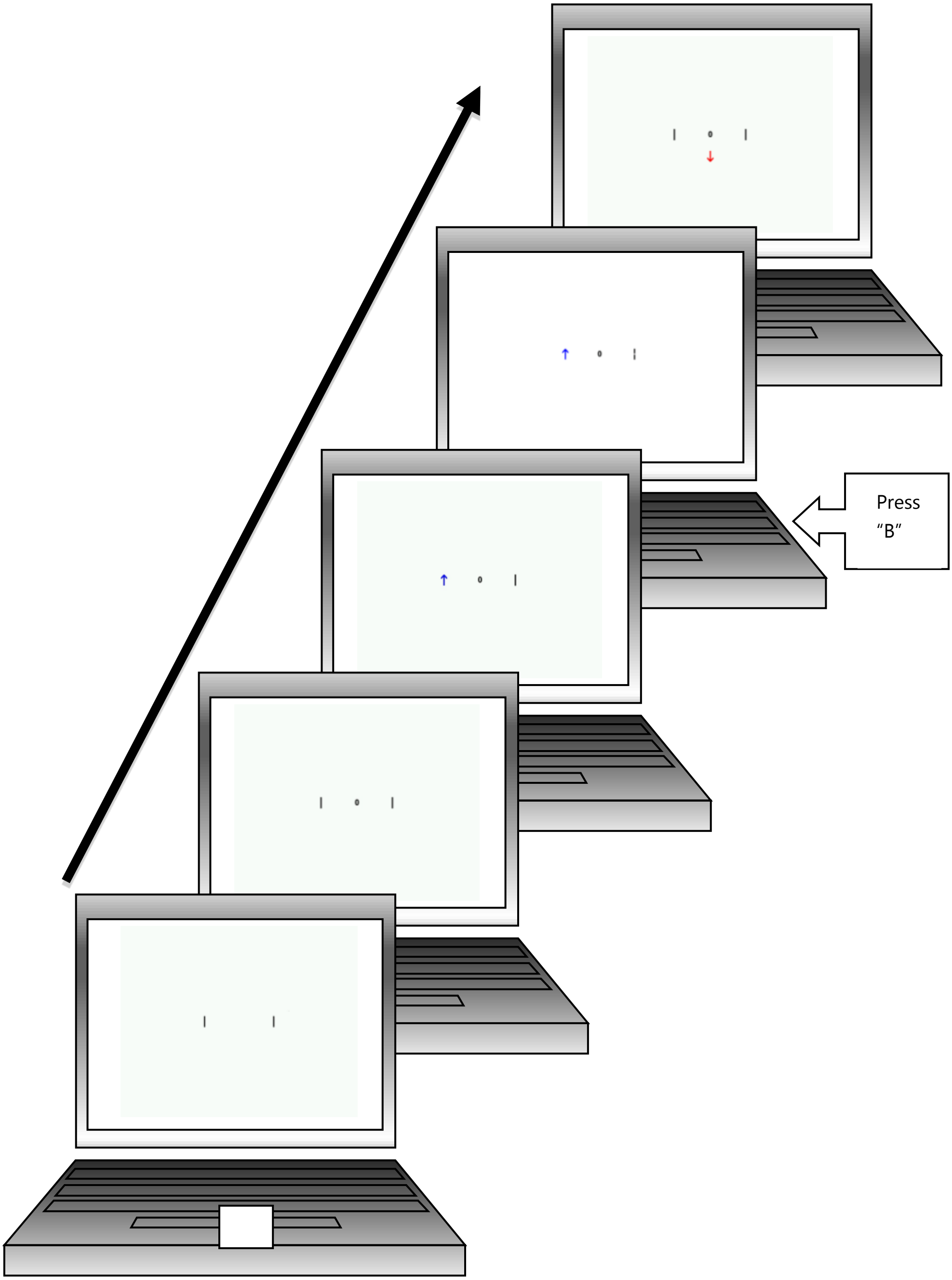
APPENDIX 2D

Examples of cued hard target, cued easy target, and uncued target

Cued hard target	Cued easy target	Uncued target
		

APPENDIX 2E

Example of screen-setup of the Spatial Orienting Task (SOT) - Example of easy cue, followed by a target in the uncued location (i.e., hard target) with subsequent slow response (i.e., negative feedback)



APPENDIX 2F

Items and response categories of self-reported substance use, subdivided by substance (alcohol, tobacco, cannabis)

Item	Substance	Question	Response categories
1	Alcohol	At how many days did you drink alcohol last week	0-7 = 0 to 7 days
2		How many glasses of alcohol did you drink last week	0-6 = 0 to 6 glasses, 7 = 7-10 glasses, 8 = 11 or more glasses
3		How many times did you drink alcohol in your lifetime?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more
4		How many times did you drink alcohol in the last twelve months?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more
5		How many times did you drink alcohol in the last 4 weeks?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more
6		At how many week days do you normally drink alcohol?	0-3 = 0 to 3 days
7		How many glasses of alcohol do you normally drink at a week day?	0-6 = 0 to 6 glasses, 7 = 7-10 glasses, 8 = 11 or more glasses per day
8		At how many weekend days do you normally drink alcohol?	0-3 = 0 to 3 days
9		How many glasses of alcohol do you normally drink at a weekend day?	0-6 = 0 to 6 glasses, 7 = 7-10 glasses, 8 = 11 or more glasses per day
10	Tobacco	Did you ever smoke, even if it was just one cigarette or a few drafts?	0 = never, 1 = 1 or 2 times, 2 = not every day, 3 = I stopped, 4 = every day
11		How many cigarettes do you normally smoke at a smoking day?	Continuous, 0 - ∞
12		How many cigarettes did you smoke in the past week?	0 = I never smoke, 1 = 0 cigs, 2 = less than 1, 3= 1-5 cigs, 4 = 6-10 cigs, 5 = 11-20, 6 = 20 or more
13		How many cigarettes did you smoke in the past four weeks?	0 = I never smoke, 1 = 0 cigs, 2 = less than 1, 3= 1-5 cigs, 4 = 6-10 cigs, 5 = 11-20, 6 = 20 or more
14	Cannabis	How many times did you use weed or hash in your lifetime?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more
15		How many times did you use weed or hash in the last twelve months?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more
16		How many times did you use weed or hash in the last four weeks?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more

CHAPTER 3

Reward-related attentional bias and adolescent substance use: a prognostic relationship?

Published as:
Van Hemel-Ruiter, M. E., de Jong, P. J., Ostafin, B. D., & Oldehinkel, A. J. (2015). Reward-Related Attentional Bias and Adolescent Substance Use: A Prognostic Relationship? *PLoS ONE 10(3): e0121058.*

ABSTRACT

Current cognitive-motivational addiction theories propose that prioritizing appetitive, reward-related information (attentional bias) plays a vital role in substance abuse behavior. Previous cross-sectional research has shown that adolescent substance use is related to reward-related attentional biases. The present study was designed to extend these findings by testing whether these reward biases have predictive value for adolescent substance use at three-year follow-up. Participants (N = 657, mean age = 16.2 years at baseline) were a sub-sample of Tracking Adolescents' Individual Lives Survey (TRAILS), a large longitudinal community cohort study. We used a spatial orienting task as a behavioral index of appetitive-related attentional processes at baseline and a substance use questionnaire at both baseline and three years follow-up. Bivariate correlational analyses showed that enhanced attentional engagement with cues that predicted potential reward and non-punishment was positively associated with substance use (alcohol, tobacco, and cannabis) three years later. However, reward bias was not predictive of changes in substance use. A post-hoc analysis in a selection of adolescents who started using illicit drugs (other than cannabis) in the follow-up period demonstrated that stronger baseline attentional engagement toward cues of non-punishment was related to a higher level of illicit drug use three years later. The finding that reward bias was not predictive for the increase in substance use in adolescents who already started using substances at baseline, but did show prognostic value in adolescents who initiated drug use in between baseline and follow-up suggests that appetitive bias might be especially important in the initiation stages of adolescent substance use.

INTRODUCTION

Substance abuse and dependence are major problems at both the individual and the societal level. Substance use often starts in adolescence (Monshouwer et al., 2008), and it has been found that a younger age at the onset of use is a risk factor for later dependence and abuse (DeWit, Adlaf, Offord & Ogborne, 2000; Grant, Stinson & Harford, 2001; Lynskey et al., 2003; Winters & Lee, 2008), with the greatest risk for youth beginning to use in the teenage years (Winters & Lee, 2008). Germane to this, there is growing evidence that appetitive, reward-related attentional bias plays a role in substance (mis)use. Through conditioning, substance-related stimuli can become cues of reward (or relief), which then attract attention. Once the cues have been noticed, they may elicit craving and behavioral dispositions to approach and consume the drug (Franken, 2003; Robinson & Berridge, 1993; 2001). There is evidence that attentional bias toward specific drug cues is related to drug behavior (Franken, 2003; Field & Cox, 2008; Lubman et al., 2000). Attentional bias toward general cues of reward should similarly increase the likelihood of drug cues attracting attention (given their status as cues of reward). That is, people who respond strongly to general reward cues might be more willing to try and use more substances, than those who are less attentive to cues of reward. Support for this idea is found in previous studies that have demonstrated that attentional biases for general reward cues are positively related to alcohol use in students (Colder & O'Connor, 2002), and to substance use in (young) adolescents (van Hemel-Ruiter, de Jong, Oldehinkel & Ostafin, 2013).

These previous studies on the relationship between substance use and attentional bias toward reward have used the Spatial Orienting Task (Derryberry & Reed, 1994) as a measure of attentional processes toward cues of general reward (Colder & O'Connor, 2002; van Hemel-Ruiter et al., 2013). This task was developed to explore to what extent people direct and hold their attention to places where a potential reward or prevention of punishment (i.e., non-punishment) are expected. In terms of Gray's Reinforcement Sensitivity Theory, the Behavioral Approach System (BAS) is proposed to be responsible for organizing behavior in response to appetitive stimuli, including reward and non-punishment Gray, 1970; 1982). Attentional biases as indexed by the spatial orienting task (SOT) have been linked to reward and punishment related processes, suggesting that this task is useful for assessing prioritized processing of both positive and negative incentives (Colder & O'Connor, 2002; Derryberry & Reed, 2002; Pratt, 2009). Although previous research has found a consistent link between adolescent substance use and high self-reported reward sensitivity (Knyazev, 2004; Lopez-Vegara et al., 2012; O'Connor & Colder, 2005; Pardo et al., 2007), relatively little research has examined whether behavioral measures of reward and punishment sensitivity are related to substance use.

Using a SOT as an index of reward-related attentional bias, it was previously found that adolescents who attended more quickly to places where a reward or non-punishment was expected reported a higher level of alcohol, tobacco, and cannabis use (van Hemel-Ruiter et al., 2013). Although these earlier findings are consistent with the idea that heightened reward-related attentional bias plays a role in substance misuse, the cross-sectional design of that previous study prevents the ability to make directional inferences regarding the relationship between reward-related attentional biases and substance use. Therefore, the present study used a longitudinal approach to examine whether a general reward-related attentional bias would show a prospective relationship with adolescent substance use at a three-year follow-up, and whether reward bias would also predict the increase in substance use within this follow-up period. First, we tested the hypothesis that an attentional bias toward cues of reward and non-punishment would be associated with high levels of prospective substance use. In line with the previous cross-sectional findings, we expected this bias to emerge as an enhanced engagement toward both rewarding cues and cues of non-punishment. To enable comparison with our previous cross-sectional findings, we again focused on the prediction of alcohol, tobacco, and cannabis use. Second, we tested if reward-related attentional bias has predictive value for prospective substance use over and above initial substance use during the baseline assessment. If reward-related attentional bias would indeed precede an increase in substance use, this would point to reward-related attentional bias as a promising focus of preventive interventions.

MATERIALS AND METHODS

Participants and Recruitment

For the current study we used the same sample as van Hemel-Ruiter et al. (2013). Participants were a sub-sample of Tracking Adolescents' Individual Lives Survey (TRAILS), a large prospective population study of Dutch adolescents with bi or triennial measurements from age 11 to at least age 25. This cohort of 2230 adolescents (Baseline: mean age = 11.09 years, *SD* = 0.56, 50.8 % female, response rate 76%) was recruited via primary schools in five northern municipalities (including urban and rural areas) and constituted of 64% of all children born between October

1989 and September 1990 (first three municipalities) or October 1990 and September 1991 (last two municipalities) in these areas (for more details, Huisman et al., 2007; de Winter et al., 2005). The present study reports data from the third (T3; from 2005 to 2007) and fourth (T4; from 2008 to 2010) assessment wave, with the fourth wave being three years following the third. In T3 a total of 1816 (81% of initial sample, mean age T3 = 16.3, range = 14.7 - 18.7), and in T4, a total of 1881 (84% of initial sample, mean age T4 = 19.1, range = 18.0 - 20.9) adolescents participated (Nederhof et al., 2012). For reasons of feasibility and costs, a focus cohort of 744 adolescents was invited to perform a series of laboratory tasks on top of the usual assessments, of which 715 (96% of initial sample) agreed to participate. Adolescents with a high risk of mental health problems had a greater chance of being selected for the experimental session. High risk was defined based on temperament (high frustration and fearfulness, low effortful control), lifetime parental psychopathology (depression, anxiety, addiction, antisocial behavior, psychoses), and living in a single-parent family. In total, 66% of the focus cohort had at least one of these risk factors. The remaining 34% were randomly selected from the low-risk TRAILS participants. Hence, the focus cohort still represented the whole range of problems seen in a normal population of adolescents, which made it possible to represent the distribution in the total TRAILS sample by means of sampling weights (for more detailed information on the selection procedure and response rates within each stratum, see van Hemel-Ruiter et al., 2013). Around 92% of this focus cohort (N = 654) had completed both the Spatial Orienting Task at T3 and the Substance Use Questionnaire (SUQ) at T3 and T4. As a result of the exclusion of 61 participants, who carried different weights, the use of this weighting procedure resulted in a deviant final weighted sample size of 657. Due to a small percentage of missing values (<0.5%) we imputed the data-set by conducting mean substitution. Descriptive statistics of the final imputed sample in T3 and T4 (weighted estimates) are presented in Table 3.1.

The experimental protocol and consent procedure were approved by the Central (Dutch) Committee on Research Involving Human Subjects (CCMO). All participating adolescents and their parents gave written informed consent.

Procedure

Laboratory Behavioral Assessment. As an index of attentional bias for appetitive stimuli we used the Spatial Orienting Task (Derryberry & Reed, 2002). The SOT was the first computer task of a larger set of experimental tests, included in the

Table 3.1
Sample Characteristics (N = 657[a])

Variable	Baseline (T3)	3-year FU (T4)
Female Gender	52.3%	52.3%
Age (mean [SD])	16.1 [0.59]	19.0 [0.54]
Servings alcohol/week previous month[b] (median [range])	4.00 [0-69.5]	6.30 [0-73.5]
Cigarettes/week previous month (median [range])	0.00 [0.0-210]	0.00 [0-224]
Frequency of cannabis use over previous month (median [range])	0.00 [0.0-40.0]	0.00 [0-40.0]
Lifetime user of illicit drugs (other than cannabis)	5.5%	13.6%
Lifetime abstainer of alcohol, tobacco and drugs	6.1%	3.1%

Note. FU = follow-up; [a] The sample size reported reflects the weighted sample size; [b] One serving of alcohol contains approximately 11 ml of pure alcohol.

third assessment wave. The test assistants received extensive training in order to optimize standardization of the experimental session. Participants were tested on weekdays, in a sound-attenuating room with blinded windows at selected locations in the participants' town of residence.

Spatial Orienting Task. The task was presented on a Philips Brilliance 190 P monitor controlled by an Intel® Pentium® 4 CPU computer using E-prime software version 1.1 (Psychology Software Tools Inc, Pittsburgh, Pennsylvania). Participants were seated 50 cm away from the screen and responses were collected on the computer's keyboard.

Task description. In collaboration with Derryberry and Reed, we programmed a SOT that was virtually identical to their original task (Derryberry & Reed, 2002). The task consisted of four positive and four negative blocks of trials (games), which alternated in sets of two, starting with two positive games. On positive blocks, participants gained 10 points for fast responses, and did not gain points for slow responses (definitions of fast and slow are given below). On negative blocks, participants lost 10 points for slow responses, and did not lose points for fast responses. Regardless of the block, ten points were lost for inaccurate responses. To enhance motivation, participants were informed that those with the highest scores in the positive games would win a price, while extremely low scores in the negative games could result in having to do the task again, until performance would be good enough. Therefore, the feedback on scores was used to enhance motivation to play the game as fast and accurate as possible.

Stimuli. Throughout each game, two vertical black bars were displayed against a white background, which marked the location of the cues and targets. Participants were instructed to fixate on the score which was presented in black at the screen's center. The score was updated after each response (see below) and remained on the screen throughout the trial. Each trial began with turning the fixation score off for 200 ms and then back on for 250 ms. Next, a cue arrow replaced one of the two vertical black bars. After a delay of 250 (short delay) or 500 ms (long delay), a target appeared. The target was a small vertical gray rectangle centered within the cue arrow (cued target) or within the vertical black bar on the opposite side of the fixation score (uncued target). Participants were told that a blue up-arrow (easy cue) signaled that a target appearing in that location (cued) would be 'easy' (i.e., own mean RT + 0.55 SD to react) and result in a sufficiently fast response about 75% of the time, whereas a target in the uncued bar's position would be 'hard' (i.e., own mean RT – 0.55 SD to react), that is, resulting in a too slow response about 75% of the time. A red down-arrow (hard cue) indicated that a cued target would be 'hard' (the response would be too slow 75% of the time) and an uncued target 'easy' (the response would be sufficiently fast 75% of the time). Additionally, they were informed that the cue would also indicate the probable location of the target, with 2/3 of the targets appearing in the cued location, and that occasionally no target would appear (catch trials). Participants were instructed to press the 'b' key as soon as they detected the target. Pressing the key before the target appeared or when no target appeared resulted in a loss of 10 points. Each block consisted of 32 cued, 16 uncued, and 8 catch trials, randomized across subjects (i.e., for every subject trials were presented in an independent order). Five hundred ms after the response (or 1 s following the delay interval on catch trials), the cue arrow and target were removed by reinstating the two black bars, and a feedback signal was presented below the central score. Feedback consisted of the same arrows as used for the cues. A blue up-arrow indicated a fast response or (accurate) non-response on catch trials. A red down-arrow signaled a slow response or (inappropriate) response on catch trials. After a delay of 250 ms, the score was updated (if changed). After a randomly selected ITI of 500 or 1000 ms, the next trial began by removing the feedback signal and blanking the score for 200 ms (see van Hemel-Ruiter et al., 2013 for more detailed descriptions of this task).

Feedback computation. At the end of each game, the participant's median RT and standard deviation were computed to calculate cut-offs for fast and slow responses on the next game of the same type (positive or negative). Consistent with the previous work of Derryberry and Reed, for easy targets, the response was labeled as fast if the RT was less than the median plus 0.55 times the standard deviation. For hard targets, a response was treated as fast if the RT was less than the median minus 0.55 times the standard deviation. If RTs equaled or exceeded these cut-offs, they were treated as slow. Because RTs tend to be about 25 ms slower after short delays, 12 ms were added to the cut-off for short-delay trials and subtracted for long-delay targets (see van Hemel-Ruiter et al., 2013 for more detailed task description, also see Derryberry & Reed, 2002. Because the response-window was adapted on-line on the basis of the participant's individual performance, there were no participants with extremely low scores.

Self-Reported Substance Use. Measures of alcohol, tobacco, cannabis, and other drug use were part of a larger self-report survey. At the third assessment wave, participants filled in these questionnaires at school, which was supervised by test assistants (see Huizink, Ferdinand, Ormel & Verhulst, 2006). At the fourth assessment wave a web-based survey method was used (see Nederhof et al., 2012). Substance use was calculated on quantity and frequency items of alcohol use (seven items, e.g., At how many days did you drink alcohol last week, How many times did you drink alcohol in your lifetime?), tobacco use (three items, e.g., Did you ever smoke, even if it was just one cigarette or a few drafts?), and cannabis use (three items, e.g., How many times did you use weed or hash in the last four weeks?; See Appendix 3A for an overview of all substance use questions). Drug use other than cannabis was left out of the substance use variable, to enable comparison with our previous cross-sectional findings (van Hemel-Ruiter et al., 2013). Because of their different scaling, standardized scores were used to calculate measures for alcohol, and cannabis use. Finally, as an index of general substance use, we used the means of the alcohol, tobacco, and cannabis measures to calculate a substance use measure (see the S1 Table in the Supporting Information for the Cronbach's alphas).

Data Reduction and Analysis

The SOT reaction time data were analyzed following Derryberry and Reed (2002). Trials with reaction times below 125 ms (probable anticipations) and above 1000 ms (probable distractions) were removed. Mean reaction times for correct responses are reported in Table 3.2.

Table 3.2
Mean score reaction times (M in ms) and standard deviations (SD) of SOT scores (N = 657 [a])

Type of game	Short Delay				Long Delay			
	Cued		Uncued		Cued		Uncued	
	Easy	Hard	Easy	Hard	Easy	Hard	Easy	Hard
	M(SD)	M(SD)	M(SD)	M(SD)	M(SD)	M(SD)	M(SD)	M(SD)
Positive	335(41)	366(47)	467(89)	470(89)	341(576)	378(67)	384(77)	377(73)
Negative	329(45)	357(52)	455(88)	458(92)	331(58)	365(67)	381(81)	373(77)

Note. SOT = Spatial Orienting Task; [a] The sample size reported reflects the weighted sample size.

Further, we computed the engagement and disengagement scores. That is, from positive game RT scores engagement towards reward was calculated by subtracting RT cued blue trials from RT cued red trials in the positive games, whereas difficulty to disengage from reward was calculated by subtracting RT uncued red trials from uncued blue trials. From negative game RT scores engagement towards non-loss was calculated by subtracting RT cued blue trials from RT cued red trials in the positive games, whereas difficulty to disengage from non-loss was calculated by subtracting RT uncued red trials from uncued blue trials. Hence, attentional bias for reward was represented in the positive games as both (1) a faster engagement toward cues of expected gain (blue arrow acting as correct cue for target; *cued blue trials*) than toward cues of expected non-gain (red arrows acting as correct cue for target; *cued red trials*) and (2) a slower disengagement from expected gain (blue arrow acting as incorrect cue for target; *uncued blue trials*) than from expected non-gain (red arrows acting as incorrect cue for target; *uncued red trials*). Analogously, attentional bias for non-punishment was represented in the negative games, by both (1) a faster engagement toward cues of expected non-loss (blue arrows acting as correct cue for target; *cued blue* trials) than toward cues of expected loss (red arrows acting as correct cue for target; *cued red trials*) and (2) slower disengagement from expected non-loss (blue arrow acting as incorrect cue for target; *uncued blue trials*) than from expected loss (red arrows acting as incorrect cue for target; *uncued red trials*). All scores were separately calculated for short-delay and long-delay trials (i.e., when there was less or more opportunity for voluntary control processes to regulate attention).

To investigate the relationship between attentional biases and prospective substance use we first performed a bivariate correlational analysis, which included prospective substance use, gender, age, all eight engagement and disengagement scores, and baseline substance use. Next, to test the unique predictive contribution of all engagement and disengagement scores, and baseline substance use in the prediction of substance use three years later we performed a stepwise hierarchical regression. Step 1 included age, gender, and baseline substance use and step 2 included the eight engagement and disengagement scores.

Table 3.3
Bivariate correlations of attentional bias scores and substance use (N = 657 [a])

		1	2	3	4	5	6	7	8	9	10	11	12
1	Prospective substance use	-											
2	Gender [b]	.12**	-										
3	Age at follow-up	.07	.02	-									
4	Attentional engagement toward reward (S-D)	.04	.03	-.07	-								
5	Difficulty disengaging from reward (S-D)	-.07	-.07*	-.01	-.04	-							
6	Attentional engagement toward non-punishment (S-D)	.11**	.03	-.09*	.29**	-.05	-						
7	Difficulty disengaging from non-punishment (S-D)	.00	.05	.04	.01	.03	-.07	-					
8	Attentional engagement toward reward (L-D)	.11**	.00	-.02	.24**	.01	.13**	-.06	-				
9	Difficulty disengaging from reward (L-D)	-.01	.00	.00	-.02	.04	-.09*	-.03	-.01	-			
10	Attentional engagement toward non-punishment (L-D)	.06	.03	-.05	.25**	.04	.20**	.04	.20**	.01	-		
11	Difficulty disengaging from non-punishment (L-D)	-.03	-.01	-.04	-.01	.04	-.08*	.00	-.08*	.04	.00	-	
12	Baseline substance use	.72**	.02	.10**	.10*	-.04	.13**	.02	.14**	-.02	.07	-.02	-

Note. S-D = short-delay; L-D = long-delay; [a] The sample size reported reflects the weighted sample size; [b] 0 = Female; 1 = Male; * $p < 0.05$; ** $p < 0.01$.

RESULTS

Reliability

Split-half correlations with Spearman-Brown corrections demonstrated substantial internal consistency for SOT mean RT's (*r*s = 0.54–0.79) whilst attentional bias scores showed only low to moderate internal consistency (*r*s = 0.00 to 0.34).

Correlation analysis

Our first hypothesis was that prospective substance use would be predicted by baseline engagement toward both rewarding cues and cues of non-punishment. Table 3.3 shows that engagement toward rewarding cues (but only for long-delay trials) and engagement toward cues of non-punishment (but only for short-delay trials) correlated weakly to prospective substance use. Additionally, prospective substance use was weakly correlated with gender, and very strongly with baseline substance use ($r = 0.72$, $p < 0.01$).

Table 3.4
Hierarchical regression model for variables explaining prospective substance use (N = 657 [a])

Variable		Beta	t	R^2 Change
Step 1				
	(Constant)		-0.10	
	Gender [b]	0.11	3.86**	
	Age	0.00	-0.00	
	Baseline Substance Use	0.71	26.13**	0.52
Step 2				
	(Constant)		-0.04	
	Gender [b]	0.10	3.80**	
	Age	0.00	-0.06	
	Baseline Substance Use	0.71	25.50**	
	Engagement toward reward (S-D)	-0.05	-1.64	
	Engagement toward non-punishment (S-D)	0.02	0.53	
	Engagement toward reward (L-D)	0.02	0.54	
	Engagement toward non-punishment (L-D)	0.02	0.68	
	Disengagement from reward (S-D)	-0.03	-1.00	
	Disengagement from non-punishment (S-D)	-0.01	-0.50	
	Disengagement from reward (L-D)	0.01	0.31	
	Disengagement from non-punishment (L-D)	-0.02	-0.70	0.00

Note. S-D = short-delay; L-D = long-delay. R^2 final model = 0.52**; Adjusted R^2 = 0.52; [a] The sample size reported reflects the weighted sample size; [b] 0 = Female; 1 = Male; * $p < 0.05$; ** $p < 0.01$.

Regression analysis

The hierarchical regression analysis showed gender, and baseline substance use predicted unique variance of adolescent substance use three years later, but the engagement and disengagement scores showed no predictive validity on top of these variables. Overall, the full model explained 52% (R^2adjusted = 0.52, F(11, 645) = 64.48, p <0.001) of all variance (Table 3.4). The model showed that male adolescents showed a larger increase in substance use than female adolescents, yet reward related attentional biases showed no predictive value for future substance use over three years follow-up.

Post-hoc analysis

That reward biases did not contribute to the increase in substance use over three years was unexpected. This could indicate that these reward biases are not involved in the increase of existing substance use, but in initial use. The incidence of alcohol, tobacco, and cannabis use at baseline was too high to explore this possibility. In contrast, only 5.5% of the adolescents in the current sample had used illicit drugs other than cannabis at baseline, while 13.4% had used these drugs three years later. We first tested the predictive value of attentional biases at T3 on illicit drug use (user/nonuser) at T4 by performing a logistic regression analysis in the subsample of non-illicit (other than cannabis) drug users at T3. The results showed that none of the attentional bias scores, but only substance use (OR = 5.25, Wald's χ^2 = 56.37, p < 0.01) at T3 could predict whether one would start using illicit drug in between T3 and T4. We therefore selected the adolescents who started using illicit drugs in between baseline and follow-up (n = 53), and examined the prospective relationship between the strength of reward-related biases and the level of subsequent illicit drug use to shed light on the relationship between reward biases and substance use in the initiation stage. First, we performed a bivariate correlation analysis including age, gender, substance use T3, all engagement and disengagement scores and illicit drug use at follow-up. The correlational analysis showed that gender, age, and engagement toward non-punishment in the long-delay trials were positively related to illicit drug use at follow-up. Subsequently, we conducted a regression analysis in the prediction of level of illicit drug use three years later and included gender, age and substance use at T3 in step 1, and engagement toward non-punishment in the long-delay trials in step 2. This full model explained 30% (R^2 adjusted = 0.24, F(4, 48) = 5.20, p < 0.01) of all variance (Table 3.5), and showed that age and engagement toward non-punishment in the long-delay trials explained unique variance. That is, within the group of adolescents who started using illicit drugs in between both measures those who were older, and those who showed stronger engagement toward longer presented cues of non-punishment reported a higher level of illicit drug use. Because of the skewed distribution of illicit drug use, we log10 transformed this variable, and repeated the analysis with this transformed variable as the dependent variable in the regression model. The results of the analysis were comparable to the original analysis. We therefore chose to report only the original analysis.

Table 3.5
Hierarchical regression model for variables explaining prospective illicit drug use (amphetamine, cocaine, magic mushrooms) in adolescents who started using illicit drugs in between baseline and follow-up (n = 52[a])

Variable		Beta	t	R^2 Change
Step 1				
	(Constant)		-2.72**	
	Gender [b]	0.31	2.44*	
	Age	0.35	2.78**	
	Substance Use T3	0.21	1.68	0.24
Step 2				
	(Constant)		-3.00**	
	Gender [b]	0.25	2.05*	
	Age	0.37	3.05**	
	Substance Use T3	0.12	0.97	
	Engagement toward non-punishment (long-delay)	0.27	2.11*	0.07

Note. R^2 final model = 0.30**; Adjusted R^2 = 0.24; [a] The sample size reported reflects the weighted sample size; [b] 0 = Female; 1 = Male; * $p < 0.05$; ** $p < 0.01$.

DISCUSSION

Previous cross-sectional research has shown that adolescent substance use is related to a relatively strong automatic engagement toward non-punishment and a relatively strong voluntary engagement toward reward (van Hemel-Ruiter et al., 2013). As an important next step, the present study tested whether these reward-related attentional biases would also show a predictive relationship with adolescent substance use at a three-year follow-up. This relationship was tested in a large representative cohort of adolescents. The criterion validity of reward-related attentional biases was supported with results showing that a relatively strong automatic engagement toward non-punishment and a relatively strong voluntary engagement toward reward correlated with adolescent substance use at three-year follow-up. However, the findings did not support the idea that reward-related attentional biases predict changes in substance use behavior. This lead to the idea that these reward biases might not be involved in the increase, but specifically in the initiation phase of substance use. The post-hoc analysis that was restricted to the subgroup of adolescents who started using illicit drugs (other than cannabis) in the three years following the assessment of the biases provided preliminary supportive evidence for reward-related attentional bias as a predictor of future drug use. Stronger voluntary engagement toward non-punishment showed independent predictive value for the prospective level of illicit drug use.

This study therefore leads to three main findings. First of all, it extends the previous finding that adolescent substance use is related to relatively strong preferential orienting of the attention toward cues of reward and non-punishment (van Hemel-Ruiter et al., 2013). That is, this study elongated the previous study by showing that reward bias was not only correlated with substance use at the same time, but also with substance use at three years follow up.

Second, the appetitive attentional biases that were correlated with substance use represented the attentional process of enhanced engagement to reward and non-punishment related cues, instead of a difficulty to disengage from these cues. It seems therefore that adolescent substance use is characterized by preferential orienting of the attention, but not by a difficulty to redirect attention away from appetitive cues. However, there is no straightforward explanation for the apparent differential involvement of short-delay vs. long-delay trials in the engagement scores for alcohol, tobacco, and cannabis use. Especially because the results showed differential patterns related to the use of different substances. We can only speculate about the differential predictive value of more automatic and more controlled attentional engagement. One possibility for this pattern could be that a strong automatic engagement toward non-punishment relative to punishment reflects a weak automatic tendency to attend to negative consequences (e.g., fear of getting a hang-over), and that a strong voluntary engagement toward reward relative to nonreward represents a heightened voluntary tendency to attend to positive outcomes (i.e., attaining a pleasant feeling after substance use). Further, a strong voluntary engagement toward non-punishment relative to punishment could reflect a weak voluntary tendency to attend to negative consequences. However, to reach a conclusive explanation, it is needed to replicate and test further these indexes related to substance use.

Finally, we found no predictive involvement of appetitive bias in the increase in substance use in adolescents who already started using substances. A post-hoc analysis did support a prognostic relationship between appetitive bias and level of future substance use in those who initiated the use of a substance (i.e., drugs) after the baseline assessment. These findings give rise to the view that perhaps appetitive bias is especially important in the initiation stages of adolescent substance use. Such a view would be in line with the idea that a heightened sensitivity for stimuli that signal unconditioned reward and relief from punishment (Gray, 1970; 1982), might predict the development of substance (ab)use. From this perspective, high attentional sensitivity to reward-related stimuli might be a risk factor for heavy initial use, and other factors for the further development and persistence of substance use once substance use behavior has reached a certain level.

As a more critical test of the relevance of attentional bias for the start of using substances such as alcohol, nicotine, and cannabis, it would be important to assess reward-related attentional bias in an even younger sample before they start using these substances. This would give the opportunity to investigate whether reward-related attentional biases precede the initiation of adolescent substance use. In addition, it would be important for future research to examine the effects of modifying attentional bias away from reward cues on subsequent substance use (cf., Fadardi & Cox, 2009; Schoenmakers et al., 2010), as this would provide important information regarding the causal status of reward bias.

Several limitations of the study should be taken into account when interpreting the results. Perhaps most important, it should be acknowledged that the effect-sizes of the predictive relationships were rather small (i.e., R^2 adj = 0.03). Nevertheless, given the relatively small range in substance use in the sample, together with the methodological restrictions of the behavioral measure used (i.e., reaction time measures such as the SOT provide only a rough indicator of the actual attentional processes), small effects are also noteworthy. Further, the importance of small effects in this research area is underscored by the considerable risks for negative health and social consequences of substance use behavior. From this perspective, the convergence of findings between the current study and previous research (van Hemel-Ruiter et al., 2013) suggests a reliable relation between attentional bias for reward and substance use that may serve as a potentially useful point of prevention or intervention. A related limitation is, that although the RT's scores showed good internal consistency, attentional bias scores showed only low to medium split-half correlations. However, for a good understanding of the reliability of this measure, also a test-retest reliability has to be performed. Nevertheless, the interpretations of the SOT scores have to be taken with caution, and more studies are needed to examine the psychometric properties of this measure. An additional point of consideration is that participants might not have been entirely honest in reporting their substance use. Yet, self-report measures of substance use have been found to be valid and reliable as long as confidentiality and anonymity is guaranteed (Del Boca & Darkes, 2003) as was the case in the present study. Lastly, the performance measure was one of the last in a longer sequence of behavioral tasks, and fatigue might have influenced participants' performance.

In summary, consistent with the view that a generally enhanced attentional bias for appetitive cues may set adolescents at risk for developing excessive substance use, this study showed that enhanced attentional engagement toward cues of reward and non-punishment was associated with adolescent substance use three years later. Although reward-related biases showed no predictive value for an increase in use between middle and late adolescence, a post-hoc analysis provided first evidence that reward biases do have predictive value for the level of illicit drug use for those who started using in the follow-up period. As a more critical test of the relevance of attentional bias in the overall initiation of substance use it would be important to test reward-related attentional bias in an even younger sample, in which participants have not already started using addictive substances. Another interesting next step would be to follow an experimental approach designed to reduce reward bias (Houben, Havermans, Nederkoorn & Jansen, 2012), and to test whether such manipulation would prevent the initiation or reduce the level of substance use in adolescents. If so, this would not only provide more direct support for the (causal) role of reward bias in adolescent substance use, but also a fresh theory-derived clinical tool to prevent the development of substance abuse and addiction.

APPENDIX 3A

Items and response categories of self-reported substance use, subdivided by substance (alcohol, tobacco, cannabis)

Item	Substance	Question	Response categories
1	Alcohol	At how many days did you drink alcohol last week	0-7 = 0 to 7 days
2		How many glasses of alcohol did you drink last week	0-6 = 0 to 6 glasses, 7 = 7-10 glasses, 8 = 11 or more glasses
3		How many times did you drink alcohol in your lifetime?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more
4		How many times did you drink alcohol in the last twelve months?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more
5		How many times did you drink alcohol in the last 4 weeks?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more
6		At how many week days do you normally drink alcohol?	0-3 = 0 to 3 days
7		How many glasses of alcohol do you normally drink at a week day?	0-6 = 0 to 6 glasses, 7 = 7-10 glasses, 8 = 11 or more glasses per day
8		At how many weekend days do you normally drink alcohol?	0-3 = 0 to 3 days
9		How many glasses of alcohol do you normally drink at a weekend day?	0-6 = 0 to 6 glasses, 7 = 7-10 glasses, 8 = 11 or more glasses per day
10	Tobacco	Did you ever smoke, even if it was just one cigarette or a few drafts?	0 = never, 1 = 1 or 2 times, 2 = not every day, 3 = I stopped, 4 = every day
11		How many cigarettes do you normally smoke at a smoking day?	Continuous, 0 - ∞
12		How many cigarettes did you smoke in the past four weeks?	0 = I never smoke, 1 = 0 cigs, 2 = less than 1, 3= 1-5 cigs, 4 = 6-10 cigs, 5 = 11-20, 6 = 20 or more
13	Cannabis	How many times did you use weed or hash in your lifetime?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more
14		How many times did you use weed or hash in the last twelve months?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more
15		How many times did you use weed or hash in the last four weeks?	1-10 = 1 to 10 times, 11 = 11-19 times, 12 = 20-39 times, 13 = 40 times or more

Note. Cronbach's alpha alcohol items: baseline = 0.87, follow-up = 0.86; Cronbach's alpha tobacco items: baseline = 0.92, follow-up = 0.93; Cronbach's alpha cannabis items: baseline = 0.92, follow-up = 0.89; Cronbach's alpha all items: baseline = 0.69, follow-up = 0.62

CHAPTER 4

Appetitive and regulatory processes in young adolescent drinkers

Published as:
Van Hemel-Ruiter, M. E., de Jong, P. J., & Wiers, R. W. (2011).
Appetitive and regulatory processes in young adolescent drinkers.
Addictive Behaviors, 36(1-2), 18-26.

ABSTRACT

Dual-process models of addiction propose that alcohol (mis)use develops because of an imbalance between a fast automatic appetitive system, in which stimuli are valued in terms of their emotional and motivational significance and a slower controlled regulatory system, which acts on deliberate considerations. This study focused on the automatic and regulatory processes that are involved in the early stages of young adolescent alcohol use. Participants were 43 young adolescent drinkers, who completed an explicit alcohol valence measure, two versions of an Affective Simon Task (AST), a working memory task and an alcohol use questionnaire. Alcohol use was associated with relatively positive self-reported valence of alcohol pictures, especially for adolescents with lower inhibition capacity. The Affective Simon Tasks did not show stronger automatic approach tendencies in heavier drinkers. This study suggests that in early stages of alcohol use appetitive valence is a more important stimulator for the initiation of alcohol use than automatic approach tendencies, and supports the view that young adolescents with low inhibition capacity are especially at risk for developing alcohol misuse. Prevention therefore should be focused on reducing the attractive valence of alcoholic drinks and strengthening the cognitive control of at-risk children.

INTRODUCTION

Recent dual-process models of addiction differentiate between a relatively automatic appetitive or impulsive system and a relatively controlled or regulatory system, both of which are assumed to be involved in the development of alcohol use and misuse (e.g., Deutsch & Strack, 2006; Evans & Coventry, 2006; Stacy & Wiers, 2010; Wiers et al., 2007). According to these models, the automatic appetitive system, in which stimuli are valued in terms of their emotional and motivational significance, automatically elicits heightened attention and triggers motivational orientation (approach or avoid). With repeated drug use, drug stimuli may acquire conditioned incentive properties, and as a consequence, they are able to grab the attention and to elicit approach behaviors (Robinson & Berridge, 1993). This same prediction of substance-related attentional bias and subjective motivational states is made by other recent models of addiction (see for a review, Field & Cox, 2008).

Additionally, current dual-process models assign a moderating role to the regulatory executive system, which is proposed to act through deliberate controlled processes. These processes are suggested to inhibit more automatic, impulsive thinking and behavior (e.g., Barrett et al., 2004; Strack & Deutsch, 2004). From this view, the automatic appetitive processes will guide alcohol-use behavior, unless the ability (e.g., cognitive resources) and motivation to regulate this behavior are available (Fazio & Towles-Schwen, 1999). The regulatory brain system is usually not fully matured before late adolescence and repeated exposure to alcohol interferes with the maturation processes, which may even cause lifelong diminished self-regulation (Moselhy, Georgiou, & Kahn, 2001; Vogel-Sprott, Easdon, Fillmore, Finn & Justus, 2001). Furthermore, alcohol intake appears to have an acute weakening effect on the controlled regulatory processes, whereas the automatic processes can even be amplified by drinking alcohol (Field, Schoenmakers, & Wiers, 2008). Consequently, together with the notion that adolescents express minimal motivation to remain abstinent, early adolescence is considered to be a sensitive stage for developing excessive alcohol use (Wiers et al., 2007).

To further our understanding of the processes that are involved in the initiation stages of drinking, it is therefore important to focus on young adolescents who just started drinking. This may provide welcome theory-derived clues for prevention and treatment. Research showed that most adolescents in the Netherlands have their first alcoholic drink between the age of eleven and fifteen. From the age of fourteen, binge drinking (i.e., drinking five or more glasses at one occasion) substantially increases and around the age of late adolescence most drinkers have considerable drinking histories (Monshouwer et al., 2008).

Therefore, the major aim of this study was to investigate the interplay of relatively automatic appetitive and regulatory processes in the early development of alcohol misuse. Recently, a variety of implicit alcohol approach measures were developed to assess automatic appetitive behavior. A series of studies have successively demonstrated automatic alcohol approach tendencies in adult and late-adolescent heavy drinkers (Field et al., 2008; Field et al., 2005; Palfai & Ostafin, 2003; Wiers et al., 2009). However, to our knowledge, there was no previous study that specifically focused on young adolescent drinkers.

To assess automatic approach tendencies, we used two modified versions of the Affective Simon Task that was originally designed by De Houwer and colleagues (AST; De Houwer et al., 2001). In these tasks, participants are shown pictures representing alcoholic or non-alcoholic drinks. Importantly, the required approach or avoidance response was not guided by the content of the picture (e.g., alcoholic drink) but by the format of the picture (i.e., portrait or landscape; Huijding & de Jong, 2005). The underlying idea is that the automatic evaluation of the picture content elicits relatively automatically (in the sense of non-intentionally) action tendencies and may thus lead to facilitation or interference with the required response. Accordingly, a picture with an attractive content is assumed to automatically elicit an approach tendency and thus to result in faster responding when the response requirement is to approach the picture and slower responding when the response requirement is to avoid the picture.

In one task, participants had to move a manikin towards or away from the picture, depending on the picture's format (AST - manikin; see e.g., De Houwer et al., 2001, exp 4). Previous research in the context of eating disorders has shown that the AST - manikin is sensitive to individual differences (Veenstra & de Jong, 2010). In the other task, participants had to push or pull pictures with a joystick (AST - joystick; as in Rinck & Becker, 2007). This task thus requires actual arm movements towards or away from the picture which may strengthen the perception of approach and avoidance (Chen & Bargh, 1999; Markman & Brendl, 2005; Rotteveel & Phaf, 2004; Tops & de Jong, 2006). In addition, the pictures reduce in size as a result of pushing, whereas they increase in size following pulling (i.e., 'zooming-effect'). This task feature elicits the visual impression of approach and avoidance. This AST - joystick has already been successfully applied in adult populations (alcohol AAT; Wiers et al., 2009; Wiers et al., 2010). For both implicit tasks, automatic approach tendencies are expressed in the difference in approach vs.

avoid (i.e., time needed to push/ move manikin away minus time needed to pull/ move manikin towards), as a function of stimulus content (see e.g., Rinck & Becker, 2007). The inclusion of two indices of automatic approach tendencies is worthwhile for two reasons. First, the reliability of underlying assumption can be improved. In other words, when the results of both measures point to the same conclusion, this conclusion can be drawn with more confidence than when using either measure alone. Second, since the way in which approach and avoid are expressed differs for both tasks, this provides the opportunity to test the relative efficacy of both tasks as a predictor of alcohol use (cf., Krieglmeyer & Deutsch, 2010).

It is suggested that automatic appetitive processes can be activated without awareness, intention, and even apart from approval (e.g., Gawronski & Strack, 2004; Strack & Deutsch, 2004). From this view, an alcohol stimulus may elicit automatic approach tendencies, independent of whether a person consciously evaluates this stimulus positive or negative. In line with this, both implicit and explicit measures of alcohol expectancies, attitudes and cognition were shown to add unique variance to the prediction of alcohol use (Jajodia & Earleywine, 2003; Palfai & Wood, 2001; Reich, Below & Goldman, 2010; Stacy, 1997; Thush & Wiers, 2007; Wiers, Van Woerden, Smulders & de Jong, 2002). Therefore, we measured both automatic tendencies to approach or avoid alcohol and more deliberate subjective appetitive evaluations of alcohol.

As an explicit appetitive measure, we included a self-report alcohol-valence rating-task (Mogg et al., 2003; Pulido, Mok, Brown, & Tapert, 2009; Wiers et al., 2009; Wiers, Rinck, Kordts, Houben & Strack, 2010). In this task, participants had to rate the appetitive valence (i.e., attractiveness) of alcohol pictures on a visual analogue scale (VAS). Research using a valence rating scale among college students, showed that positive appetitive evaluations of alcohol cues were positively related to alcohol use (Drobes, Carter & Goldman, 2009; Pulido et al., 2009). In a similar vein, previous studies using other explicit measures frequently showed that adolescent substance use is characterized by stronger positive explicit alcohol outcome expectancies (Christiansen, Smith, Roehling & Goldman, 1989; Drobes et al., 2009; Goldman, Del Boca & Darkes, 1999; Palfai & Wood, 2001; Stacy, 1997; Thush & Wiers, 2007; Thush et al., 2007, 2008; Wiers et al., 1997). These self-reported expectancies were especially found to be strong correlates of concurrent alcohol use, whereas in prospective studies these findings were less strong, in particular after controlling for previous alcohol use (Jones et al., 2001; Sher et al., 1996). As a positive appetitive evaluation of alcohol will logically contribute to people's motivation for using alcoholic drinks, we expected alcohol use in early adolescents to be positively related to subjective appetitive valence of alcohol. In line with this, a previous study found positive explicit alcohol valence to be correlated with positive explicit alcohol expectancies (Drobes et al., 2009).

As a second issue, we explored whether the relationships between subjective appetitive valence and alcohol (mis)use as well as between automatic approach tendencies and alcohol (mis)use is moderated by executive control. Previous research provided preliminary evidence indicating that indeed the predictive validity of automatic appetitive processes for alcohol misuse in adults as well as in adolescents is restricted to individuals with relatively weak executive control (Farris et al., 2010; Grenard et al., 2008; Houben & Wiers, 2009; Thush et al., 2008). It seems reasonable to assume that also the predictive value of explicit appetitive valence for alcohol use would be especially pronounced in individuals with weak executive control. It is likely that similar to automatic approach tendencies also subjective appetitive evaluations reflect short-term ratifications (i.e., that beer looks really tasty), whereas executive control makes long-term consequences (i.e., drinking alcohol will make me feel sick) more available (e.g., Thush et al., 2008). Accordingly, we expected that the relationship between subjective appetitive valence and alcohol approach tendencies on the one hand and alcohol use on the other hand would be especially pronounced in young adolescents with relatively low working memory capacity (as a proxy of executive control). To test this, we included a random number generation task (RNG; Jahanshahi, Saleem, Ho, Dirnberger, & Fuller, 2006) as a quick and easy measure of working memory capacity (WMC). This measure assesses the executive functions of inhibition, which reflects the ability to deliberately inhibit dominant, automatic, or prepotent responses when necessary (Miyake, Friedman, Emerson, Witzki, & Howerter, 2000); a function that has been argued to be critically involved in the development and maintenance of addictive behaviors (Wiers et al., 2007).

METHOD

Participants and recruitment

Participants were recruited from a Dutch low-level secondary school. After principals' approval, students of second to fourth classes were invited to participate. Students were informed that the study concerned alcohol-drinking behaviors, and that participants would have to perform a series of computer tasks and fill in questionnaires. The underage students who agreed to participate in this study received an information letter and an informed consent form for their parents as well. A total of 55 students (24 male and 31 female) agreed to participate and returned the signed parental informed consent form. At the alcohol use questionnaire, three participants reported no use of alcohol ever in their lives and another nine reported no drinks in the last month. All twelve were excluded from analyses. A total number of 43 high school students (21 male and 22 female), aged 13 – 17 years (M = 15.09, *SD* = 0.97) thus remained in the final analyses. Self-reported mean alcohol use was 6.71 Dutch standard alcoholic drinks per week (*SD* = 7.67). A substantial proportion of these adolescents (65 %) indicated having one or more binges (five or more Dutch standard alcoholic drinks on one occasion) in the past two weeks. The study was approved by the Ethical Committee Psychology of the Psychology Faculty of the University of Groningen.

Material

Alcohol use. Alcohol use was measured through a shortened version of a self-report Dutch alcohol use questionnaire (Wiers et al., 1997), based on the timeline follow-back method (Sobell & Sobell, 1990). Participants were asked to estimate how many alcoholic drinks they normally drink on each day of the week, on how many occasions they drank alcohol in the last four weeks and on how many days of past month they consumed five standard glasses or more (ranging from 'I never drink' to 'seven times or more' on a 6-point Likert scale). We transformed every alcoholic consumption to standard Dutch glasses (i.e., about 11 ml of pure alcohol). A measure for alcohol consumption was calculated by taking the standardized scores of three measures: frequency of alcohol use, mean number of glasses on a drinking day (quantity) and number of binges in the last two weeks (cronbach's alpha = 0.65).

Implicit Measures. Computer tasks were performed at an AMD - Athlon XP1400 laptop computers with 14 inch 60 Hz screen (resolution of 1024 × 768). Participants were seated at a distance of 50 centimeters from the computer screen in an active position. They were asked to read the instructions that were shown at the computer screen carefully and were instructed explicitly to react as fast as possible and to make as little errors as possible. Two modified version of the Affective Simon Task (AST; designed by De Houwer et al., 2001) were used to assess automatic approach tendencies: the AST - manikin and the AST - joystick (based on the AAT; Rinck & Becker, 2007).

AST – manikin. Each trial started with the appearance of a picture in the middle of a black screen and a white manikin above or beneath the picture. Participants had to move the manikin towards or away from the picture by pressing the arrow buttons (i.e., ↑ or ↓) five times. With every button press the legs of the manikin changed size, which created an actual movement sensation. The picture disappeared when a correct movement was made (i.e., when by correct approach the manikin crossed the picture border or by correct avoidance the manikin crossed the screen border). In order to get an equal travel distance in both formats, high and wide pictures had the same height (i.e., high pictures were 270 × 384 pixels and wide pictures 545 × 384 pixels). The test pictures were presented in random order.

AST – joystick. A 'Logitech Attack 3' joystick was attached to the computer and fixed at the table in between an exact distance of the participant and the computer screen. It was ensured that joystick push motions were directed towards and pull motions away from participants' body. Participants started each trial by a push on the trigger, which made a picture appear at the black screen. A joystick push or pull movement made the picture smaller or larger and eventually disappear. High pictures were 330 × 468 pixels and wide pictures 468 × 330 pixels, whereas picture size was equal in both formats. The test pictures were presented in a pseudo-random order, i.e., we made one random order with the restriction that no more than three pictures of the same category were presented consecutively (as in Rinck & Becker, 2007) and used this fixed order for all participants. We used a fixed order across participants to reduce method variance. This is assumed to enhance the sensitivity of the ASTs as a measure of individual differences, which is important in view of the aim of the present study (cf., Asendorpf, Banse, & Mücke, 2002).

Stimuli. To prevent carry-over effects we made two sets of pictures (set A and set B), each of ten alcohol pictures and ten soda pictures that were matched on content and appearance. All soda pictures and half of the alcohol pictures were selected from a set that was used in an alcohol AAT study with students (Wiers et al., 2009). We made ten supplementary alcohol pictures from popular drinks among young adolescents. We presented one set in the AST - manikin and the other set in the AST - joystick to half of the participants and the reverse to the other half of the participants.

Design. The AST - manikin as well as the AST - joystick consisted of a practice block of 20 trials, followed by two test blocks of 100 trials each. Each block had 40 alcohol trials and 40 soda trials. Stimuli were pictures of alcoholic drinks or sodas, which were presented at a black background. Every picture was presented four times per block, twice in portrait (high) and twice in landscape (wide) format. Furthermore, there were 20 neutral trials (i.e., empty white frames presented on a black background; ten times high and ten times wide format). Half of the participants was ordered to approach (pull/ move manikin towards) high pictures and avoid (pull/ move manikin away from) wide pictures and half had to approach wide pictures and avoid high pictures. Task order (first AST - manikin or first AST - joystick) and instructions (approach wide/avoid high in AST - manikin and/or AST - joystick; approach high/avoid wide in AST - manikin and/or AST - joystick) were counterbalanced across participants.

Subjective appetitive valence. A computerized Visual Analog Scale (VAS) which was programmed in E-prime was used to assess subjective appetitive valence for alcohol pictures. We used the same pictures as in the implicit tasks allowing to make straightforward comparisons between subjective valence and automatic approach tendencies. Each alcohol and soda picture was presented in random order at the computer screen. Participants had to rate the affective valence for each picture on a VAS, anchored at extreme left end for 'dat ziet er vies uit' ('that looks really disgusting') and extreme right end for 'dat ziet er lekker uit' ('that looks really tasty'), by placing a dash mark where they thought appropriate. The dash was set by a mouse click on the VAS, and if necessary it was possible to subsequently move it to the appropriate place. It was emphasized that they were to judge the attractiveness of the total picture, not just the drink as a concept.

Random Number Generation Task (RNG; Jahanshahi et al., 2006). RNG was taken with response pace at one digit per second (which was indicated by a metronome adjusted to 60 bpm). Participants were instructed to generate a random sequence of digits ranging from 1-10, for a period of 100 beats (100 seconds), by naming one digit with each tone. To explain the concept of randomness we used Baddeley's (1966) analogue of picking a digit from a hat, reading this digit out loud, place it back in the hat, shake it and take the next digit. We underlined that the concept of randomness would not include supremacy of repetitions or adjacent number values. Participants were told to listen to the rhythm of tones and adjust their speed when they would fell behind or walk in front of this rhythm. A total of 100 numbers were entered, which were written down and used to generate the critical inhibition component, composed of the standardized mean score on 'TPI', and the reversed standardized mean scores on 'Runs', 'A', and 'RNG' (cronbach's alpha, 0.93) using the RcCalc Program (Towse & Neil, 1998).

Procedure

The teachers' room was temporarily set up as a computer lab. Two laptop computers were set up for computer-based assessments, in order to be able to test two students at one time. Before starting participants were informed about the study and signed informed consent. The assessments were administered in a set order: first, the RNG task was taken orally; second the implicit computer tasks (AST - joystick and AST - manikin, balanced in order across participants) and the VAS rating task; and finally the paper-and-pencil questionnaires; demographic questionnaire and alcohol use questionnaire. The entire assessment took about one period (50 minutes). After completing the test, participants were thanked for their participation and received a small present (i.e., a box of chocolates).

RESULTS

Preliminary analyses

AST – manikin. Mean reaction times longer than 3 SD (5848 ms) and trials with first key press before 200 ms were removed as outliers. A measure for approach tendency (AST - manikin effect) was obtained by subtracting median approach reaction time from median avoidance reaction time; a larger AST - manikin effect therefore represents a larger approach tendency. Table 4.1 shows the mean AST - manikin reaction time data.

AST – joystick. One participant with error trial percentage above 3 SD (13%) was discarded as outlier. Another participant was omitted due to testing error; the used set of pictures accidentally was equal for AST - joystick and AST - manikin. From the remaining participants (95% of the initial participants) AST - joystick error trials (i.e., incorrect complete responses; a 4.4%) as well as trials below 200 ms and above 3 SD (1526 ms) were excluded from analysis. A measure for approach tendency (AST - joystick effect) was obtained by subtracting median approach reaction time from median avoidance reaction time; a larger AST - joystick effect therefore represents a larger approach tendency. Table 4.1 shows the mean AST-joystick reaction time data.

Table 4.1

Mean score reaction times of AST - manikin and AST - joystick .

	Alcohol				Soda			
	Approach		Avoid		Approach		Avoid	
	M	(SD)	M	(SD)	M	(SD)	M	(SD)
AST - manikin	1324	(105)	1406	(135)	1313	(120)	1420	(125)
AST - joystick	757	(98)	747	(102)	749	(99)	744	(93)

Note. AST = affective simon task; SD = standard deviation; Mean scores are calculated by subtracting median approach reaction time from median avoidance reaction time; More positive scores therefore represent larger approach tendencies.

Table 4.2

Bivariate correlations of implicit and explicit measures and alcohol use

	1	2	3	4	5	6	7	8	9
1 Age	-								
2 Gender	-.53**	-							
3 Alcohol Use	.16	-.05	-						
4 Alcohol AST - manikin effect	-.17	.01	-.27	-					
5 Sodas AST - manikin effect	-.23	.19	-.06	.36*	-				
6 Alcohol AST - joystick effect	-.12	.00	-.32*	.27	.08	-			
7 Sodas AST - joystick effect	-.22	.26	-.14	.05	.11	.61**	-		
8 Subjective alcohol valence	.06	-.31*	.37*	.13	-.11	-.03	-.10	-	
9 Subjective soda valence	-.09	.12	-.08	.20	.03	-.27	-.06	.11	-

Note. AST = affective simon task; * p < 0.05 (two tailed); ** p < 0.01 (two tailed).

Bivariate analyses

Table 4.2 shows that alcohol use correlates with alcohol AST - joystick effect (r = -0.32, p = 0.04) and with subjective alcohol valence (r = 0.37, p = 0.01). Furthermore, alcohol AST - manikin effect showed borderline correlation with alcohol use (r = -0.27, p = 0.08), and a trend to a correlation was found with alcohol AST - joystick effect (r = 0.27, p = 0.1). Implicit measures were not correlated with self-reported alcohol or soda valence (all ps > 0.2).

Controlling for alcohol valence, partial correlations between alcohol AST - joystick effect and alcohol use remained significant (r = -0.34, p = 0.03) and borderline significant between alcohol AST - manikin effect and alcohol use (r = -0.28, p = 0.09). Beyond subjective alcohol valence, the relationship between alcohol

AST - joystick effect and alcohol use still explained unique variance, albeit remarkably negative and less convincing for the relationship between alcohol AST - manikin effect and alcohol use.

Table 4.3
Summary of three regression models for valence and AST variables predicting alcohol use

		Model 1		Model 2		Model 3	
Variable		Sign	ΔR^2	Sign	ΔR^2	Sign	ΔR^2
Step 1							
	(Constant)	ns		ns		ns	
	Age	ns		ns		ns	
	Gender	ns		ns		ns	
Step 2	Subjective soda valence	ns		ns		ns	
	Subjective alcohol valence	<0.01		<0.01		<0.01	
Step 3	Soda AST - manikin effect	ns		##		ns	
	Soda AST - joystick effect	##		ns		ns	
Step 4	Alcohol AST - manikin effect	<0.05	0.09*	##		ns	
	Alcohol AST - joystick effect	##		<0.05	0.11*	<0.1	0.12
		R^2 = 0.29		R^2 = 0.34		R^2 = 0.36	

Note. AST = affective simon task; ## Variable not included in the model; * p < 0.05. ** p < 0.01.

Hierarchical linear regression analyses

To test the relative importance of positive subjective alcohol valence and enhanced implicit alcohol approach tendencies in the prediction of early alcohol use we performed a series of hierarchical linear regressions, which also enabled us to test the relative efficacy of both Affective Simon Tasks. The first two models tested whether each implicit measure (in model 1 the AST - manikin, in model 2 the AST - joystick) separately could explain unique variance in alcohol use beyond subjective alcohol valence. The last model tested the hypothesis that each implicit measure could explain unique variance in alcohol use beyond subjective alcohol valence and beyond each other's effects. Therefore, next to subjective alcohol valence, in the first model we included only AST - manikin effect as a predictor, in the second model only AST - joystick effect and in the final model both AST - manikin and AST - joystick effects. In all three models a stepwise hierarchical procedure was used. In step 1 age and gender were entered into the regression equation as background variables. In step 2 both alcohol valence and soda valence scores were added, to get insight in the unique contribution of alcohol valence and adjust for general valence. Next, the implicit approach effects (model 1 only AST - manikin, model 2 only AST - joystick, model 3 both AST - manikin and AST - joystick) for soda trials were entered to correct for general appetitive approach tendencies. In the final step we added alcohol approach effects (model 1 only AST - manikin, model 2 only AST - joystick, model 3 both AST - manikin and AST - joystick) to the model (see Table 4.3). The alpha level was set to 0.05 for all analyses.

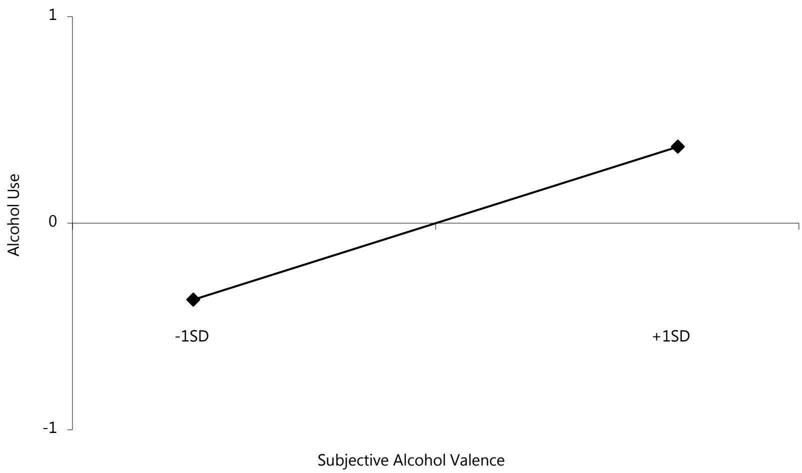
As predicted, subjective alcohol valence was a significant predictor for alcohol use, and in the first two models the AST was a significant predictor for alcohol use as well, beyond subjective alcohol valence and above background variables, soda valence, and soda approach effect. Overall, the full models explained 29% (model 1 alcohol AST - manikin effect, R^2 adjusted = 0.18, $F(6,36) = 2.50$, $p = 0.04$) and 34% (model 2 alcohol AST - joystick effect, R^2 adjusted = 0.23, $F(6,34) = 2.97$, $p = 0.02$) of all variance. The third model showed that the alcohol AST - joystick effect still reached borderline significance beyond alcohol valence ($p = 0.06$), and above background variables, soda valence, and soda approach effect, but the alcohol AST - manikin effect did not ($p > 0.2$). Jointly both implicit measures were borderline significant in the prediction of alcohol use (model 3 step 4 $\Delta R^2 = 0.12$, $p = 0.07$). This full model explained 36% of all variance (R^2 adjusted = 0.20, $F(8,32) = 2.25$, $p = 0.05$). We build a trimmed model by removing all variables that were not (borderline) significant in the explanation of alcohol use. This trimmed model (see Table 4.4) shows that 14% of the variance of alcohol use can be explained by subjective valence for alcoholic drinks ($p = 0.01$) and that another unique 10% of this variance can be explained by alcohol AST - joystick effect ($p = 0.01$). Overall, the final trimmed model explained 24% of all variance (R^2 adjusted = 0.20. $F(1,38) = 4.91$, $p = 0.03$). Figure 4.1 shows the relationship between subjective alcohol valence and alcohol use; participants who reported to drink more alcohol showed more positive subjective valence for alcohol. Figure 4.2 shows that there is a negative relationship between alcohol AST - joystick effect and self reported alcohol use. Contrary to our expectations, participants who reported to drink more alcohol demonstrated a negative alcohol AST - joystick effect; they were faster to push than to pull alcohol pictures.

Table 4.4
Trimmed hierarchical regression models for variables predicting alcohol use (N = 41)

Variable		β	t	R^2 Change
Step 1				
	(Constant)		-2.36*	
	Subjective alcohol valence	0.37	2.52*	0.14
Step 2				
	(Constant)		-2.51*	
	Subjective alcohol valence	0.37	2.58*	
	Alcohol AST - joystick effect	-0.31	-2.22*	0.10

Note. R^2 final model = 0.24 ($p < 0.05$); Adjusted R^2 = 0.20; * $p < 0.05$.

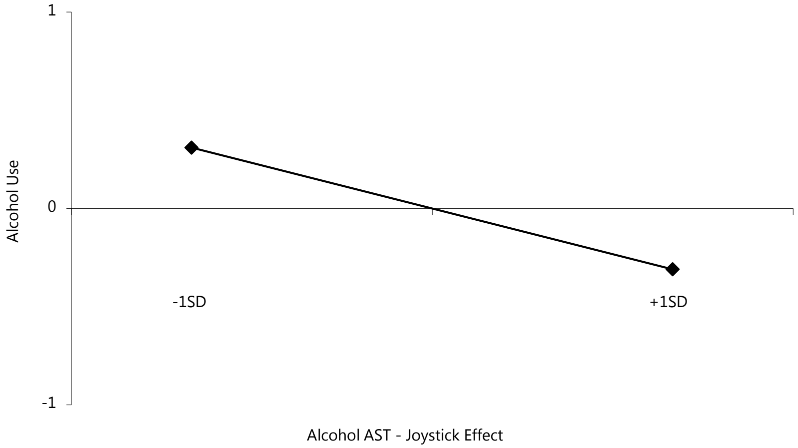
Figure 4.1
Alcohol use as a function of low versus high subjective alcohol valence (respectively 1SD below and above mean score



Note. AST = affective simon task; SD = standard deviation.

Figure 4.2

Alcohol use as a function of avoidance versus approach tendencies measured with the AST - joystick (respectively 1SD below and above mean AST - joystick score), controlled for explicit alcohol evaluations



Note. *AST = affective simon task;* SD = standard deviation; Mean AST - joystick scores are calculated by subtracting median approach reaction time from median avoidance reaction time.

Influence of working memory capacity

Bivariate analysis (Table 4.5) showed no correlation of RNG inhibition with alcohol use, alcohol AST - manikin effect or alcohol AST - joystick effect (all *ps* > 0.1). We explored the possibility of a moderating influence of working memory capacity by means of a hierarchical linear regression moderator analysis. After centering all variables, we entered subjective alcohol valence in the first step and alcohol AST - joystick effect in the second. Because the AST - manikin had no additive value in predicting alcohol use, we did not include this variable. Next we included the moderator variable RNG inhibition. A moderating effect expresses when the moderator variable is not significant in explaining variance in the dependent variable, but the interaction with the independent variable is. In the final step we included the interaction variables between the independent variables (subjective alcohol valence and alcohol AST - joystick effect) and the moderator variable; a total of two interaction variables.

Table 4.5

Bivariate correlations of implicit and explicit measures and working memory capacity

	1	2	3	4	5
1 Alcohol use	-				
2 Subjective alcohol valence	.37*	-			
3 Alcohol AST - manikin effect	-.27	.13	-		
4 Alcohol AST - joystick effect	-.32*	-.03	.27	-	
5 RNG inhibiting capacity	-.01	.06	-.25	.01	-

Note. AST = affective simon task; RNG = random number generation; * p < 0.05 (two tailed).

Table 4.6

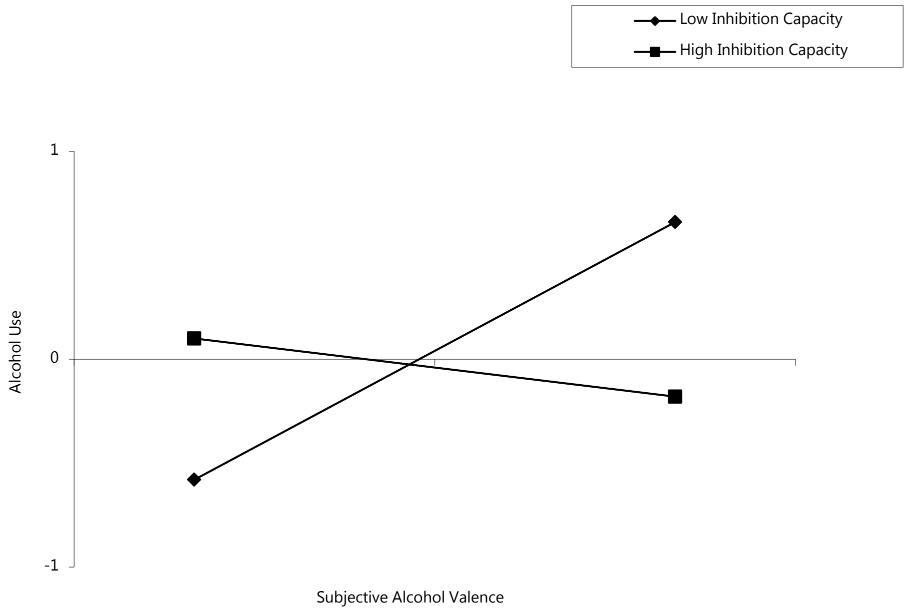
Hierarchical moderator regression models for variables explaining alcohol use (N = 41)

Variable		β	t	R^2 Change
1	(Constant)		0.28	
	Subjective alcohol valence	0.37	2.52*	0.14
2	(Constant)		0.29	
	Subjective alcohol valence	0.37	2.58*	
	Alcohol AST - joystick effect	-0.31	-2.22*	0.10
3	(Constant)		0.31	
	Subjective alcohol valence	0.37	2.57*	
	Alcohol AST - joystick effect	-0.31	-2.19*	
	RNG inhibiting capacity	-0.07	-0.49	0.01
4	(Constant)		0.48	
	Subjective alcohol valence	0.24	1.68	
	Alcohol AST - joystick effect	-0.38	-2.80**	
	RNG inhibiting capacity	-0.04	-0.28	
	Subjective alcohol valence*RNG inhibiting capacity	-0.38	-2.60*	0.12

Note. AST = affective simon task; RNG random number generation; R^2 final model = 0.36 (p < 0.05); Adjusted R^2 = 0.29; * p < 0.05. ** p < 0.01.

The final model showed that alcohol AST - joystick effect (*p* = 0.01) and the interaction variable subjective alcohol valence*RNG inhibition (*p* = 0.02) were significant in the prediction of alcohol use, whereas the variable subjective alcohol valence was no longer significant (*p* = 0.1). This full model was sufficient for an explanation of 36% of the variance in alcohol use. Next, we trimmed the model by removing the non-significant interaction alcohol AST – joystick effect*RNG inhibition, which showed that beyond the 33% of the variance in alcohol use that can be explained by subjective alcohol valence and alcohol AST - joystick effect, 12% can be explained by the interaction of subjective alcohol valence*RNG inhibition (see Table 4.6). Overall, the final trimmed model explained 36% of all variance (R^2 adjusted = 0.29, $F(4,36) = 5.13$, $p < 0.01$, see also Table 4.6). Figure 4.3 shows that in participants with low inhibition capacity subjective alcohol valence positively predict self reported alcohol use, whereas in participants with high inhibition capacity, there seems not to be such a relationship; more positive valence for alcohol does not seem to lead to more alcohol use.

Figure 4.3
Alcohol use as a function of low versus high subjective alcohol valence (respectively 1SD below and above mean score) and low and high inhibiting capacity measured with the Random Number Generation Task (respectively 1SD below and above mean inhibition score).



Note. SD = standard deviation.

DISCUSSION

The major results can be summarized as follows: early adolescents who drank more showed (i) relatively weak automatic approach tendencies towards alcohol and (ii) relatively positive self-reported appetitive valence for alcoholic drinks, which was especially expressed among adolescents with relatively low inhibitory capacity.

Subjective appetitive valence

The positive association between the subjective appetitive valence of alcohol and the extent of alcohol use is in line with previous research among late adolescents (Drobes et al., 2009; Pulido et al., 2009). These findings support the notion that positive evaluations of alcohol may be an important driving force in adolescents' drinking behavior. Further, these results are in line with the frequently replicated finding that adolescent heavy drinkers were characterized by stronger positive explicit outcome expectancies and attitudes (Christiansen et al., 1989; Drobes et al., 2009; Goldman et al., 1999; Palfai & Wood, 2001; Stacy, 1997; Thush & Wiers, 2007; Thush et al., 2007; Thush et al., 2008; Wiers, Hoogeveen, Sergeant & Gunning, 1997). Interestingly, our results indicated that the subjective appetitive valence for alcohol was a stronger predictor of alcohol use among adolescents with relatively low inhibitory capacity. This finding supports the view that immediate positive features of alcoholic drinks may promote drinking behavior especially in those adolescents who are less able to regulate their impulsive behaviors (i.e., those with low WMC).

At first sight, this finding seems to be inconsistent with previous findings showing that explicit outcome expectancies were stronger predictors for alcohol use in adolescents with higher WMC (Thush et al., 2008). Yet, there seems to be an important difference between the self-reported measures that were used in this study and those used in the earlier study of Thush and colleagues: whereas outcome expectancies can be considered as explicitly endorsed attitudes (see e.g., Hofmann, Gschwendner, Friese, Wiers & Schmitt, 2008; Wiers & Stacy, 2010), self-reported appetitive valence can be considered as a cue-reactivity measure, especially with the current use of pictorial rather than more abstract verbal stimuli. It seems reasonable to assume that adolescents with higher WMC have better cognitive capacities than their low-WMC peers to consider relevant long-term alcohol outcome expectancies and thus, to moderate their positive associations and to inhibit direct appetitive responses. Therefore, (longer term) outcome expectancies will play a more important role in relatively high WMC individuals' drinking behavior, whereas direct appetitive features will play a more important role in low WMC adolescents.

It should be acknowledged, however, that the cross-sectional design of our study does not allow any firm conclusion regarding the direction of the present relationship between subjective appetitive valence of alcohol and alcohol use. Therefore, the present findings should be interpreted with care. To be on more solid ground in this respect, it would be important to test further the proposed interrelationship in a longitudinal design. To further test the moderating influence of inhibitory control, it would be interesting to experimentally manipulate adolescents' inhibitory capacities (Hofmann, Deutsch, Lancaster, & Banaji, 2010). From a clinical perspective, it would be especially relevant to see whether increasing one's inhibitory capacity (cf., Siegle, Ghinassi, & Thase, 2007) would indeed lower the influence of a positive appetitive valence of alcohol on actual alcohol use. If so, this would point to the relevance of training cognitive control in children who are at risk for developing alcohol misuse.

Automatic approach tendencies

A series of previous studies showed that heavy drinkers are characterized by relatively strong automatic approach tendencies towards alcohol (Field et al., 2005; Field, Schoenmakers & Wiers, 2008; Palfai & Ostafin, 2003; Wiers et al., 2009). These enhanced approach tendencies have been argued to play an important role in the generation of persistent alcohol abuse and misuse (Wiers et al., 2007). Interestingly, and in apparent conflict with the important role attributed to automatic approach tendencies in alcohol misuse, the present study showed no indication of stronger approach tendencies in early-adolescent heavy drinkers. Moreover, relatively heavy drinkers showed even weaker approach tendencies (or stronger avoidance tendencies) than light drinkers, which is dissimilar to previous findings in late-adolescent and adult studies. By and large, this pattern of results was similar for both implicit tasks that were included in the present study, attesting to the validity of this finding.

To explain this finding, we have to consider that the present study differed from previous alcohol approach studies in that the participants were (i) younger and (ii) drank less alcohol than participants included in the previous automatic alcohol approach studies. Because of their younger age, they most probably had a shorter history of alcohol use as well. To our knowledge, only two studies explored implicit alcohol cognitions among early adolescents. The first study, using a Single Target Implicit Associations Task (ST-IAT), found implicit alcohol-arousal associations in twelve-year-old boys who just started drinking alcohol (Thush & Wiers, 2007). However, the other recent IAT study found negative implicit associations to be predictive of alcohol use in eleven year olds (Pieters, van der Vorst, Engels, & Wiers, 2010). In summary, although various implicit studies among late adolescents and adults have shown that heavy drinkers are characterized by alcohol approach tendencies, results of implicit cognition studies in early adolescence seem to be less equivocal. Therefore, an interesting topic for future research is to further examine the development of implicit appetitive processes in young adolescents who just started to drink alcohol.

It has been proposed that repeated alcohol use strengthens the emotional and motivational significance of alcohol, which leads to selective attentional processing and relatively automatic approach tendencies. These alcohol approach tendencies are shown in people who have been drinking excessively for several years. In young drinkers, who drink less alcohol and for a shorter period of time, this process may not yet have come to large effects. However, it remains to be explained why young adolescents that drink relatively heavy, showed even weaker approach tendencies (or stronger avoidance tendencies) than light drinkers. By now, there is abundant evidence that implicit measures are highly sensitive to context effects, such that the same object can elicit different automatic evaluations, depending on the context in which it is encountered (Blair, 2002; Ferguson & Bargh, 2007; Mitchell, Nosek & Banaji, 2003). Adolescents who drink alcohol more frequently are likely to have both stronger positive and stronger negative alcohol associations than incidental drinkers. The negative associations may relate to undesirable physical experiences but also to other persons' responses to their drinking behavior. That is, drinking at a young age might provoke negative reactions of parents, teachers and other adults, and these experiences are likely to be stored as associations in memory (Pieters et al., 2010). Further, a recent study on this issue implies that when one encounters counter-attitudinal information, the attention to available context cues is enhanced. As a result, a contextualized representation is formed (Gawronski, Rydell, Vervliet, & De Houwer, 2010). In this view, the contextual cues (i.e., school environment) may have made the negative associations (i.e., the teachers' counter-attitudinal negative reactions about drinking alcohol) more readily accessible than the more positive alcohol associations, giving rise to avoidance rather than approach tendencies in early-adolescent heavy drinkers. Obviously, the present findings are far from conclusive in this respect, and to arrive at more solid conclusions, it would be important to experimentally manipulate measurement context (e.g., testing approach behaviors in both a 'drinking context' and a 'non-drinking context'; cf., Huijding, de Jong, Wiers, & Verkooijen, 2005). Furthermore, it should be noted that the results of this study do not seem to indicate that a stronger automatic avoidance tendency actually results in less drinking, yet that more positive appetitive valence is a stronger indicator for drinking alcohol. In line with this, there is growing evidence that short-term appetitive associations are predictive for alcohol use, whereas especially long-term explicit outcome expectancies seem to be important contributors for the regulation of drinking behavior (cf., Wiers & Stacy, 2010).

More generally, the results of our study should be interpreted with some caution, due to a number of limitations. First, the present study relied on a modest sample size. Although there was considerable variance in drinking behaviors, it remains to be seen whether the present findings also generalize to other samples of adolescents. In addition, because participation was voluntary, some form of selection bias may have influenced the results. For example, it cannot be ruled out that adolescents who drank more refused to participate because they did not want anyone to know how much they drank. Furthermore, it is conceivable that participants were not entirely honest in reporting their alcohol use, because most of them had not yet reached the age of sixteen at which one is legally permitted to drink alcohol in the Netherlands (Brener, Billy, & Grady, 2003). Although it should be noted that self-report measures of alcohol use have generally been found to be valid and reliable as long as confidentiality is assured (Sobell & Sobell, 1990). Another possible limitation is the fixed order of the ASTs, the valence rating scale and the alcohol use questionnaire; it might be that order effects have played a role in the current sample. However, this fixed sequence was chosen as an optimal method in order to minimize differential carry-over and priming effects. Additionally, since the same pictures were used in the ASTs and the valence rating scale, the scores of the latter measure may have been influenced by this previous experience with the pictures. However, all participants were confronted with the same pictures at an equal frequency. Further, in this task the participants had to rate on a scale from 'tasty' to 'disgusting', which are words that could be subject to personal interpretation. This interpretation may have influenced the results. Next, the affective evaluation of alcohol stimuli was measured uni-dimensionally. However, it cannot be ruled out that positive and negative evaluations are at least somewhat independent, as results with unipolar IATs suggest (Jajodia & Earleywine, 2003; Houben & Wiers, 2006). Further, the unexpected moderation effects could be related to the measure used here (RNG), which was different from the measures used in previous moderation studies (Grenard et al., 2008; Houben & Wiers, 2009; Thush et al., 2008). Finally, this study was cross-sectional, which makes it hard to unravel the causal influences in the pattern of results. For example, more positive appetitive evaluations of alcohol may have led to more alcohol use, but the experience with drinking alcohol may have caused a more positive appetitive evaluation of alcoholic drinks as well.

In conclusion, the present results seem to indicate that early-adolescent drinkers are characterized by a relatively positive deliberate affective evaluation of alcoholic drinks together with lower inhibiting capacity. Unlike for older adolescents and adults, automatic approach tendencies do not seem to be involved in early adolescents' alcohol (mis)use. Instead, early-adolescent relatively heavy drinkers showed automatic avoidance tendencies away from alcohol, which might be indicative of a negative conditioned response. As a consequence, in the early beginnings of alcohol use, there might be opportunities of prevention and intervention. First, this could be achieved by altering information provided by the direct environment. For example, adolescents can be prevented from drinking alcohol by decreasing the subjective attractive valence of alcoholic drinks. Preliminary results on this issue demonstrated that evaluative conditioning of alcohol stimuli with negative stimuli correlated with more negative implicit attitudes towards alcohol and less self-reported alcohol use one week later (Houben, Havermans & Wiers, 2010). As alcohol advertisements are obviously major contributors to the development of a positive appetitive attitude to alcohol, they should be restricted from exposure to children and adolescents. A further opportunity for prevention could be achieved by increasing the number of negative responses from the environment, especially in the context where adolescents initially start drinking. Additionally, early adolescents with weak inhibitory capacities might benefit from interventions that aim at strengthening their controlled inhibiting processes, such as working memory training, which has been found effective in children and adolescents with inhibitory problems (e.g., Klingberg et al., 2005).

CHAPTER 5

Reward sensitivity, attentional bias, and executive control in early adolescent alcohol use

Published as:
Van Hemel-Ruiter, M. E., de Jong, P. J., Ostafin, B. D., & Wiers, R. W. (2015). Reward sensitivity, attentional bias, and executive control in early adolescent alcohol use. *Addictive Behaviors, 40*, 84-90.

ABSTRACT

This study examined whether attentional bias for alcohol stimuli was associated with alcohol use in young adolescents, and whether the frequently demonstrated relationship between reward sensitivity and adolescent alcohol use would be partly mediated by attentional bias for alcohol cues. In addition, this study investigated the potential moderating role of executive control (EC), and tested whether the relationship between alcohol-related attentional bias and alcohol use was especially present in young adolescents with weak EC. Participants were 86 adolescents (mean age = 14.86), who completed a Visual Probe Task (VPT) as an index of attentional bias, a flanker-task based Attention Network Task (ANT) as an index of EC, the sensitivity of punishment and sensitivity of reward questionnaire (SPSRQ) as an index of reward sensitivity, and an alcohol use questionnaire. High reward sensitivity, high alcohol-related attentional bias, and weak EC were all related to alcohol use. The relationship between reward sensitivity and alcohol use was not mediated by alcohol-related attentional bias. As hypothesized, attentional bias was only associated with alcohol use in participants with weak EC. Together, the present findings are consistent with the view that high reward sensitivity and low EC may be considered as risk factors for adolescent alcohol use. The independent contribution of reward sensitivity and attentional bias might suggest that adolescents who are highly reward sensitive and display an attentional bias for alcohol cues are at even higher risk for excessive alcohol use and developing alcohol abuse problems. Future research using a longitudinal approach would allow an examination of these risk factors on subsequent alcohol use. Treatment implications are discussed, including the importance of strengthening EC and reducing the rewarding value of alcohol use.

INTRODUCTION

There is considerable evidence supporting the view that alcohol-related stimuli capture the attention of people who use or abuse alcohol (see for review, Field & Cox, 2008). Using the Visual Probe Task (VPT), previous studies have demonstrated an alcohol-related attentional bias in heavy users of alcohol when picture pairs were presented for a longer period of time, such as 500–2000 ms (e.g., Field et al., 2004; Miller & Fillmore, 2010; Townshend & Duka, 2001). In addition, recent studies have found that controlled executive processes (e.g., Executive Control, EC) moderate the relationship between automatic appetitive processes (e.g., attentional bias) and alcohol use. These findings suggest that relatively weak executive functioning increases the influence of appetitive processes on alcohol use, and that especially people with weak EC are at risk to develop excessive alcohol use (Farris et al., 2010; Friese et al., 2010; Houben & Wiers, 2009; Peeters et al., 2012, 2013; Thush et al., 2008). However, not much is known about the role of attentional bias and the possible moderating influence of EC in (early) adolescent alcohol use.

It has been hypothesized that an alcohol-related attentional bias develops by the process of classical conditioning. That is, by repeated experience of the rewarding effects of drug-taking, alcohol-related cues would become associated with these rewarding effects and would consequently acquire the ability to grab the user's attention (e.g., Franken, 2003; Robinson & Berridge, 1993, 2001). Following this perspective, adolescents with high reward sensitivity could be especially at risk for developing attentional bias for alcohol cues. Germane to this, it has been argued that people's responding to appetitive cues in the environment depends on their trait reward sensitivity (Gray, 1970, 1982). People high on reward sensitivity are sensitive to stimuli that signal unconditioned reward and the relief from punishment. In the development of early adolescent alcohol use this would imply that the initial responses to alcohol-related cues would vary as a function of adolescents' reward sensitivity, whereas the repeated experience of the effects of alcohol use would subsequently shape the development of alcohol-related attentional bias. In line with this view, previous research has found a consistent link between adolescent substance use and high reward sensitivity (Knyazev, 2004; Lopez-Vergara et al., 2012; O'Connor & Colder, 2005; Pardo et al., 2007; van Hemel-Ruiter et al., 2013). Moreover, reward sensitivity has been found to be a significant predictor of reactivity to alcohol cues (Glautier, Bankart & Williams, 2000; Kambouropoulos & Staiger, 2001, 2004; Zisserson & Palfai, 2007). Of the few studies that have examined attentional bias for alcohol cues in adolescents, none have included measures of reward sensitivity. Thus it remains to be tested whether individuals with high reward sensitivity also show stronger alcohol attentional bias and whether the previous findings of a relationship between reward sensitivity and alcohol use might be (partly) mediated by attentional bias for alcohol cues. Therefore, the first aim of this study was to test further the interrelationships between reward sensitivity, attentional bias for alcohol cues, and early adolescent alcohol use.

The few studies that have examined attentional bias for alcohol cues in adolescent samples found evidence for an attentional bias in heavy drinking adolescents (16–18 years: Field et al., 2007a), and high-risk adolescents (12–16 years: Pieters et al., 2011; 15–20 years: Zetteler et al., 2006), but not in an unselected group of adolescents (15–21 years: Willem et al., 2013). The results of the latter study showed a moderating role for self-reported attentional control in the relationship between attentional bias and alcohol use such that the relation between attentional bias and alcohol use was significant for participants with strong attentional control but not for those with weak attentional control. The direction of this finding was unexpected and is difficult to explain. Given the debate regarding whether self-report methods are adequate assessments of EC capacity (cf., Reinholdt-Dunne, Mogg & Bradley, 2009; Wiers et al., 2010), the present study used a performance measure of EC to test further if EC moderates the relationship between attentional bias for alcohol cues and common adolescent alcohol use. Based on previous research investigating the moderating role of EC processes on automatic processes (Farris et al., 2010; Friese et al., 2010; Houben & Wiers, 2009; Peeters et al., 2012, 2013; Thush et al., 2008) we expected that especially adolescents with weak EC capacity would show a relationship between alcohol attentional bias and alcohol use. Thus the present study extends previous research in two important ways. First, this study examines the relationship between reward sensitivity and alcohol attentional bias and tests whether the previously reported relationship between reward sensitivity and adolescent alcohol use is mediated by attentional bias. Second, the study investigates the potential moderating role of EC on the relationship between alcohol-related attentional bias and alcohol use in (young) adolescents by using a performance measure instead of a self-report (subjective) index of EC.

In short the present study tested if i) reward sensitivity would be positively related to adolescent alcohol use, ii) this relationship would be mediated by attentional bias for alcohol pictures, and iii) EC moderates the relationship between attentional bias for alcohol pictures and alcohol use, such that the relation is demonstrated in individuals with weak (but not strong) EC.

METHOD

Participants and recruitment

Participants were recruited from two different Dutch secondary schools. A total of 88 adolescents in between 12 and 18 years of age agreed to participate and returned the signed informed consent forms. One participant was excluded because of more than 25% missing on the SPSRQ, and one because of more than 25% errors on the ANT. This resulted in a total of 86 participants (37 male and 49 female; mean age = 14.86, *SD* = 1.37). Descriptive statistics are presented in Table 5.1.

Table 5.1
Sample Characteristics (N = 86)

Variable	Mean (*SD*) or percentage
Female Gender	57%
Age	14.86 (1.37)
Servings of alcohol/week over previous month [a]	3.84 (5.20)
Lifetime Abstainer of alcohol	15.1%

Note. SD = standard deviation; [a] One serving of alcohol contains approximately 11 ml of pure alcohol.

Assessments and outcome measures

Questionnaire measures.

Self-reported alcohol use. Alcohol use was measured using a substance use questionnaire developed by TRAILS (Tracking Adolescents' Individual Lives Survey, see van Hemel-Ruiter et al., 2013). Alcohol use was calculated as an aggregate of the standardized scores of the eight quantity and frequency items (e.g., “At how many of the weekdays do you normally drink alcohol?”; Cronbach's alpha = 0.91). As the aggregate alcohol use variable demonstrated a non-normal distribution, a log10 transformation was conducted. The statistical significance of the results did not differ when the analyses were conducted with either the raw or the transformed variables. For ease of interpretation, we report the results based on the raw scores.

Reward sensitivity and punishment sensitivity. The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ; Torrubia, Ávila, Moltó & Caseras, 2001) is a self-report measure of reward sensitivity (RS; 24 items, e.g., “Do you often do things to get praised?") and punishment sensitivity (PS; 24 items, e.g., "Do you often refrain from doing something because you are afraid of it being illegal?"). Participants can respond to these questions with either yes or no. RS and PS are calculated by summing the 24 questions of which participant answered yes. The total score can thus range from 0 to 24, and a higher score reflects a higher reward sensitivity or punishment sensitivity. Cronbach's alpha for reward sensitivity = 0.77, for punishment sensitivity = 0.86.

Computerized measures.

Attentional bias. Attentional bias was assessed with a VPT (MacLeod et al., 1986). In this task we used pictures of three different categories: alcohol, tobacco, and cannabis. For the purpose of the current study only the alcohol trials are relevant. Each category consisted of ten different picture pairs, which were composed of a substance-related picture and a neutral picture. The neutral pictures were matched on composition and brightness. Another eight pairs of neutral pictures were used as practice trials at the beginning of the task, and as buffer trials in between the switch between different categories of substances. All pictures were 95 mm high and 95 mm wide.

Each trial started with a fixation cross which was presented for 500 ms in the middle of the screen. Participants were instructed to attend to the fixation cross. Next, the cross disappeared and two pictures were presented (a substance-related and a neutral picture), each on one side of the screen, for a period of 500 or 1250 ms. After disappearance of the pictures a small arrow (probe) pointing upward or downward was presented at the location of either one of the pictures. Participants had to respond to the arrow direction by pressing the corresponding button on the keyboard as quickly and accurately as possible. The next trial started 500 or 1250 ms after each response. The probe was presented equally often on the right and on the left side, and was presented equally often upward and downward. Substance-related pictures were presented equally often on the right as on the left side, and for half of the trials the picture pairs were presented for 500 ms and half for 1250 ms.

The VPT started with 16 practice trials, in which participants received feedback about their accuracy, followed by two blocks of 120 critical trials. Each block was preceded by 2 buffer trials with substance–neutral picture pairs that were not presented during the critical trials. Within each block, each picture pair was presented four times. The alcohol, tobacco, and cannabis trials were randomly distributed and the 500 ms and 1250 ms presentation time trials were intermixed in each block. Both response time and accuracy were recorded.

Executive control. The Attention Network Task (ANT; Fan, McCandliss, Sommer, Raz & Posner, 2002) is a task designed to measure the alerting, orienting, and executive function of spatial attention, and is a combination of the cued reaction time (Posner, 1980) and the flanker task (Eriksen & Eriksen, 1974). Each trial started with a fixation cross which was presented for 400 ms in the middle of the screen. Participants were told to attend to the fixation cross. Next, a row of five horizontal black lines (one central arrow plus four flankers) was presented above or below the fixation cross, with arrowheads pointing left or right. The target is a left or right-facing arrowhead at the center. The target was "flanked" on either side by two arrows in the same direction (congruent condition), the opposite direction (incongruent condition) or by two horizontal lines (neutral condition). Participants had to respond to the target by pressing the corresponding button on the response box as quickly and accurately as possible. Before the target appeared, a warning cue was presented to signal the upcoming target. There were four warning conditions: a center cue, which was presented at the center location (replacing the fixation cross), a double cue, which were two asterisks presented above and below the fixation cross, or a spatial cue which was an asterisk presented at the exact location of the upcoming target, or no cue at all.

The ANT started with 24 practice trials in which participants received feedback about their mean response time and accuracy, followed by three blocks of 96 critical trials each. Trials were presented in random order, with all types of warning cue and types of flankers presented evenly frequently, and as many target arrows left as right.

Procedure

Participants were tested in a quiet room at school. Two laptop computers were set up for computer-based assessments in separate corners of one room, in order to be able to test two participants at one time. The measures as discussed in this article were part of a larger assessment of five computerized tasks and four questionnaires. The measures were administered in a set order: first, the VPT, and three other computer tasks, then the ANT, and finally the paper-and-pencil questionnaires including the demographic questionnaire, substance use questionnaire, and the SPSRQ. Computer tasks were presented at a 14-inch Acer laptop computer with a 60 Hz screen (1024 × 768 resolution) using E-prime software version 2.0 (Psychology Software Tools Inc., Pittsburgh, Pennsylvania).

Participants were seated 50 cm away from the screen and responses were collected on the keyboard. The entire assessment took about 75 min.

Data reduction and analysis

VPT trials with an incorrect response (4.5%) or with reaction times 3 SD below (probable anticipations) or above (probable distractions) the mean (1.5%) were removed. Mean reaction times for correct responses are reported in Table 5.2. We computed attentional bias (AB) scores by subtracting the mean reaction time on alcohol trials from the mean reaction times on corresponding neutral trials. This resulted in two attentional bias scores: for alcohol pictures that were presented 500 ms or 1250 ms. A higher AB score means a stronger attentional bias toward alcohol-related pictures compared to neutral pictures.

Table 5.2

Mean reaction times for alcohol and neutral stimuli during the VPT 500 ms and VPT 1250 ms

	Alcohol Stimuli M(SD)	Neutral Stimuli M(SD)
VPT 500 ms	659(99)	665(97)
VPT 1250 ms	649(98)	653(103)

Note. VPT = Visual Probe Task; M = mean; SD = standard deviation.

ANT trials with reaction times 3 SD below (probable anticipations) or above (probable distractions) the mean (2.0%), or with an incorrect response (5.4%) were removed. Mean reaction times for correct responses for congruent and incongruent trials are reported in Table 5.3. The EC effect was calculated by subtracting the mean RT of all congruent flanking conditions, summed across cue types, from the mean RT of incongruent flanking conditions (see Fan et al., 2002). A higher score on EC therefore reflects a weaker EC function.

Missing value analysis on the questionnaires showed that 0.7% of the items was not completed. We imputed the single items of the alcohol questionnaire and the SPSRQ by conducting mean substitution.

Table 5.3

Mean reaction times for congruent and incongruent trials during the ANT

	Congruent Trials M(*SD*)	Incongruent trials M(*SD*)
ANT	533(73)	644(97)

Note. ANT = Attention Network Task; M = mean; SD = standard deviation.

RESULTS

Bivariate analyses

First, we performed a bivariate correlation analysis to explore the relationship between age, gender, RS and PS, alcohol attentional bias, EC and alcohol use. Table 5.4 shows that alcohol use was positively correlated with age, and RS, and negatively with gender and PS. It further shows that AB was unrelated to RS and PS. Thus the present findings were inconsistent with the hypothesis that a relationship between reward sensitivity and alcohol use would be mediated by alcohol attentional bias. In addition, there was no evidence for a direct relationship between alcohol use and AB or EC. To investigate the hypothesized moderating role of EC on the relationship between AB and alcohol use, we performed a regression analysis.

Table 5.4

Bivariate correlations among measures SPSRQ (SR and SP), alcohol attentional bias and EC, as well as age and gender

	1	2	3	4	5	6	7	8
1 Age	-							
2 Gender[a]	-.07	-						
3 Alcohol Use	.48**	-.23*	-					
4 Reward Sensitivity	.22*	-.25*	.40**	-				
5 Punishment Sensitivity	-.16	.19	-.27*	-.15	-			
6 Alcohol attentional bias 500 ms	.11	.07	.12	.16	-.08	-		
7 Alcohol attentional bias 1250 ms	.06	.08	.20	.01	-.16	.04	-	
8 Executive control	.27*	-.06	.00	.22*	.05	-.04	-.03	-

Note. SPSRQ = Sensitivity to Punishment and Sensitivity to Reward Questionnaire; SR = sensitivity to reward; SP = sensitivity to punishment; EC = executive control; [a] Male = 1, female = 2; * $p < 0.05$ (two tailed); ** $p < 0.01$ (two tailed).

The relationship between adolescent alcohol use, reward sensitivity, attentional bias, and executive control

To investigate the hypothesized relationship between adolescent alcohol use and reward sensitivity (RS), alcohol attentional bias (AB500 ms and AB1250 ms) and the interaction between attentional bias and EC, we performed a hierarchical regression analysis. We also included punishment sensitivity as the correlation analysis showed a significant negative association between punishment sensitivity and alcohol use. Because gender and age correlated strongly with alcohol use, they were included in the model as covariates. This is especially relevant regarding the positive relation between age and EC, and age and alcohol use, and the expectation that alcohol use would be explained by weaker EC. Therefore, in the first step we included age and gender as control variables. In step 2 we included RS, PS, AB500 ms, AB1250 ms, and EC and in step 3 the interaction-effects of AB500 ms × EC, and AB1250 ms × EC. This model (Table 5.5) explained 43% (R^2 adj = 0.37, $F(9,85)$ = 6.45, p < 0.001) of the variance in adolescent alcohol use, with age and RS being significant, and gender, EC and the interaction AB1250 ms × EC approaching significance.

Table 5.5
Hierarchical regression model for variables explaining alcohol use (N = 86)

Variable		Beta	t	p-value	R^2 Change
Step 1					
	(Constant)		1.94	0.06	
	Gender	-0.19	-2.03*	0.05	
	Age	0.47	4.93**	<0.001	0.27
Step 2					
	(Constant)		1.35	0.18	
	Gender	-0.13	-1.41	0.16	
	Age	0.43	4.64**	<0.001	
	Reward Sensitivity	0.29	3.07**	<0.01	
	Punishment Sensitivity	-0.09	-1.01	0.32	
	Attentional Bias 500 ms	0.06	0.62	0.54	
	Attentional Bias 1250 ms	0.17	1.90	0.06	
	Executive Control	-0.18	-1.92	0.06	0.15
Step 3					
	(Constant)		1.46	0.15	
	Gender	-0.14	-1.53	0.13	
	Age	0.44	4.70**	<0.001	
	Reward Sensitivity	0.26	2.70**	0.01	
	Punishment Sensitivity	-0.11	-1.14	0.26	
	Attentional Bias 500 ms	0.05	0.59	0.56	
	Attentional Bias 1250 ms	0.10	1.01	0.32	
	Executive Control	-0.16	-1.69	0.10	
	AB500ms*EC	-0.01	-0.09	0.93	
	AB1250ms*EC	-0.15	-1.48	0.14	0.02

Note. R^2 final model = 0.43**; Adjusted R^2 = 0.37; IV's were centered before analysis; * p < 0.05; ** p < 0.01.

Table 5.6
Trimmed hierarchical regression model for variables explaining alcohol use (N = 86)

Variable		Beta	t	p-value	R^2 Change
Step 1					
	(Constant)		1.94	0.06	
	Gender	-0.19	-2.03*	0.05	
	Age	0.47	4.93**	<0.001	0.27
Step 2					
	(Constant)		1.50	0.14	
	Gender	-0.14	-1.56	0.12	
	Age	0.44	4.85**	<0.001	
	Reward Sensitivity	0.31	3.36**	<0.01	
	Attentional Bias 1250 ms	0.19	2.14*	0.04	
	Executive Control	-0.19	-2.10*	0.04	0.14
Step 3					
	(Constant)		1.63	0.11	
	Gender	-0.15	-1.71	0.09	
	Age	0.45	4.98**	<0/001	
	Reward Sensitivity	0.28	3.03**	<0.01	
	Attentional Bias 1250 ms	0.13	1.30	0.20	
	Executive Control	-0.18	-1.94	0.06	
	AB1250ms*EC	-0.14	-1.39	0.17	0.01

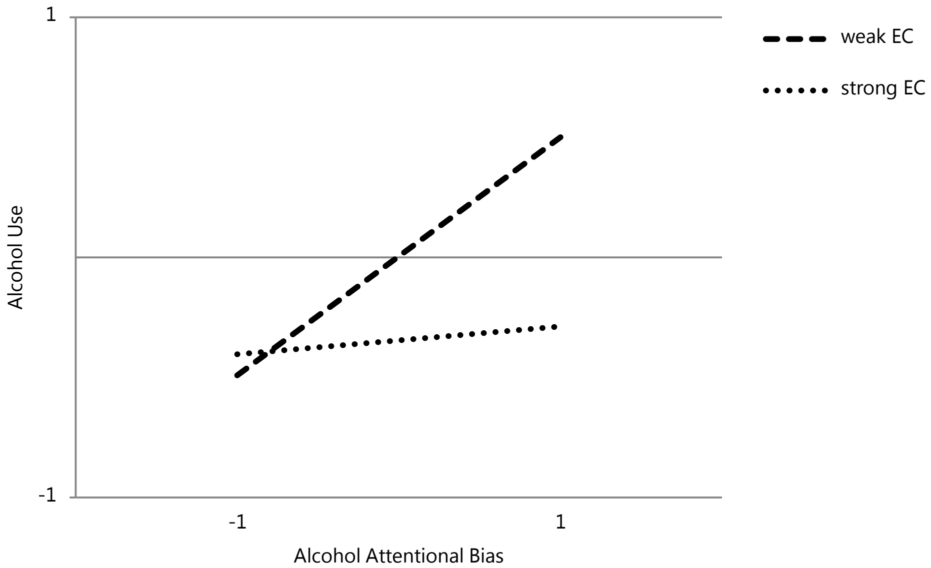
Note. R^2 final model = 0.42**; Adjusted R^2 = 0.38; IV's were centered before analysis; * p < 0.05; ** p < 0.01.

We subsequently trimmed the model, leaving only the predictors that were significant or approached significance. This trimmed model (Table 5.6) explained 42% (R^2 adj = 0.38, F(6,85) = 9.51, p < 0.001) of the variance in adolescent alcohol use. The results of step 2 show that older age, stronger reward sensitivity, stronger AB for cues presented for 1250 ms and weaker EC were associated with higher levels of alcohol use. However, when the interaction of AB 1250 ms × EC was entered in step 3, the main effects of both AB 1250 ms and EC did not reach significance anymore. Further, the interaction effect between attentional bias and EC was not significantly related to alcohol use.

Although the corresponding interaction was not significant, we exploratory tested our a priori hypothesis that only in adolescents with weak EC, AB and alcohol use would be related. We calculated simple slopes separately for adolescents with weak and strong EC. A visual representation of the interaction effect is presented in Figure 5.1. The simple slopes for attentional bias at weak EC (β = 0.20, p = 0.03) and strong EC (β = 0.05, p = 0.73) show that only for adolescents with weak EC, AB

1250 ms was significantly related to alcohol use. That is, in adolescents with weak EC, a stronger attentional bias for alcohol cues that were presented for 1250 ms was related to a higher level of alcohol use.

Figure 5.1
Alcohol use as a function of low versus high attentional bias (respectively 1SD below and above mean score) and low and high EC (respectively 1SD below and above mean score)



Note. EC = executive control; [a] Higher attentional bias score reflects more positive attentional bias for alcohol cues.

Post-hoc analyses: are there specific roles for gender and age?

The finding that gender correlated with RS as well as alcohol use, gives rise to the idea that gender might be a moderating factor in the relation between RS and alcohol use. We explored the possibility of a moderating influence of gender by means of a hierarchical linear regression moderator analysis. After centering all variables, we entered gender and RS in the first step and the gender × RS interaction variable in the second. A moderating effect expresses when the moderator variable is not significant in explaining variance in the dependent variable, but the interaction with the independent variable is. The final model showed that indeed gender was not significant in explaining variance in alcohol use (t = − 1.32, p = 0.19), but also the interaction effect was not significant (t = 1.05, p = 0.30). Only RS was a significant independent contributor to the explanation of alcohol use (t = 3.68, p < 0.01). Thus, RS was strongly related to adolescent alcohol use, and this was not different for boys and girls.

The correlation analysis further showed that age correlated positively with RS. Although age was included as a covariate in the linear regression analysis, we post-hoc built a mediation model in which we included RS as a mediator for the relation between age and alcohol use. That is, we tested whether the relation between age and alcohol use could be explained by RS. Therefore, according to Baron and Kenny (1986), we first carried out three regression analyses in which we tested whether 1) age was predictive for RS, 2) age was predictive for alcohol use, 3) RS had a significant unique effect on alcohol use, and 4) the contribution of age to the explanation of alcohol use shrinked when RS was added to the equation. The results showed that age was significantly related to alcohol use (B = 0.275, p < 0.001), and RS (B = 0.72, p = 0.04). RS contributed uniquely to the explanation of alcohol use when age was in the model (B = 0.05, p < 0.01). In the full model also age remained a significant contributor in the explanation of alcohol use (B = 0. 24, p < 0.001). The Sobel test (Baron & Kenny, 1986) showed that the indirect effect of age via RS was different from zero (p < 0.01). Therefore, the mediation analysis showed that RS partly mediated the relation between age and alcohol use.

DISCUSSION

This study examined the relation between alcohol use, EC and attentional biases toward alcohol cues. The major results can be summarized as follows: (i) alcohol use was related to strong reward sensitivity, ii) among the predictor variables, reward sensitivity predicted unique variance of alcohol use, (iii) attentional bias toward alcohol cues was not related to reward sensitivity, and (iv) alcohol attentional bias and drinking were related in participants with weak EC but not in those with strong EC.

The current finding that adolescents with higher reward sensitivity reported higher levels of alcohol use is in line with previous research among adolescents (Colder et al., 2013; Jonker, Ostafin, Glashouwer, van Hemel-Ruiter & de Jong, 2014; Knyazev, 2004; Lopez-Vergara et al., 2012; O'Connor & Colder, 2005; Pardo et al., 2007). These results suggest that in the early stages, reward sensitivity may promote adolescent alcohol use. Consistent with such view, recent research using performance measures of reward and punishment sensitivity showed that reactivity to rewarding cues was positively related to concurrent (Colder & O'Connor, 2002; van Hemel-Ruiter et al., 2013) and prospective adolescent alcohol use (van Hemel-

Ruiter, de Jong, Ostafin, & Oldehinkel, 2015a), and that the increase in reward sensitivity over two years was a significant predictor of increase in young adolescent alcohol use over these years (Colder et al., 2013).

We expected that the relationship between alcohol use and reward sensitivity would be partly mediated by alcohol-related attentional bias. The findings did not support this hypothesis, as reward did not show a meaningful relationship with attentional bias. Thus the present findings did not substantiate the view that high reward sensitivity would set adolescents at risk for developing attentional bias for alcohol cues.

The post-hoc analysis of a possible moderating role of gender in the relationship between reward sensitivity and alcohol use showed that this relation did not differ between boys and girls. Thus, although boys showed stronger reward sensitivity than girls, this difference could not explain the higher alcohol consumption of boys, related to girls. Therefore, while research has shown that some of the risk factors related to problematic alcohol use during adolescence apply only to boys or girls (see e.g., Schulte, Ramo & Brown, 2009; Weichold, Wiesner & Silbereisen, 2014), this study gives no indication that the role of reward sensitivity in adolescent alcohol use is different for boys and girls.

Further, the post-hoc mediation analysis showed that the relation between age and alcohol use was partly mediated by reward sensitivity. That is, part of the relation between age and alcohol use could be explained by the increase of reward sensitivity when adolescents grow older. This finding is in line with recent research showing that reward sensitivity increased during adolescence and that increases in reward sensitivity were related to increases in substance use (Colder et al., 2013). However, due to the correlational nature of this study is it not possible to conclude about individual growth trajectories on the basis of the present findings.

Although alcohol use was related to punishment sensitivity, (a) the bivariate correlation was weaker than between alcohol use and reward sensitivity and (b) the regression analysis showed that punishment sensitivity did not continue to predict variance of alcohol use when reward sensitivity was included. These findings suggest that the negative consequences of alcohol consumption might be less critical in motivating behavior than the rewarding consequences (cf., Bijttebier et al., 2009).

Extending previous research on the role of attentional bias and executive control in adolescent alcohol use (Farris et al., 2010; Field et al., 2007a; Friese et al., 2010; Houben & Wiers, 2009; Peeters et al., 2012; 2013; Pieters et al., 2011; Thush et al., 2008; Willem et al., 2013; Zetteler et al., 2006) the current study showed that young adolescents who demonstrated a stronger attentional bias toward alcohol cues reported a higher level of alcohol use. Although EC did not significantly moderate the relationship between attentional bias and alcohol use, the exploratory analysis showed that alcohol-related attentional bias was only related to alcohol use in adolescents with weak EC. In this regard it seems relevant to consider that in the present sample the experience with alcohol use was limited and as a group the current participants reported only a low level of substance use. Together with the notion that participants were relatively young, this might suggest that in the present sample the attentional bias might not have come to large effects yet (cf., van Hemel-Ruiter, de Jong, & Wiers, 2011). Therefore, the difference in attentional bias as well as alcohol use between weak and strong EC adolescents might have been too small for the moderation effect to reach the level of significance. The additional finding that weak EC per se was associated with higher levels of alcohol use (although this relationship was only marginally significant after entering the interaction of attentional bias and attentional control) is in line with previous studies which showed that controlled executive processes (e.g., EC) were associated with the development and maintenance of alcohol use disorders (e.g., Finn & Hall, 2004; Gunn & Finn, 2013; Nigg et al., 2006). Although further research is needed on this topic, these findings might suggest that executive functioning is a risk factor in both a direct and an indirect way. That is, adolescents with weak EC might have trouble controlling their alcohol intake as well as resisting the attentional capture of alcohol-related cues.

The finding that only in the 1250 ms condition AB was related to alcohol use in adolescents with weaker EC can be explained by the fact that with a longer stimulus presentation time there is more time for cognitive processes to influence participants' responding. Therefore, for those with stronger EC it will be easier to counter the automatic influence of alcohol cues on behavior. Further, these results are in line with previous studies which have consistently demonstrated that heavy substance users showed an attentional bias for stimuli that were presented for longer stimulus presentation times (i.e., 2000 ms), but found mixed results with shorter stimulus duration times (i.e., 200 ms or 500 ms; Bradley et al., 2004; Bradley et al., 2003; Field et al., 2006; Field et al., 2004; Townshend & Duka, 2001).

Together, the present findings are consistent with the view that high reward sensitivity and low EC may be considered as risk factors for adolescent alcohol use. For those with high reward sensitivity, the positive effects of alcohol may have more impact than for those with low reward sensitivity and may therefore lower the threshold for future use. In the same vein, it seems reasonable to assume that for those who have difficulty to disengage their attention from alcohol cues, the threshold for developing craving will be lowered which in turn may promote actual alcohol consumption. The independent contribution of reward sensitivity and attentional bias might implicate that people who are highly reward sensitive and display an attentional bias for alcohol cues are at even higher risk for excessive alcohol use and developing alcohol abuse problems.

It should be acknowledged, however, that the cross-sectional design precludes inferences regarding the direction of the relationship between reward sensitivity, EC, and alcohol use. Future research using a longitudinal approach would allow an examination of the risk factors of reward sensitivity and EC on subsequent alcohol use. To the extent that reward sensitivity and EC prove to be risk factors for heavy alcohol use, interventions should focus on these variables. First, interventions could target the rewarding valence of alcohol. Related to this, recent studies have demonstrated a decrease in alcohol consumption after evaluative conditioning (Houben et al., 2010a; Houben, Schoenmakers & Wiers, 2010b) and pairing rewarding stimuli with situational cues signaling that approach is unwanted (Houben, Havermans, Nederkoorn & Jansen, 2012). Second, interventions could focus on increasing EC. In line with this, preliminary results demonstrated that increasing working memory capacity indeed resulted in a decrease in alcohol intake (Houben, Wiers, & Jansen, 2011). Further, due to the limited sample size of this study we were not able to compare gender differences for all variables, while there are clues that the role of automatic and controlled processes in adolescent substance use may differ for boys and girls (see e.g., Pieters et al., 2011; Willem et al., 2013).

Finally, other aspects of the study limit the inferences that can be made from the results. First, because participation was voluntary, some form of selection bias might have influenced the results. Adolescents who used higher levels of substances might have refused to participate because they did not want anyone to know how much they used. In addition, participants might not be entirely honest in reporting their alcohol use, because most of them had not yet reached the legal age of sixteen[1] to use alcohol in The Netherlands (Brener et al., 2003). However, self-report measures of substance use have been found to be valid and reliable as long as confidentiality and anonymity is guaranteed (Del Boca & Darkes, 2003). Further, because the present study was part of a larger study on cognitive biases in substance use, the VPT contained alcohol, tobacco, and cannabis pictures. As a consequence, the number of critical alcohol-related pictures in each presentation time (i.e., 500 ms and 1250 ms) was rather low (40), which might have had a negative impact on the sensitivity of the current task. Finally, the ANT was the last computer task in a series of five. This might have influenced the results, for example due to fatigue.

In sum, the present study showed that higher reward sensitivity and lower EC was related to early adolescent alcohol use. In addition, it demonstrated that stronger attentional bias for alcohol-related pictures was related to higher levels of alcohol use, but only in adolescents with weak attentional control. The results suggest that high reward sensitivity and weak EC might be seen as potential risk factors for adolescent alcohol use.

CHAPTER 6

Attentional bias and executive control in treatment-seeking substance-dependent adolescents: a cross-sectional and follow-up study

Submitted for publication as:
Van Hemel-Ruiter, M. E., Wiers, R.W., Brook, F. G., & de Jong, P. J.
Attentional bias and executive control in treatment-seeking substance-dependent adolescents: a cross-sectional and follow-up study.

ABSTRACT

Background Research in adults shows that substance dependent individuals demonstrate attentional bias for substance-related stimuli. This study investigated the role of attentional bias in adolescents diagnosed with alcohol, cannabis, amphetamine or GHB dependency on entering therapy and six months later, and the role of executive control (EC) as a moderator of the relationship between problem severity and attentional bias.

Methods Seventy-eight substance-dependent adolescent patients (mean age = 19.5), and 64 controls (mean age = 19.0) were tested. Thirty-eight patients took part at 6-month follow-up. Attentional bias was indexed by a Visual Probe Task, EC by the Attention Network Task, problem severity by the short Alcohol (or Drug) Use Disorder Identification Test and the Severity of Dependence Questionnaire.

Results Patients demonstrated an attentional bias for substance stimuli presented for 500 ms and 1250 ms, with the latter related to severity of dependence. They showed no reduced EC, and EC did not moderate the relationship between attentional bias and dependency. Substance use, dependency, and attentional bias remained unchanged in the 6 month follow-up period.

Conclusions Substance dependent adolescents showed a stronger relatively early as well as maintained attentional bias toward substance cues. A stronger maintained attention was related to higher severity of dependence. No evidence emerged to sustain the view that EC might play an important role in adolescent substance use. The finding that follow-up attentional bias and problem severity were not decreased is consistent with the view that traditional addiction treatments may benefit from attentional bias modification procedures.

INTRODUCTION

Addiction is a serious problem worldwide, both at the individual and the societal level. Epidemiologic studies have demonstrated that the prevalence of alcohol and drug use and abuse increases with age during adolescence and peaks in young adulthood (Hibell et al., 2012; Johnston et al, 2014; SAMHSA, 2014; Van Laar et al., 2013). Therefore, it is important to increase knowledge of factors that contribute to the development of alcohol and drug use problems.

Current models of addictive behavior propose that attentional bias (AB) plays a central role in the persistence of substance (ab)use (e.g., Franken, 2003). In line with this, there is considerable evidence supporting the view that substance-related stimuli capture the attention of people who use or abuse these addictive substances (Field & Cox, 2008). The selective attention for alcohol or drug-related stimuli is assumed to activate the feeling of craving, which further promotes AB for the substance and subsequent drug-seeking behavior (Franken, 2003). Further, research has shown that substance abusers' executive functioning is affected (e.g., Cox & Klinger, 2004; Lubman, Yücel & Pantelis, 2004; Wiers et al., 2007, but see Wiers et al., 2015a), and it has been argued that substance users with reduced Executive Control (EC) are especially susceptible to the attention-grabbing properties of substance-related stimuli (Field & Cox, 2008), because they are less able to regulate their attention (Fazio & Towles-Schwen, 1999; Wiers et al., 2007).

Thus far research on substance-related AB has focused on adult populations. Using various paradigms, these studies have demonstrated AB in non-clinical and clinical alcohol and drug users (see for review, Field & Cox, 2008; Sinclair et al., 2010). AB for substance cues has been linked to craving (see for meta-analysis, Field et al., 2009), relapse, and to the escalation of drug problems (Garland, Franken & Howard, 2012; Marhe et al., 2013; Waters et al., 2012). However, recent critical reviews demonstrate that there is inconsistent evidence regarding the predictive relationship between AB assessed in clinical settings and subsequent relapse (Christiansen et al., 2015; Field, Marhe & Franken, 2014).

For a proper appreciation of the role of AB in addictive behaviors it is important to investigate the role of AB in adolescent substance use and abuse. There are only a few studies that have examined AB for substance-related stimuli in adolescents, and all of them focused on alcohol use in nonclinical settings. These studies found evidence for an AB in heavy drinking adolescents (16-18 years: Field et al., 2007a), and high-risk adolescents (12-16 years: Pieters et al., 2011; 15-20 years: Zetteler et al., 2006), but not in unselected groups of adolescents (12-18 years: van Hemel-

Ruiter, de Jong, Ostafin & Wiers, 2015b; 15-21 years: Willem et al., 2013; see for review: Wiers et al., 2015a).

The present study aimed to extend this research, by investigating substance-related AB in treatment-seeking adolescents and young adults ("youth", 12-25 year-olds), diagnosed with a substance use dependency, and including a control group. The large majority of youth enrolling in addiction therapy are abusers of cannabis or alcohol. This applies both to the U.S. (Johnston et al, 2014; SAMHSA, 2014) as well as for Europe (EMCDDA, 2015; Van Laar et al., 2013). In the Netherlands, cocaine, amphetamine, and gamma hydroxybutyrate (GHB) are, with some distance, the next most used illicit drugs among adolescent treatment seekers. Of those, cocaine use is declining, while the use of GHB has been rising since 2007 (Wisselink et al., 2013). Previous studies about the role of substance-specific AB mainly focused on alcohol- or cannabis users, and there are some studies available that focused on cocaine or heroin users. Given the prevalence of adolescent alcohol, cannabis, amphetamine, and GHB abusers, we decided to focus on these groups for the current study.

The major aim of this study was to test whether treatment-seeking substance abusing youth diagnosed with alcohol, cannabis, amphetamine, or GHB abuse or dependency, were characterized by an AB for personally relevant substance stimuli. To index substance-specific AB we used a visual probe task (VPT) similar to the VPT designed by Field et al. (2004). To investigate the time-course of AB, different exposure durations (SOA, stimulus onset asynchrony) were used in this task. In the present study we used an SOA of 500 ms, which is found to be a robust condition demonstrating AB (e.g., Cisler & Koster, 2010, Mogg & Bradley, 1998), and is thought to reflect relative early attentional processes. We further used a longer SOA of 1250 ms, as a reflection of maintained attention, as previous studies have shown that especially biases in maintained attention are relevant in substance use problems (e.g., Field & Cox, 2008). Based on the prevalence of misuse in Dutch treatment settings, we included four categories of substance-related stimuli in the present VPT: alcohol, cannabis, amphetamine, and GHB. This enabled computing AB scores for the personally relevant substance of each participant.

Cognitive models of addiction further propose that individual differences in cognitive control will modulate the relationship between automatically triggered appetitive processes (e.g., AB) and problem severity (Field & Cox, 2008). However, there are some inconsistencies in previous research with some studies showing that indeed the predictive validity of automatically triggered appetitive processes (e.g., AB) toward alcohol was restricted to individuals with relatively weak executive functions (Grenard et al., 2008; Houben & Wiers, 2009; Peeters et al., 2012, 2013; Thush et al., 2008; van Hemel-Ruiter et al., 2015b), and some studies that did not find such a moderating influence of executive functioning on automatic processes (Christiansen, Cole, Goudie & Field, 2012; Cousijn et al., 2013; Pieters et al., 2012; van Hemel-Ruiter et al., 2011).

The second aim of the current study was therefore to test whether treatment-seeking adolescent substance abusers are characterized by a lowered EC, and whether the relationship between substance-specific AB and problem severity is moderated by EC. To assess individual differences in EC, we used the Attention Network Task (Fan et al., 2002), as a combination of the cued reaction time (Posner, 1980) and the flanker task (Eriksen & Eriksen, 1974). This behavioral reaction time task has been developed to measure the efficiency of three attentional networks (i.e., alerting system, orienting system, and executive attention). Participants respond to a central target arrow and EC of attention is assessed from the interference effect on RT of task-irrelevant flankers (arrows which point in an incongruent direction to the central target arrow). Previous research has shown that this task is suitable for the use in young and clinical samples (Howell, Osternig, van Donkelaar, Mayr & Chou, 2013; Keehn, Lincoln, Müller & Townsend, 2010; Racer et al., 2011), and has good test-retest reliability (Fan et al., 2002; Ishigami & Klein, 2010, 2011). Recent studies using the ANT to measure executive attentional control within undergraduate samples showed that AB for alcohol stimuli was related to alcohol use only in weak EC adolescents (van Hemel-Ruiter et al., 2015b), and that there was a relationship between fear-level and heightened threat-related AB only in weak EC individuals (Hou et al., 2014; Reinholdt-Dunne et al., 2009). In addition, we investigated if substance-related AB and EC changed during therapy. There is some evidence that AB is reversed in abstinent smokers (Peuker & Bizarro, 2014), reversed or decreased in abstinent alcoholics (Noël et al., 2006; Townshend & Duka, 2001; Vollstädt-Klein et al., 2009), and decreased in treated cocaine and heroin abusers (Gardini, Caffarra & Venneri, 2009). In this study we therefore also included a follow-up assessment for the patient group, in order to investigate whether AB and EC had changed six months after entering treatment, and if so, whether this change was related to changes in problem severity.

In short, the present study was designed to investigate AB and EC in a clinical sample of substance abusing youth. Healthy peers served as a control group. According to cognitive motivational models of addiction, we hypothesized that substance abusing youth would be characterized by an AB for personally relevant substance stimuli. We expected this bias to appear at both relatively short (500 ms) and relatively long (1250 ms) presentation times. In addition, based on the findings that people with relatively weak EC abilities are at risk for developing substance misuse and dependency (de Wit, 2009; Verdejo-García & Pérez-García, 2007), we hypothesized that youth diagnosed with substance dependency would be characterized by a relatively weak EC, compared to the control group. As a subsidiary issue, we expected that ABs would be decreased six months after entering treatment, along with substance use and problem severity. Since common therapies are aimed at increasing control over behavior (e.g., cognitive behavior therapy; see e.g., Beck, 2011), and there are indications that prolonged abstinence is beneficial for cognitive functioning (Fernandez-Serrano, Perez-Garcia & Verdejo-Garcia, 2011), we further expected that EC would increase.

METHOD

Participants and Recruitment

Participants were 78 alcohol- or drug-dependent patients (12-25 years) and 64 adolescent or young adult control participants. Youth between 12 and 25 years old who entered intake procedure at VNN Addiction Care, who were diagnosed with alcohol, cannabis, amphetamine, or GHB use disorder were eligible for this study. Patients were excluded if they were diagnosed with gambling disorder, or entered treatment for problematic gaming. Controls were healthy youth matched at group level for age, gender, and educational level with the patient group.

Patients were recruited at intake procedure of VNN Addiction Care, a large addiction care facility in the northern part of the Netherlands. The therapist leading the intake invited the patients to participate in a study about the development of substance use and abuse, which consisted of two sessions of 90 minutes each. Originally, the study also included a third assessment, which was dropped halfway through data collection, based on the large attrition between baseline and follow-up. A total of 111 patients agreed to participate in the study, of which 33 were excluded in the next step. Three were in treatment for problems other than alcohol or drug dependence (i.e., gambling), one fell out of the age-range, four moved to another residence, seventeen changed their minds about participation, and eight did not respond to our repeated attempts to contact them via the telephone. Baseline assessment started during or immediately after the intake procedure (which took three to four weeks), with follow-up assessments taking place at approximately six months after the baseline assessment. At baseline, two patients were excluded for not having a diagnosis of alcohol or drug abuse or dependence (i.e., their substance use did not meet criteria for dependency), one due to too many errors on the ANT at baseline (i.e., > 25%), three patients due to a VPT or ANT score that was larger than 3SD from the group mean. The final baseline patient sample therefore resulted in a total of 72 participants (48 male and 24 female; mean age = 19.7, *SD* = 2.8; see Table 6.1 for group characteristics). Twenty patients (26.3%) reported that they had not used their primary substance over the previous month. Patients mainly received assertive community treatment, or cognitive behavioural treatment, but the exact approach and duration of treatment highly varied between patients. Medication was no standard component of treatment.

Almost half of the patients who were assessed at baseline also completed the assessment at 6-month follow-up (N = 38). A group of 28 participants did not want to participate anymore during the follow-up assessment, and we were unable to get in contact with another twelve participants. In the follow-up analysis, the data of two participants had to be removed due to too many errors on the ANT (i.e., > 25%) or an ANT score that was larger than 3SD from the group mean. Therefore, for the analysis of the longitudinal data there remained 70 participants in the study, with 32 (46%) who completed both assessments.

Control participants were recruited via schools and by word–of–mouth, for participation in a study about the development of substance use and abuse, which consisted of one session of 90 minutes. They were included for the study if they matched the patient group on the basis of age, gender, and educational level. They were allowed to be recreational users of alcohol and drugs, but were excluded from the study if they had a diagnosis of alcohol or drug dependency. Two controls had to be excluded from analysis due to a coding error (i.e., output of computer tasks were coded the same for both participants) and one due to an ANT score that was larger than 3SD from the group mean. The final control sample therefore resulted in a total of 61 participants (42 male and 19 female; mean age = 19.0, *SD* = 2.4).

All participants gave their written informed consent, and for under-aged participants parents gave written informed consent as well. Both patients and controls received a gift-voucher of 5 euros per session after completion. Descriptive statistics are presented in Table 6.1. The study was approved by the Medical Ethical Committee of the University Medical Centre Groningen.

Table 6.1

Means and standard deviations of variables as a function of group

	Patients n = 72	Controls n = 62	
Variable	Mean (SD)	Mean (SD)	t or U statistic
Gender, % female	32%	31%	2148.0
Age	19.69 (2.83)	19.00 (2.37)	1.52
Educational Level [a]	2.82 (0.79)	3.03 (0.58)	1874.5
Primary diagnosis alcohol dependence (n,%)	10 (14%)	-	
Primary diagnosis cannabis dependence (n,%)	49 (68%)	-	
Primary diagnosis amphetamine dependence (n,%)	10 (14%)	-	
Primary diagnosis GHB dependence (n,%)	3 (4%)	-	
Substance use previous month (AUDIT/DUDIT)	5.93 (4.56)	1.43 (1.03)	8.11**
Severity of dependence (SDS)	5.76 (4.06)	0.27 (0.72)	11.3**
Substance AB 500 ms	19.00 (36.50)	1.60 (11.84)	3.82**
Substance AB 1250 ms	7.39 (25.33)	-0.19 (11.00)	2.30*
EC[b]	108.86 (40.45)	100.07 (32.62)	1.36

Note. SD = standard deviation; GHB = gamma hydroxybutyrate; AUDIT = alcohol use disorder identification test; DUDIT = drug use disorder identification test; SDS = severity of dependence scale; [a] educational level in categories of '1' to '4', where '1' stands for primary education, '2' for lower secondary education, '3' for upper secondary education or lower tertiary education and '4' for higher tertiary education; [b] higher score means a weaker EC; ** p < 0.01 (2-tailed); * p < 0.05 (2-tailed).

Questionnaire measure

Self-reported substance use. Alcohol use was measured by a shortened version of the Alcohol Use Disorder Identification Test (AUDIT: Saunders, Aasland, Babor, de la Fuente & Grant, 1993), which included only questions about frequency and quantity of use (e.g., "At how many days in the weekend did you use alcohol in the previous month?" And "How many glasses did you consume on a drinking day?"). In the current study, the questions were formulated related to the past month. Cannabis use was measured by a shortened version of the Cannabis Use Disorder Identification Test (CUDIT: Adamson & Sellman, 2003), which consisted of three items about cannabis use in the previous month (e.g., "How many times did you use cannabis in the previous month?"). Because there were no comparable questionnaires available, we constructed a SUDIT and a GUDIT, which contained the same questions as the short CUDIT, but now related to amphetamine (speed) use and GHB use respectively. For ease of understanding we named the drug use questionnaires DUDIT. Scores could lie in between 0 and 12 and the higher the score on the AUDIT or DUDIT the higher the level of substance use. Internal reliability of these questionnaires was good to excellent, with Cronbach's alpha ranging from 0.86 to 0.99.

Self-reported severity of dependence. Level of dependency was measured by the Severity of Dependence Scale (SDS: Gossop, Best, Marsden & Strang, 1997). The Severity of Dependence Scale (SDS) is a 5-item questionnaire that provides a score indicating the severity of dependence on alcohol or drugs. Each of the five items is scored on a 4-point scale (0-3). The total score for severity of dependence was calculated by the addition of the score on the five items. A higher score reflects a higher level of dependence. Reliability as indexed by internal consistency of the SDS was good to excellent with Cronbach's alpha ranging from 0.71 to 0.92.

Computerized Measures.

Substance-specific AB. AB was measured with the Visual Probe Task (VPT: MacLeod et al., 1986). In this task we used pictures of four different categories: alcohol, cannabis, amphetamine and GHB. Each category consisted of ten different picture pairs, which were composed of a substance-related picture and a neutral picture. The neutral pictures were matched on composition and brightness. Another fourteen pairs of neutral pictures were used as practice trials at the beginning of the task, and as buffer trials in the switch between different categories of substances. All pictures were 100 mm high and 100 mm wide.

Each trial started with a fixation cross which was presented for 500 ms in the middle of the screen. Participants were told to attend to the fixation cross. Next, the cross disappeared and two pictures were presented (a substance-related and a neutral picture), each on one side of the screen, for a period of 500 or 1250 ms. After disappearance of the pictures a small arrow pointing upwards or downwards was presented at the location of either one of the pictures. Participants had to respond to the arrow by pressing the corresponding button on the response box as quickly and accurately as possible. The next trial started 500 or 1250 ms after each response. The probe was presented equally often on the right and on the left side, and was presented equally often upwards as downwards. For half of the trials the picture pairs were presented for 500 ms whereas for the other half of trials the pairs were presented for 1250 ms. The location of the neutral (and substance-related) picture was balanced across trials.

The VPT started with 16 practice trials, in which participants received feedback about their accuracy, followed by four blocks of critical trials. For each category of substance we created subsets in which the ten picture pairs were presented twice. Thus, we created a subset of 20 alcohol trials, a subset of 20 cannabis trials, a subset of 20 amphetamine trials, and a subset of 20 GHB trials. In each block those four subsets were presented twice. Subsets were pseudo-randomly distributed, with the restriction that the same subset could not be presented in sequence, and that the same subset could not be used as a starting subset of more than one block. Each subset was preceded by 3 neutral buffer trials. Trials within the subsets were distributed pseudo-randomly, with the prescription that during the whole task each picture pair was presented evenly in 500 ms and 1250 ms, with as many probes right as left and up as down, and as many neutral pictures right as left, and that within blocks as many picture pairs were presented for 500 ms and 1250 ms, with as many probes right as left and up as down, and as many neutral pictures right as left. Response time and accuracy were recorded.

Executive Control. The Attention Network Task (ANT: Fan et al., 2002) is designed to measure the alerting, orienting, and executive function of spatial attention. Each trial started with a fixation cross which was presented for 400 ms in the middle of the screen. Participants were told to attend to the fixation cross. Next, a row of five horizontal black lines (one central arrow plus four flankers) was presented above or below the fixation cross, with arrowheads pointing left or right. The target is a left or right arrowhead at the center. The target was "flanked" on either side by two arrows in the same direction (congruent condition), the opposite direction (incongruent condition) or by two horizontal lines (neutral condition). Participants had to respond to the target by pressing the corresponding button on the response box as quickly and accurately as possible. Before appearance of the target a warning cue was presented, to signal the upcoming target. This could be one of four warning conditions: a center cue, which was presented at the center location (replacing the fixation cross), a double cue, which were two asterisks presented above and below the fixation cross, or a spatial cue which was an asterisk presented at the exact location of the upcoming target, or no cue at all.

The ANT started with 24 practice trials in which participants received feedback about their mean response time and accuracy, followed by three blocks of 96 critical trials each. Trials were presented in random order, with all types of warning cue and types of flankers presented evenly frequent, and as many target arrows left as right.

Procedure

Patients were tested in a quiet room at various locations of the treatment center in or near the patient's town of residence. Controls were tested in a quiet room located in the university or schools in or near the patient's town of residence. Measures were administered in a fixed order, and were part of a larger assessment, which further included a computerized Self-Assessment Manikin to assess valence and arousal (see van Hemel-Ruiter et al., 2011), and four questionnaires that were not part of the current study (i.e., Desire to Alcohol/Desire to Drugs Questionnaire, Sensitivity to Punishment and Sensitivity to Reward Questionnaire, Attentional Control Questionnaire, and a Motivation to Change Questionnaire). The VPT and ANT were the first computer tasks of the assessment and the questionnaires were administered after completion of the computer tasks. Computer tasks were presented on a 14 inch Acer laptop computer with a 60 Hz screen (1024 x 768 resolution) using E-prime software version 2.0 (Psychology Software Tools Inc., Pittsburg, Pennsylvania). Participants were seated 50 cm away from the screen and responses were collected with a response box.

Data Reduction and Analysis

VPT trials with reaction times 3SD below (probable anticipations) or above (probable distractions) the mean (baseline 4.1%, FU 4.4%), or with an incorrect response (1.3% baseline, 1.3% FU) were removed (cf., van Hemel-Ruiter et al., 2015b). We computed AB scores by subtracting the mean reaction time on substance trials from the mean reaction times on corresponding neutral trials. This resulted in AB scores for alcohol, cannabis, amphetamine and GHB. A higher AB score means a stronger AB towards substance-related pictures compared to neutral pictures.

Then, a measure of substance-specific AB was calculated in the patient group by selecting only the AB score that was related to the primary diagnosis of substance use (e.g., when the primary substance was cannabis, then the cannabis AB score was used for analysis), and in the control group by calculating a mean AB score for all four substances (i.e., AB alcohol + cannabis + amphetamine + GHB/4).

ANT trials with reaction times 3SD below (probable anticipations) or above (probable distractions) the mean (baseline 5.1%, FU 6.3%), or with an incorrect response (baseline 1.8%, FU 1.4%) were removed (van Hemel-Ruiter et al., 2015b). The EC effect was calculated by subtracting the mean RT of all congruent flanking conditions, summed across cue types, from the mean RT of incongruent flanking conditions (see Fan et al., 2002). A higher score on this total score means a *weaker* EC.

Measures of substance-specific use and dependency were calculated in the patient group by selecting the alcohol or drug questionnaire (e.g., when the primary substance was amphetamine, the DUDIT, SDS-D was used for analysis) and in the control group by calculating a mean score for alcohol and drug questionnaire (e.g., AUDIT+DUDIT/2).

Because of the different frames of the research questions (i.e., one cross-sectional, one longitudinal), the study results will be reported in two parts. Part 1 will report the results of the baseline study of clients and controls. Part 2 will report the results of the longitudinal patient study (i.e., baseline and follow-up).

RESULTS

Part 1 – baseline

Group characteristics, patients and controls baseline. Independent t-tests were used to compare age, gender, educational level, substance use, and severity of dependence between the groups. As can be seen from Table 6.1, the matching of the groups on age, gender, and educational level was successful. The patient group reported higher substance use and severity of dependence than the control group.

Exploration of substance-specific AB scores. We first explored whether ABs for the various substances differed between patients and controls. We therefore made subsamples of patients based on diagnosis (alcohol, cannabis, amphetamine, or GHB dependency). Some patients were diagnosed with more than one substance use dependency. Hence, these patients were selected for more subsamples. For each of the substances, we carried out independent t-tests to examine whether patients with a dependency diagnosis differed from controls (see Table 6.2). Overall, patients showed a larger AB than controls (with the exception of GHB AB 500 ms), but this difference only reached significance for cannabis AB 500 ms and 1250 ms and amphetamine AB 500 ms. As can be seen in Table 6.2, there was an acceptable number of cannabis-dependent patients (n = 54), but the number of patients dependent on alcohol (n = 22), amphetamine (n =20), and especially GHB (n = 3) was small, which implied relatively low statistical power to find differences between patients and controls for these subgroups. Further, one sample t-tests showed that for patients diagnosed with the related substance use dependency, cannabis AB 500 ms and 1250 ms, and amphetamine AB 500 ms were significantly larger than zero. Although not for other substances, controls showed significant cannabis AB 500 ms. This latter finding was unexpected and influenced the calculation of a mean AB score for the controls. However, the finding that cannabis-dependent patients showed a significantly larger cannabis AB than controls was taken to justify the use of a mean AB score for the control group as a reference category.

Table 6.2
Attentional bias scores for patients diagnosed with alcohol, cannabis, amphetamine or GHB dependency

	Alcohol		Cannabis		Amphetamine		GHB	
	Patients	controls	patients	controls	patients	controls	Patients	controls
	n = 22	n = 61	n = 54	n = 61	n = 20	n = 61	n = 3	n = 61
AB	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
500 ms	-3.11 (21.4)	-3.67 (22.8)	26.13 (42.9)*	10.23 (20.6)	12.06 (34.3)*	-1.63 (23.2)	-2.59 (36.8)	1.48 (19.4)
1250 ms	-0.14 (29.3)	-3.03 (19.6)	11.36 (30.7)*	1.29 (19.7)	4.52 (26.5)	-2.25 (22.1)	7.52 (5.9)	3.22 (30.0)

Note.: AB = attentional bias; SD = standard deviation; * score significantly ($p < 0.05$) differs between patients and controls.

Table 6.3
Mean VPT reaction times for primary substance cues and neutral cues

	Patients		Controls	
	n = 72		n = 61	
	Substance cue	Neutral cue	Substance cue	Neutral cue
SOA	Mean RT (sd)	Mean RT (sd)	Mean RT (sd)	Mean RT (sd)
500 ms	574 (75)**	593 (82)	568 (83)	569 (82)
1250 ms	568 (74)*	575 (73)	558 (83)	557 (82)

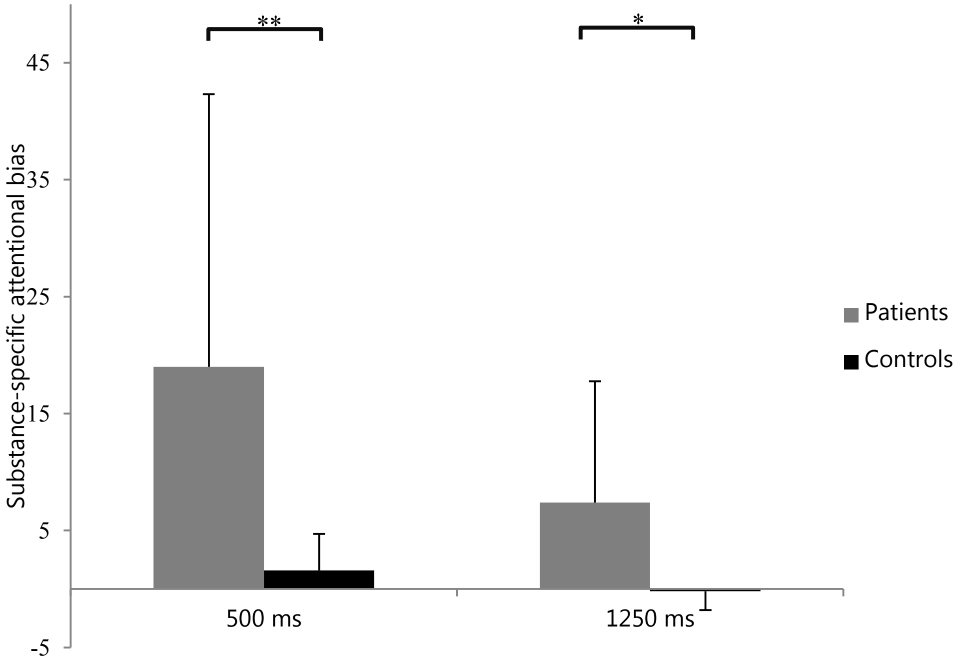
Note. VPT = visual probe task; RT = reaction time; * RT on substance cue significantly ($p < 0.05$) differs from RT on neutral cue; ** RT on substance cue significantly ($p < 0.01$) differs from RT on neutral cue.

AB in patients versus controls. First, we explored whether patients and controls showed an substance AB by comparing the mean response time for probes that were presented on the location cued by the substance stimuli (congruent trials) to the mean response time for probes that were presented on the location cued by the neutral control stimuli (incongruent trials). For the patient group, the analysis was restricted to congruent and incongruent trials displaying pictures of their primary substance of abuse. Table 6.3 shows that for both the 500 ms and 1250 ms trials patients were significantly faster on congruent than on incongruent trials. For controls there was no overall difference in response time between congruent and incongruent trials.

In addition, patients and controls were compared on AB measures by means of a 2 (WS, SOA: 500 ms, 1250 ms) x 2 (BS, group: patient, control) mixed ANOVA.

Most important for the current context, there was a main effect of group (*F*(1,131) = 14.25, $p < 0.001$) indicating that patients generally demonstrated stronger AB for substance-related pictures (see Figure 6.1). Further, there was a main effect of SOA (*F*(1,131) = 6.37, $p = 0.01$) that was similar for both groups as evidenced by the absence of a significant interaction effect of SOA*group (*F*(1,131) = 3.42, $p = 0.07$). As can be seen in Table 6.3, this indicates that the AB was generally stronger for 500 ms than for 1250 ms trials. Although the interaction-effect was not significant, effect-size calculation showed that the difference between patients and controls was medium to large for the 500 ms SOA (Cohen's $d = 0.7$) and small to medium for the 1250 ms SOA (Cohen's $d = 0.4$)

Figure 6.1
Mean 500 ms and 1250 ms attentional biases for patients and controls



Note. * p < 0.05 (two tailed); ** p < 0.01 (two tailed).

Because the largest group of patients were diagnosed with cannabis dependence, we made a subsample of patients diagnosed with cannabis dependency (n = 54), and repeated the analyses for the cannabis-dependent group versus controls, using cannabis AB as dependent variable. The results of these analyses were comparable with the above-mentioned tests, in that patients and controls differed in cannabis AB, and that cannabis AB was highest for active using patients ($F(2,112) = 8.59$, $p < 0.01$). This latter difference was significant for both cannabis AB 500 ms (mean difference between controls and active using cannabis dependent patients = 19.85, $p < 0.01$), and cannabis AB 1250 ms (mean difference between controls and active using cannabis dependent patients = 12.79, $p = 0.02$).

AB in active using and abstinent patients. Because some of the patients had already been abstinent during the previous month (n = 18), and some had not (n = 54), we used post-hoc comparisons of abstinent patients with controls regarding their AB scores by means of a 3 (BS, group: active using patients, abstinent patients, controls) ANOVA for 500 ms and 1250 ms separately, with Fisher's LSD post-hoc tests. The results showed that AB differed between using patients and controls for stimuli that were presented for both 500 ms (mean difference = 19.5, $p < 0.001$), and 1250 ms (mean difference = 8.1, $p = 0.03$), but not between abstinent patients and controls (mean difference AB500ms = 11.2, $p = 0.14$; mean difference AB1250ms = 6.2, $p = 0.26$) or abstinent and using patients (mean difference AB500ms = 8.3, $p = 0.28$; mean difference AB1250ms = 1.9, $p = 0.73$). Results thus showed that substance-related AB was highest for active using patients, and lowest for controls. Post-hoc one-sample t-tests further showed that in the group of active using patients ABes significantly differed from zero (AB 500 ms: mean = 21.08, $p < 0.001$; AB 1250 ms: mean = 7.86, $p = 0.02$), whereas AB effects did not differ from zero within the group of abstinent patients.

Executive attention in patients and controls. A (group: patient, control) ANOVA to compare patients and controls with respect to executive attention indicated that ANT performance did not differ between patients and controls ($F(1,131) = 1.86$, $p = 0.18$). We post-hoc compared active using patients, abstinent patients and controls on ANT performance by means of a 3 (BS, group: active using patients, abstinent patients, controls) ANOVA. Again, the main effect of group was not significant ($F(2,130) = 1.56$, $p = 0.21$).

Moderating effect of cognitive control on the relationship between substance-specific AB and problem severity. Because of the skewed distribution, we first log10 transformed the SDS to obtain a more normal distribution. Correlational analysis showed that within the group of substance-dependent youth, severity of dependence was positively correlated with AB1250ms ($r = 0.25$, $p = 0.04$) but not with AB500ms ($r = 0.09$, $p = 0.48$) or EC ($r = - 0.20$, $p = 0.09$). We used a hierarchical regression analysis to investigate whether EC moderated the relation between AB1250ms and severity of dependence. In step 1 AB1250ms and EC were included and in step 2 the interaction between AB1250ms and EC. This model explained 11% (R^2adj = 0.07, F(5,71) = 2.76, p = 0.05) of the variance in severity of dependence. The results of step 1 show that AB1250ms was positively, and EC was marginally negatively associated with higher severity of dependence (see Table 6.4). However, when the interaction of AB 1250ms x EC was entered in step 2, the main effect of AB 1250 ms appeared to have no independent significant value in the prediction of problem severity. Further, contrary to the expectations, the interaction effect between AB and EC was not significantly related to severity of dependence.

Table 6.4
Moderator regression analysis in the prediction of severity of dependence (n = 72)

Variable		Beta	T	p-value	R^2 Change
Step 1					
	(Constant)		33.33	< 0.001	
	Attentional Bias 1250 ms	0.26	2.28	0.03	
	EC[a]	-0.22	-1.92	0.06	0.11
Step 2					
	(Constant)		32.35	<0.001	
	Attentional Bias 1250 ms	0.30	1.08	0.29	
	EC[a]	-0.21	-1.81	0.07	
	AB1250ms*EC	-0.04	-0.15	0.88	0.00

Note. EC = Executive control; AB = attentional bias; R^2 final model = 0.11*; Adjusted R^2 = 0.07; *p = 0.05; [a] Higher score means weaker EC.

Part 2

Group characteristics, baseline and follow-up. Almost half of the patient participants who were assessed at baseline also completed the assessment at 6 months follow-up (N = 38). A group of 28 participants did not want to participate anymore in the follow-up assessment, and we were unable to get in contact with another twelve participants. Due to the exclusion of seven participants, we kept 70 patients in the study of whom 32 completed both assessments. Of those, 20 were still in treatment at the time of the follow-up assessment.

To test whether patients who remained in the study differed from patients who dropped out, we conducted independent t-tests on baseline measures. These analyses showed that patients who dropped out differed from patients who remained in the study on gender (i.e., 6 female/26 male in completers, 17 female/21 male in drop-outs; Mann-Whitney $U = 450$, $p = 0.02$), but not on age, diagnosis of primary substance, level of substance use, dependency, AB 500ms, AB1250ms, or EC at baseline. Further, although the drop-out rate was quite high, there was no reason to assume that the reason why participants dropped-out was related to research-outcome. We therefore treated the missing data as missing at random and applied multiple imputation in order to estimate the follow-up missing-data. We imputed the missing data in SPSS using M = 40 imputations, and to avoid bias due to missingness we used baseline variables that might be predictive for missingness at follow-up (age and gender, AB and EC variables and substance use variables) as indicators in the model (Sterne et al., 2009). We used this imputed data-set for the following analyses and report the pooled results. Paired-samples t-tests showed that neither substance use nor level of dependency were significantly decreased six months after entrance of treatment (see Table 6.5). As a check-up we repeated all following analyses for the complete cases only, and results were comparable to the results of the imputed data-set.

Table 6.5

Paired samples t-test between baseline and follow-up scores, N = 70[a]

Variable	Baseline Mean (SD)	Follow-up Mean (SD)	T-statistics
Substance use previous month (AUDIT/DUDIT)	5.79 (4.59)	5.37 (5.10)	0.38
Severity of dependence (SDS)	5.63 (4.01)	4.68 (5.63)	0.95
Substance Attentional Bias 500 ms	19.31 (36.96)	10.45 (36.72)	1.34
Substance Attentional Bias 1250 ms	7.31 (25.64)	8.90 (42.74)	-0.18
EC[b]	107.63 (40.08)	86.29 (40.41)	3.22**

Note. [a] Based on the imputed data-set; [b] Higher score means weaker EC; SD = standard deviation; EC = executive control; ** p < 0.01.

Course of AB and executive control. We tested whether ABs decreased between baseline and follow-up by means of paired-samples t-tests. As can be seen in Table 6.5, there was no significant difference between baseline and follow-up for the AB scores. The results further showed that EC significantly increased from baseline to follow-up (mean increase = 21.34, $t(110) = 3.22$, $p < 0.01$). Bivariate Pearson correlations between baseline and 6-month follow-up scores were significant for AB 500ms ($r2= 0.39$, $p = 0.01$) and EC ($r2 = 0.60$, $p < 0.001$), but not for AB 1250 ms ($r2 = 0.09$, $p = 0.57$).

Changes in problem severity, ABs and EC. We subsequently tested whether problem severity differences between baseline and follow-up were related to differences in ABs or EC between baseline and follow-up. We therefore calculated difference scores for both ABs, for EC, and severity of dependence. By means of a multivariate regression analysis we tested to what extent the change in severity of dependence could be predicted by change in AB and EC. This model was not significant in the explanation of change in severity of dependence (R^2 adj = 0.18, $F(3,66) = 6.77$, $p = 0.07$). Thus there was no convincing relationship between changes in severity of dependence and changes in AB or EC.

DISCUSSION

This study investigated AB and EC in a sample of treatment-seeking substance dependent youth, compared to a control group. The major results can be summarized as follows: First, substance-dependent youth showed a stronger AB for stimuli representing the primary substance of abuse than the non-abusing controls, both when presented for 500 ms and 1250 ms. Second, patients did not demonstrate a relatively low EC, compared with matched controls. Further, in the substance-dependent group, higher self-reported severity of dependence was positively related to stronger AB for stimuli that were presented for 1250 ms, and this relationship appeared independent of EC. Finally, congruent with the finding that substance dependency remained unaffected at 6-month follow-up, also AB for substance cues was similar at baseline and at follow-up six months after entering treatment. However, there was an unexpected increase in EC at 6-month follow-up.

The finding that substance-dependent youth were characterized by an AB for relevant substance stimuli is in line with previous research showing a heightened AB for substance stimuli that were presented for 500ms or longer in alcohol and drug abusers (see for review, Field & Cox, 2008), and the few adolescent studies that investigated AB for alcohol in heavy drinking and at-risk adolescents (Field et al., 2007a; Pieters et al., 2011; Zetteler et al., 2006; see for review, Wiers et al., 2015b).

The post-hoc comparison sheds some light on the course of substance-related AB, in that the highest AB was found in substance dependent youth who were current users, and the lowest in the control group. The finding that ABs were absent in abstinent patients is in line with previous studies in abstinent alcoholics showing an absence of AB for alcohol stimuli that were presented for 500 ms or longer (Field et al., 2013; Noël et al., 2006), or even a bias away from those stimuli (Townshend & Duka, 2007; Vollstädt-Klein et al., 2009). This absence of AB for maintaining attention on substance stimuli in abstinent patients might be explained by their explicit wish to remain abstinent.

The inclusion of two stimuli presentation times demonstrated some differences between the role of early attentional processes and maintained attention in addiction. The results showed that there was a large difference between patients and controls for stimuli that were presented for 500 ms, but only a moderate difference for stimuli that were presented for 1250 ms. Interestingly, within the patient group those with stronger maintained attention reported the highest severity of dependence. The hypothesized "vigilance-avoidance" pattern of AB (see, Noël et al., 2006) might account for the relationship between AB for 1250 ms and severity of dependence. Those patients who already were abstinent or moderated their substance use (which indicates a smaller severity of dependence) might have developed a strategy in which they tried to redirect their attention away from substance stimuli, which is easier when there is more time for exerting voluntary control (i.e., 1250 ms condition). However, before making any strong conclusions, it is necessary to test the robustness of this finding by replicating this research in a larger group of substance dependent adolescent patients.

Based on previous findings that substance-abusing individuals are characterized by a lowered executive functioning (Lubman et al., 2004; de Wit, 2009; Verdejo-García & Pérez-García, 2007), we expected to find a lowered EC in the patient group compared to controls. However, we did not find such a difference in the current study. Further, in apparent contrast to previous research that found a moderating role of executive functions in the relationship of appetitive processes and alcohol use functions (Grenard et al., 2008; Houben & Wiers, 2009; Peeters et al., 2012, 2013; Thush et al., 2008; van Hemel-Ruiter et al., 2015b), the current study did not show evidence for a moderating effect of EC on the relation between AB and problem severity. However, there were also previous studies that failed to find a moderating role of executive functions on appetitive processes and substance use (Christiansen et al., 2012; Cousijn et al., 2013; Pieters et al., 2012; van Hemel-Ruiter et al., 2011). One explanation for this finding could be that the role of lowered EC plays a less critical role than often assumed. In addition, since EC is not a unitary construct, it could also be that the ANT does not index the components of

EC that are relevant for AB in substance use. However, this seems not very convincing as a previous study using the ANT to index EC did find evidence for EC moderating the relationship between AB and substance use in heavy drinking students (van Hemel-Ruiter et al., 2015b). Moreover, a series of studies in the context of internalizing symptoms similarly showed evidence for ANT performance as a moderator of the relationship between AB for threat cues and symptoms of anxiety (Hou et al., 2014; Reinholdt-Dunne et al., 2009). Another reason for the current failure to find a moderating influence of EC on the relationship between AB and substance use might be found in the characteristics of the current sample. The current study investigated AB in substance-dependent patients, whereas previous studies were mainly focused on subclinical ranges of alcohol users. To arrive at more definitive conclusions about the role of EC in adolescent substance abuse, it would be important to replicate these findings by using additional indices of EC.

The follow-up assessment of the patient group six months after entering treatment demonstrated that, contrary to expectations, AB had not systematically decreased. However, also the severity of substance dependency and substance use had not decreased. Thus the finding that overall AB remained unaffected is entirely consistent with the starting point that AB is involved in the maintenance of substance misuse. The absence of an effect of the intervention may also explain why this study failed to find a convincing relationship between the reduction in symptoms and a reduction in bias.

The finding that the enhanced AB in patients remained unaffected during the six month period after entering treatment points to the potential relevance of adding treatment components that directly address enhanced AB. Related to this, a first small clinical study showed that ABs can be decreased by means of an AB modification (ABM) training, and that this decrease in AB is related to a decreased relapse-rate in alcoholic patients (Schoenmakers et al., 2010). Further, also other forms of Cognitive Bias Modification have proven successful as add-on to regular treatment for alcoholism (Eberl et al., 2013; Wiers et al., 2011, 2013). Perhaps then conventional treatments might benefit from an add-on ABM intervention, to decrease ABs for personally relevant substance stimuli. The training of these ABs might help patients to automatically attend away from substance cues, which might be supplemental to the conventional therapies aimed at more overt behaviors that are under voluntary control. Germane to this, it has been suggested that ABM might especially be successful when combined with CBT or Motivational Enhancement Therapy (MET: Wiers et al., 2015b); two interventions that are commonly integrated in adolescent addiction treatment programs. Future studies are therefore needed to investigate the effects of an add-on ABM to treatment as usual in adolescent substance-dependent patients.

Although substance use remained largely stable between baseline and six months after entering treatment, EC increased. One explanation could be that the EC increase reflects a learning effect (Ishigami and Klein, 2011). Further, it could be that EC was increased due to the interventions. It could also be that the EC increase reflects normal maturation of the adolescent cognitive processes. Recent research showed that especially in males attentional control continues to increase until at least age 21 (Gur et al., 2012). One way to solve this ambiguity in future research would be to use a between-groups design with half of the participants only being tested at follow-up, or , alternatively, test the control group at follow-up too.

The current study sheds some light on the role and course of substance-specific AB and EC in an adolescent substance-dependent patient group. However, there are some limitations that need attention. First of all, despite our intensive efforts to keep participants in our study, the follow-up component of the present study suffered from a substantial amount of dropout. Most of the patients were in outpatient treatment, which complicated the contact with participants and reduced opportunities to keep the patients in the study. However, we multiple imputed the data-set and completers did not differ at intake from drop-outs (except from gender). Further, results from original data analysis and imputed data analysis did not differ. Second, several authors concluded on the basis of the poor internal consistency of the visual probe task, that this task is unreliable and cannot be used as an index of individual differences in AB (see e.g., Ataya et al., 2012). However, other authors (e.g., Huntjens, Rijkeboer, Krakau & de Jong, 2014) have argued that internal consistency might not be an adequate index of reliability in performance measures especially when the target stimuli (here substance cues) are task-irrelevant and participants' performance profits most from ignoring the target stimuli and to focus on the task at hand (here probe identification). Moreover, its current ability to differentiate between patients and controls seem to speak to its reliability (see also Mogg, Mathews & Eysenck, 1992). Third, it is important to note that for drawing conclusions about changes in AB from the early stages of treatment to 6-months follow up, it is critical that the VPT has satisfactory test-retest reliability. In apparent conflict with this requirement, previous studies that examined the test-retest reliability of the VPT seem to converge to the conclusion that the test-retest reliability of this index of AB is relatively poor (e.g., Marks, Pike, Stoops & Rush, 2014; Schmukle, 2005; Spiegelhalder et al., 2011). However, thus far, these studies relied on non-clinical samples and showed only weak or no overall reaction time based AB effects to begin with. Thus it remains important for future research to examine whether the test-retest reliability within clinical groups is or is not sufficient to draw meaningful conclusions about changes in AB over time. Fourth, the naturalistic setting was not only a strength but also a limitation of our study. It was impossible to direct the inclusion procedure strictly, and thus intake and therapy sometimes intertwined, and in other cases intake and therapy were weeks apart because of patient no-shows. In this way some participants already received one or more therapy sessions and some were already abstinent for a shorter or longer time, before the first assessment within this study took place. This might have influenced the results, although this also has provided some insight in the difference in substance-related AB between still using and abstinent patients. A further limitation related to the naturalistic character of this study is that the current follow-up assessment was at a time when a large number of patients were still in treatment. Although the initial design was to follow participants for a longer period of time, the actuality involved such a large dropout that we had to cancel this third assessment. Unfortunately, we were therefore not able to investigate the longer-term course of substance-specific AB during the treatment period and right after. Furthermore, by taking the AB scores for the different groups of substance abusers together, this might have washed out effects for specific sub-groups. However, the finding of an effect of this composite score also indicates that related processes are involved with dependency of different substances. But it cannot be ruled out that the results might be mainly driven by the difference in cannabis AB between patients and controls. Therefore, it is to be recommended that future studies aim at recruiting alcohol, amphetamine, and GHB using patients, to be able to test whether the relevance of AB may vary as a function of substance. Finally, it should be acknowledged that we used a fixed task order implying that the ANT was always performed after the VPT. Although previous research using a similar order did found differences in ANT performance as a function of alcohol use in early adolescents (van Hemel-Ruiter et al., 2015), it cannot be ruled out that this order may have reduced the sensitivity of the ANT to detect differences between the current patient and control groups.

Taken together, the results of the current study indicate that treatment-seeking substance-dependent youth were characterized by an AB for personally relevant substance stimuli, which was found to be both a bias in early attentional processes and in maintenance of the attention, with only the latter related to problem severity. The novel findings of demonstrating ABs in i) substance dependent youth and ii) for a variety of personally relevant substance cues (alcohol, cannabis, amphetamine and GHB), add to the existing literature demonstrating alcohol ABs in heavy substance users, substance dependent patients and at-risk adolescents. Further, the results of this study showed no decreased EC in substance-dependent adolescent patients, and level of EC did not moderate the relationship between AB and substance dependency. Together these findings are consistent with the view that traditional addiction treatments may benefit from an additional CBM intervention aimed at decreasing substance-related AB.

CHAPTER 7

General discussion

There is ample evidence that adult substance users and addicted persons are characterized by cognitive biases for substance-related stimuli such as approach and attentional biases (Field & Cox, 2008; Stacy & Wiers, 2010). It has also been found that these cognitive biases are predictive for the strength of substance use problems, and relapse-risk (Cox et al., 2002, 2007; Marissen et al., 2006; Streeter et al., 2008). In addition, there is evidence that these cognitive biases are especially related to substance use in people characterized by a weak executive control (Farris, et al., 2010; Friese et al., 2010; Grenard et al., 2008; Houben & Wiers, 2009; Thush et al., 2008; Willem et al., 2013). However, less is known about the role of these biases and the interplay with cognitive control in adolescent substance use and in the transition from recreational to harmful use. This gap in knowledge is important to fill, as adolescent substance use is an important risk factor for the development of substance use disorders (DeWit et al., 2000; Grant et al., 2001; Lynskey et al., 2003; Winters & Lee, 2008).

This dissertation presented a series of studies on automatic and controlled cognitive processes in the context of adolescent alcohol and drug use and dependency. More specifically, the current studies were designed to examine whether (i) adolescent substance use is related to and can be explained by attentional bias toward general rewards, (ii) attentional and approach biases toward alcohol cues are related to young adolescent alcohol use, (iii) adolescents diagnosed with substance abuse or dependency are characterized by an attentional bias for substance related stimuli, and (iv) this substance-related attentional bias mediates the relationship between reward sensitivity and adolescent substance use. Furthermore, following the available evidence on the moderating role of executive controlled processes, it was investigated whether (v) the association between cognitive biases and substance use would be especially pronounced in (young) adolescents with weak executive functions. The current chapter will first summarize the outcomes of the individual studies, then connect and conceptually integrate the major findings, and conclude with suggestions for further research and clinical implications.

MAIN FINDINGS

The role of reward sensitivity in adolescent substance use

The first series of studies described in Chapter 2, 3 and 4 investigated the relationship between reward sensitivity and adolescent substance use. First of all, the study in Chapter 4 showed that adolescents who demonstrated stronger self-reported reward sensitivity also reported heavier use of alcohol. Further, Chapter 2 provided some insight in the attentional processes of reward sensitivity. Adolescents who demonstrated a stronger engagement towards a location that predicted reward and non-punishment reported higher levels of self-reported substance use (i.e., alcohol, tobacco, cannabis). In addition, enhanced automatic attention or orienting towards places of expected non-punishment and enhanced more voluntary or maintained attention towards places of expected reward showed unique predicting value for adolescent substance use. These results suggest that the crucial substance-related attentional biases involve enhanced engagement with cues of reward and non-punishment, whereas problems with disengaging from cues of reward and non-punishment seemed less relevant for explaining adolescent substance use. In other words, when it comes to adolescent heavy substance users, attention is attracted and held more strongly to cues predicting reward compared to cues predicting frustrative nonreward, and to cues predicting nonpunisment compared to cues predicting punishment. On the one hand, a strong automatic engagement towards non-punishment relative to engagement toward punishment could reflect weak automatic fear of negative consequences (e.g., fear of getting a hang-over). On the other hand, a strong voluntary engagement towards reward could represent a heightened voluntary drive to receive rewards (e.g., attaining pleasant feelings after drug use).

The longitudinal study described in Chapter 3 showed that baseline reward biases were also predictive for substance use three years later. However, in contrast to our expectations, reward-related biases were not indicative for an increase in substance use over the next three years. Increase in adolescent substance use could thus not be explained by the strength of their earlier reward-related attentional biases. Nevertheless, the post-hoc analysis in Chapter 3 demonstrated that enhanced voluntary or maintained attention towards places of expected non-punishment was predictive for the level of illicit drug use in those adolescents who initiated the use of these drugs in between baseline and follow-up three years later. An interpretation of this finding could be that people who are striving for non-punishment (which might be avoiding pain, negative thoughts, feelings and situations) are most vulnerable for initiating illicit-drug use. This is in line with the idea that a heightened sensitivity for stimuli that signal unconditioned reward and relief from punishment might predict the development of substance (ab)use (Gray, 1970, 1982). From this perspective, high attentional sensitivity to reward-related stimuli, as indicated by a strong attentional engagement to reward and non-punishment, might be a risk factor for a fast increase after initial substance use, whereas other factors may be more important for the further development and persistence of substance use once substance use behavior has reached a certain level.

Together, the studies described in Chapters 2, 3, and 4 provide consistent evidence for a relationship between adolescent substance use and reward sensitivity as measured by both self-report and behavioral measures. First, the studies described in these chapters all show that reward sensitivity is related to substance use in young, normative adolescents. However, reward sensitivity was not predictive for the increase in substance use over three years. Thus, reward sensitivity might especially play a role in the initiation of adolescent substance use, but not in the transition from recreational to harmful use. It is likely that adolescents whose attention is captured strongly by signals of reward or non-punishment will start using alcohol or other addictive substances. That is, when their attention is captured by the rewarding value of addictive substances, this might more or less automatically guide their behavior towards these substances (cf. Robinson & Berridge, 1993, 2000, 2003). The study described in Chapter 3 demonstrated a prospective relationship between reward-related biases and substance use three years later, and showed that those adolescents who were heavier users at baseline also were heavier users at follow-up. Therefore, (young) adolescents who show heightened attentional bias towards appetitive stimuli might be at risk for initiating substance use at a younger age and subsequently for developing substance use problems. Future research might benefit from designs developed to test the predictive role of reward sensitivity on the initiation of substance use in adolescents who have not used any alcohol and other addictive substances before. Then, it might also be relevant to test the increase in reward sensitivity and its relation with the increase in substance use (cf., Urošević et al., 2015). Further longitudinal research into substance-related cognitive biases (e.g., attentional bias, approach bias) might benefit from the inclusion of a (behavioral) measure of reward sensitivity, to increase insight in the developmental pathways of reward sensitivity and cognitive biases in the prediction of the initiation and escalation of adolescent substance use.

The role of self-reported appraisal of alcohol cues in adolescent alcohol use

The study presented in Chapter 4 showed that young adolescents who reported more positive subjective appetitive evaluations of alcohol stimuli also reported higher levels of alcohol use. Germane to this, a previous study showed increased brain activation in alcohol abusing adolescents in response to pictures of alcohol advertisements, which was related with their frequency of drinking and urges to drink alcohol (Tapert et al., 2003). It therefore might be that alcohol cues (e.g., advertisements) that have been linked to drinking experiences might enhance escalation of drinking in adolescents. In addition, our study showed that the relation between appetitive evaluations and alcohol use was especially strong in adolescents who showed a weak executive control. This finding suggests that the positive features of alcoholic drinks may promote drinking behavior (and further escalation of drinking) especially in those adolescents who are less able to regulate their drinking behavior (i.e., those with low executive functions). Adolescents with impaired executive functions might thus be especially vulnerable for developing excessive alcohol use.

However, due to the cross-sectional nature of the study it is not possible to draw any conclusions regarding the direction of this relationship. It is therefore needed to expand the current research with longitudinal research investigating the proposed interrelationship between explicit valence and adolescent substance use, and the moderating influence of executive control. Concluding, this study showed that appetitive alcohol evaluation and adolescent alcohol use were positively related, but future longitudinal studies are required to inform about the direction of this relationship.

The role of automatic approach tendencies and adolescent alcohol use

One way appetitive, reward-related processes might influence adolescent substance use could be via promoting automatic approach tendencies. The study in Chapter 4 investigated whether indeed automatic approach tendencies were related to young adolescent substance use. Unexpectedly, this study did not show evidence for a positive correlation between automatic alcohol approach tendencies and alcohol use, but just the opposite. That is, those adolescents who reported higher levels of alcohol use showed a relatively strong tendency to avoid rather than to approach alcohol cues. In this study we used two measures of alcohol approach tendencies - a manikin and a joystick version – which yielded comparable results. The fact that the negative relationship between approach tendencies and alcohol use was found for both measures of approach tendencies seems to indicate that this finding was robust, and not just an artifact of the measures that were used. This finding was interpreted in the light of contextual influences; the contextual cues (i.e., school environment) may have made negative associations with drinking alcohol more readily available, which might have activated avoidance rather than approach associations in those adolescent drinkers (cf. Roefs et al., 2006). Recent studies measuring alcohol approach bias in adolescents demonstrated a relation between alcohol approach tendencies and alcohol use in (sub)samples of young high-risk adolescents (Peeters et al., 2012), male adolescents with permissive parents (Pieters et al., 2012), and male adolescents and young adults (Willem et al., 2013). Further, a predictive role of alcohol approach tendencies for future alcohol use was found in (sub)samples of high-risk low cognitive control adolescents (Peeters et al., 2012, 2013), and adolescents with weak explicit negative expectancies (Pieters et al., 2014), but not in a group of normative adolescents (Janssen et al., 2015). This pattern of findings suggests that alcohol approach tendencies seem to be involved in adolescent alcohol use, but that the exact characteristics of adolescents for whom this concerns are still unclear. It is possible that the absence of a relation between alcohol approach tendencies and alcohol use in the current project represents the relatively low-risk nature of our sample. Related to this, a recent study failed to find evidence that baseline alcohol approach tendencies in nondrinking or light drinking young adolescents could predict drinking behavior six to 18 months later (Janssen et al., 2015). Taken together, it seems likely that alcohol approach bias plays a role in the further development of already existing risky drinking and not so much in the development of early drinking (cf., Janssen et al., 2015). To further increase insight in the role of approach tendencies in adolescent alcohol use, more longitudinal studies are needed, which investigate alcohol approach tendencies at different time points (i.e., before and after the start of alcohol use, and preferably over a long period of time) using both low-risk and high-risk samples of adolescents.

The role of attentional bias in adolescent substance use

Related to the role of approach tendencies in adolescent alcohol use, we were also interested in the role of attentional processes in adolescent alcohol use. In the study described in Chapter 5 we measured attentional bias for alcohol stimuli in an unselected group of adolescents. First, we expected that the relationship between reward-sensitivity and adolescent alcohol use would be mediated by alcohol attentional bias. More specifically, we expected that stronger reward sensitivity would be related to attentional bias for alcohol stimuli, which in its turn would be related to alcohol use. However, we did not find such a relationship between reward sensitivity and alcohol attentional bias in this study. With respect to the relation between attentional bias and alcohol use it was found that stronger attentional bias for alcohol cues that were presented for a relatively long duration (1250 ms) but not for a shorter duration (500 ms), was related to adolescent alcohol use. To expand these findings, we conducted a study in a clinical sample of treatment-seeking substance-dependent adolescents to increase insight in attentional processes in substance-dependent adolescents (Chapter 6). The participants of this study were heavy users of alcohol, cannabis, amphetamine and/or GHB, and attentional biases scores for their specific primary substance were measured. In this study we found that, compared to a matched unselected group of adolescents, substance-dependent adolescents demonstrated a stronger attentional bias for substance stimuli that were presented for both a shorter (500 ms) and a longer duration (1250 ms). Thus, patients showed relatively strong engagement towards substance cues as well as a relatively strong tendency to maintain their attention to these cues. In addition, we found that a stronger maintained attention (but not stronger engagement) towards substance cues was related to problem severity. In this study we also again measured attentional bias after a 6-month period in which the substance-dependent patients received treatment of any kind and length. Consistent with the absence of a decrease in substance use and problem severity, also the attentional bias remained unaffected within this time interval.

To sum up, our results did not provide evidence to support the view that the relation between reward sensitivity and adolescent alcohol use is mediated by alcohol attentional bias. Thus, the findings did not substantiate the view that high reward sensitivity would set adolescents at risk for developing attentional bias for alcohol cues. The results did, however, provide evidence for a relationship between alcohol attentional bias and young adolescent alcohol use, but only when stimuli were presented for a relatively long duration. Further, the results of our patient study (Chapter 6) showed that substance-dependent adolescents are characterized by a bias in both the engagement and maintenance of the attention towards substance cues. These findings are in line with previous research on attentional bias for alcohol in adolescents, demonstrating alcohol attentional bias in adolescents with alcohol-dependent parents (15-20 years, as indexed with a Stroop task; Zetteler et al., 2006), and in heavy drinking adolescents (16-18 years, as indexed with a Stroop task; Field et al., 2007a), attentional bias related to alcohol use in young adolescents with an enhanced genetic risk (12-16 years, indexed with 1500 ms VPT; Pieters, et al., 2011), and a predictive role of attentional bias for adolescent alcohol use later on (12-18 years, as indexed with 1000 ms VPT, but no effects using Stroop task; Janssen et al., 2015). However, the results are dissimilar to two other previous studies that did not find alcohol attentional bias cross-sectional related to alcohol use in normative samples of adolescents (15-21 years, as indexed with 750 ms VPT; Willem et al., 2013; 12-16 years, as indexed with 1500 ms VPT; Pieters, et al., 2014; 12-18 years, as indexed with 1000 ms VPT and Stroop task; Janssen et al., 2015). This latter study showed that baseline alcohol attentional bias was predictive for alcohol use six and 18 months later, but only in those adolescents who already had started drinking alcohol at baseline (Janssen et al., 2015).

The differences between these studies complicate direct comparison of the results. First, in some studies risk-groups of adolescents were used, compared to normative samples of adolescents in other studies. Second, it is suggested that the VPT and the Stroop task tap into different underlying components of information processing (Mogg & Bradley, 2002). The task demands differ between the Stoop task and the VPT, with the Stroop task demanding inhibiting irrelevant word meaning, and the VPT demanding scanning visual displays. Further, there is also debate about whether the Stroop interference scores reflect a fast automatic or a slower voluntary strategic process (Franken, Gootjes & van Strien, 2009; Phaf & Kan, 2007; Thomas, Johnstone & Gonsalvez, 2007). And last, the different presentation times of the VPT used in the studies described above are suggested to indicate different attentional processes (from attentional engagement to maintained attention). Zooming in on the studies that used the VPT as attentional bias measure, there is a same trend as in adult substance-related attentional bias (for review, Field & Cox, 2008). It seems that substance use behavior is especially related to a maintained attention toward substance stimuli.

Despite the use of different samples and measures in the above mentioned studies, the results seem most consistent with the view that attentional bias plays a role not so much in the early beginnings of alcohol use, but more in the maintenance and escalation of already existing excessive or risky drinking patterns. In order to further our understanding of the role of attentional bias in adolescent alcohol use, more (longitudinal) research is needed, preferably including young naïve alcohol users as well as excessive adolescent drinkers, and multiple measures of attentional bias in one study.

The study in substance abusing adolescent patients is one of the first that considered attentional bias in this specific group. One recent patient study demonstrated an attentional bias for cannabis cues in cannabis dependent adolescents using a Stroop task (Cousijn et al., in press). The study described in Chapter 6 expands the previous research by showing that substance dependent adolescents demonstrate biases in the engagement and maintenance of attention to substance-related cues. That maintenance of attention was also associated with the severity of dependence, which shows that attention bias for substance cues goes hand in hand with substance use (problems). One way to test whether this attentional bias is causally involved in substance use (problems) would be to train the attention away from substance cues and to see whether modifying attentional bias would also have a decreasing effect on substance use (problems). Further, the finding that substance use, dependency and substance-related attentional biases were not decreased after a six-month treatment period, underscores the highly persistent condition of addiction. In this respect interventions aimed at manipulating substance-related attentional biases might also have clinical relevance as a supplement to traditional addiction treatments.

The role of executive control in adolescent substance use

Three studies investigated the role of executive control in adolescent substance use. The research did not show evidence for a moderating influence of cognitive control on the relationship between alcohol approach tendencies and adolescent alcohol use (Chapter 4). Yet there was evidence that cognitive control moderated the relation between self-reported appetitive valence and adolescent alcohol use (Chapter 4), and the relationship between alcohol attentional bias and adolescent alcohol use (Chapter 5). However, unexpectedly, we did not find a similar moderating relationship between attentional bias and cognitive control in the clinical sample of substance-dependent adolescents (Chapter 6). These findings indicate that in adolescents with weak cognitive control the extent to which they evaluate alcohol positively as well as the way they direct their attention toward alcohol (but not the way they have the tendency to approach alcohol) are predictive for their alcohol use. However, this statement is very speculative, given the still inconsistent findings of previous studies with respect to the influence of executive functions. Some studies did indeed demonstrate that the predictive validity of automatically triggered appetitive processes (i.e., attentional bias, approach bias, and associations) toward alcohol was restricted to individuals with relatively weak executive functions (Grenard et al., 2008; Houben and Wiers, 2009; Peeters et al., 2012, 2013; Thush et al., 2008), and some studies did not find such a moderating role of executive functioning on automatic processes (Pieters et al., 2012, 2014). In these studies the tasks that were used to index executive functioning were different than the ones that were used in our studies (i.e., Self Ordered Pointing Task (SOPT), Stroop task). These different tasks might tap into different aspects of executive functions. However, the use of different tasks is not enough to explain the difference in findings. The fact is that using the SOPT and the Stroop task, some studies did find a moderating role of executive functions and some did not. The difference in findings could better be explained by the differences in population. The studies that did find a moderating role of executive functions used older adolescents (Grenard et al, 2008; Houben & Wiers, 2009; Thush et al., 2008) or at-risk adolescents who already started drinking alcohol (Peeters et al., 2012, 2013), whereas the studies that failed to find a moderating role used normative samples of adolescents (Pieters, et al., 2012, 2014). The finding in our patient study that executive control did not moderate the relation between substance-related attentional bias and substance dependence is in line with recent studies in cannabis-dependent adolescents that also failed to find a moderating role of cognitive control in the relation between cannabis attentional bias and cannabis use and dependence (Cousijn et al., 2013, in press).

One interpretation of these results might be that executive functions play only a minor role in adolescents who just start to drink alcohol, but that in older or at-risk adolescents who already started to drink more alcohol those with weak executive functions are more at risk to use higher levels of alcohol. The finding that in the clinical samples such a moderating relationship did not exist is somewhat harder to explain. It could be that the role of executive control differs in alcohol and cannabis users (since our study also included mainly cannabis users), but this is somewhat hard to substantiate. It could also be that in adolescents who already use excessive amounts of a substance the automatic processes have grown so strong, that the controlled processes simply are not strong enough to control their substance use.

We further also found mixed results regarding the relationship between executive control and substance use per se. The studies described in Chapter 4 and 6 did not find such a relationship, whereas the study in Chapter 5 did find a negative relation between executive control and adolescent alcohol use. Thus, although the results of the study in Chapter 5 seem to indicate that weak executive control could be a vulnerability factor for developing substance (ab)use, the results of the studies in Chapters 4 and 6 do not further substantiate such interpretation. The differences in findings might have been partly due to the use of different measures (i.e., the RNG task in Chapter 4, and the ANT in Chapters 5 and 6), but this cannot explain all, since the ANT measure did (Chapter 5) and did not (Chapter 6) show a relation between strength of executive control and substance use. Another explanation of the differences might be related to differences between samples of participants included in the studies. More specifically, our patient study included many cannabis-dependent adolescents, whereas the normative studies were conducted among alcohol using adolescents. Two recent studies in cannabis (ab)users also failed to find reduced executive control compared to a control group (Cousijn et al., 2013, in press). It could thus be that the role of executive control is different in alcohol users and cannabis users, or even absent in cannabis users.

Future (preferably longitudinal) research is therefore needed on this issue. It is recommended to include two executive control measures, to be able to compare the effects. Further, clinical studies in samples of adolescent patients diagnosed with different substance use disorders (to start with alcohol use dependency and cannabis use dependency) might increase insight in the automatic and controlled processes in adolescent substance dependency.

INTEGRATION OF PRESENT FINDINGS

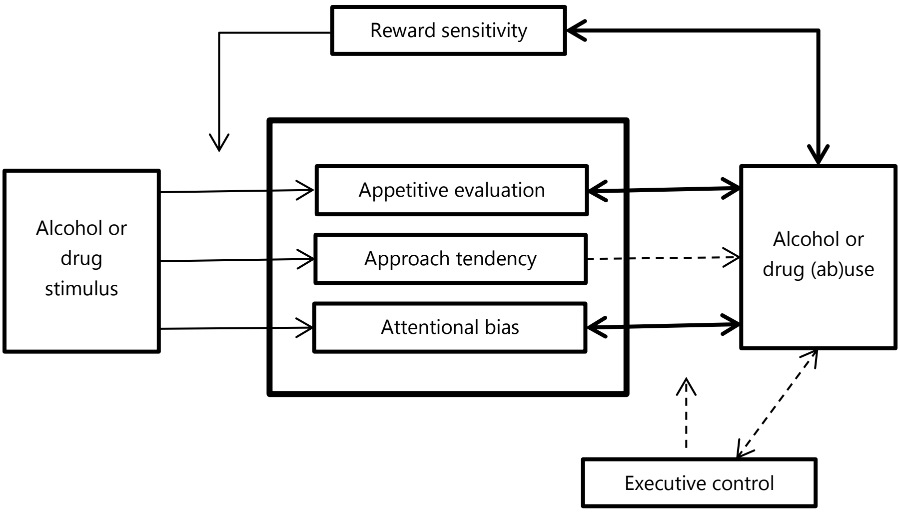
Integrated model

In Chapter 1, a model was proposed that links the pathways that might be involved in the initiation stages of adolescent substance use and in the transition towards harmful use (Figure 1.1). Figure 7.1 presents the same model integrating the findings of the studies that are described. Most of the pathways have been tested in this dissertation, although this has been done in a largely cross-sectional manner. The pathways that are shown in this model are not intended to be exhaustive, but are meant to illustrate the variables described in this dissertation. In this model the dense lines are those relationships for which we found (at least some) supportive evidence in the studies that are part of this dissertation. The dotted lines are those relationships, which were not supported by the present studies or for which the evidence is mixed. The thin lines represent assumed relations that were not explicitly tested in this thesis.

The new aspect in this model is the inclusion of appetitive evaluation. It might be that the explicit appetitive evaluation (or rewarding value) of an addictive substance is a factor that attracts young individuals to those substances and seduces them to try it (cf. Tapert et al., 2003). One aspect that we did not include in our studies but might have been interesting to look at is whether explicit appetitive value of a substance moderates the relation between reward sensitivity and the use of this substance. It might well be that especially in those who are sensitive for reward, and striving to gain rewards, this appetitive value contributes to an individual’s motivation to use substances. It might also be that individuals who are highly sensitive to rewards, evaluate substance cues as more appetitive. More research on this issue is therefore needed to reach more conclusive results.

Figure 7.1

Model for the interplay of approach bias and attention bias, appetitive evaluation, reward sensitivity and executive control in adolescent substance use



Note. The dark arrows represent relations that are supported by this dissertation and seem to be involved in adolescent substance (ab)use. The dotted arrows represent relations which are not or not supported by the present studies, or for which the evidence is mixed. The light arrows represent assumed relations which were not explicitly tested in this dissertation.

Theoretically, it has been suggested that both relatively controlled and relatively automatic processes are important factors in the development of adolescent alcohol (ab)use (e.g., Wiers et al., 2007). More specifically, it is proposed that strong automatic approach tendencies, and attention towards substance-related cues and weak cognitive control are predictive of subsequent adolescent substance use. The studies that were presented in this dissertation partly support this notion, and provide insights into factors that might be involved in the very early stages of adolescent substance use. The current project showed that in normative samples of adolescents appetitive (or reward-related) attentional biases are related to substance use and predictive for the initiation of substance use, but not for the increase in substance use. Further, this project showed that alcohol use was related to appetitive valence of alcohol cues, and a maintained attentional bias for alcohol cues in weak cognitive control adolescents, but not to an approach tendency towards alcohol cues.

These findings suggest that early adolescent substance use might be driven by the appetitive (rewarding) value of these cues, which is in line with a large body of literature showing a relation between reward sensitivity and substance use (problems) (see for review, Bijttebier et al, 2009). Thus, individuals who focus their attention (automatically) on appetitive cues, who are more sensitive for reward and evaluate substance cues as more appetitive are also more likely to engage in substance use. Then, following the first experiences with substance use, and with the rewarding effects of substance use, brain systems may start to sensitize, and automatic cognitive processes (e.g., approach tendencies and attention bias) may start to develop and grow stronger (see e.g., Wiers et al., 2007, Robinson & Berridge, 1993). That reward sensitivity does not seem to play a role in this development to harmful use substantiates the suggestion that in the transition from recreational to harmful substance use other processes have become more important factors. It could therefore be that individuals who are highly reward sensitive first initiate substance use because of the expected rewarding effects, which leads to a quick increase in use. With this repeated substance use automatic cognitive biases might develop, which subsequently might lead to a further increase in substance use and a possible development of substance-related problems. The finding that in our normative samples of adolescents alcohol use was related to attentional bias in weak cognitive control adolescents only, but not to a heightened approach tendency for alcohol might indeed indicate that the development of these automatic processes has only just started. Combining these findings with recent studies investigating the role of cognitive biases in adolescent substance use indicates that the associations between cognitive biases (i.e., approach tendencies and attentional bias) and substance use in adolescence might only hold for specific subgroups (e.g., high-risk adolescents, adolescents with genetic disposition, boys with permissive parents, adolescents with explicit negative expectancies, adolescents with weak cognitive control; see for review, Wiers et al., 2015a).

Our patient study showed that attentional bias for substance cues was related to substance dependency, and that this association was unrelated to cognitive control. Further, the patient group as such was characterized by a strong attentional engagement and maintenance towards substance cues. The suggestion that attentional biases develop by repeated substance use is underscored by this finding. However, we found no supportive evidence for a moderating role of cognitive control in the relation between attentional biases and substance use (problems). The hypothesis that especially weak cognitive control adolescents might be susceptible for developing substance use problems is thus not supported by our research.

Attentional bias, reward sensitivity and executive control

Figure 7.2 depicts a heuristic model representing the involvement of attentional engagement and maintained attention, reward sensitivity, and executive control in substance use and abuse. In this model the dense lines are those relationships for which we found (at least some) supportive evidence in the studies that are part of this dissertation. The dotted lines are those relationships, which were not supported by the present studies or for which the evidence is mixed. The thin lines represent assumed relations that were not explicitly tested in this thesis.

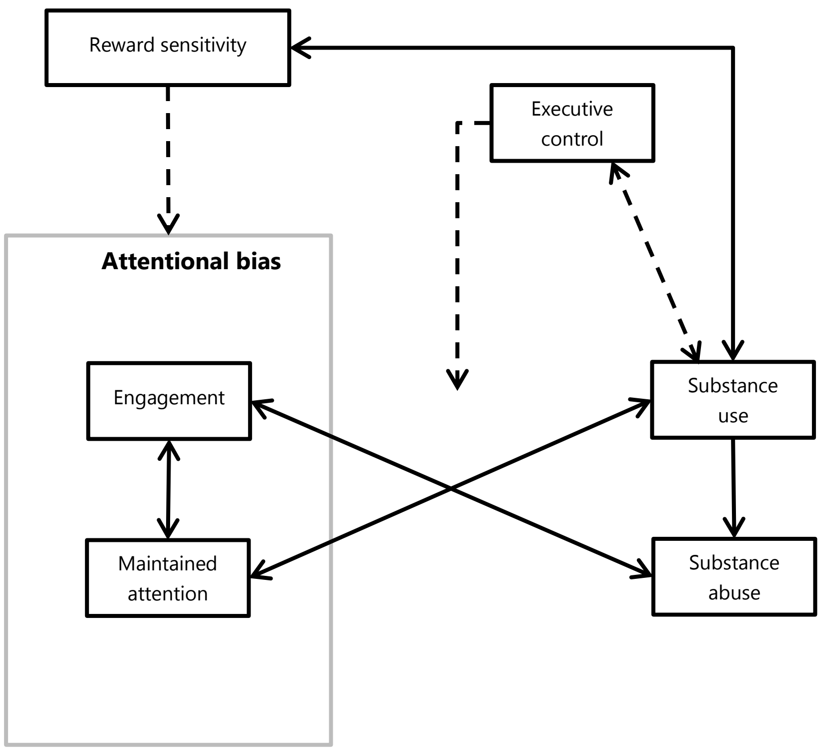
This model specifies how attentional processes might influence adolescent substance use, and the transition to substance abuse. The empirical findings support the involvement of reward sensitivity in early adolescent substance use, and are consistent with the hypothesis that adolescents with high reward sensitivity would be especially at risk for initiating in substance use. The empirical findings provide no support for the hypothesized mediating role of substance-related attentional biases in the association between general appetitive bias and adolescent substance use. However, we only were able to test this relationship using a self-report measure of reward sensitivity. It could therefore be interesting to test this hypothesized relationship using a self-report and a behavioral measure of reward sensitivity (i.e., with the latter generating reward-related attentional bias), which enables testing whether more general appetitive bias is related to substance-specific attentional bias, and/or to self-reported reward sensitivity.

Further, the hypothesized relationships between substance-related attentional biases and substance use and substance abuse were supported. We found evidence for a correlational relationship between substance-related attentional bias and substance use and dependency (Chapter 5 and 6). Specifically, we found that especially attentional bias for stimuli that were presented for a long duration (i.e., maintained attention) was related to substance use, and also to severity of dependence in adolescents diagnosed with a substance use disorder. Although we did not find a correlational relationship between engagement of attention and substance dependency, the adolescent patients were characterized by both a bias in the engagement of attention towards substance cues and in the maintenance of the attention.

In Chapter 5 we found that impaired executive control was related to heavier alcohol use, but we did not find such a relationship in a comparable adolescent sample (Chapter 4) or in substance-dependent adolescents (Chapter 6). We also found some differential results regarding the hypothesized moderating role of executive control. That is, in Chapter 5 we found that only in adolescents with weaker executive control there was a relationship between alcohol attentional bias and alcohol use, but we did not find evidence for such a relationship in substance-dependent adolescents (Chapter 6).

Figure 7.2

Model for the interplay of attentional engagement and maintained attention, reward sensitivity and executive control in adolescent substance use and abuse



Note. The dark arrows represent relations that are supported by this dissertation and seem to be involved in adolescent substance (ab)use. The dotted arrows represent relations which are not or not supported by the present studies, or for which the evidence is mixed. The light arrows represent assumed relations which were not explicitly tested in this dissertation.

These findings shed some light on the cognitive processes that are possibly involved in substance (ab)use. Consistent with the hypothesized "vigilance-avoidance" pattern of attentional biases (Noel et al., 2006) attention might first be drawn towards, and then directed away from the substance stimulus. In adolescents who first start using substances, attention might be drawn equally strongly towards substance cues, and their use might thereafter be influenced by how long they will maintain their attention on this cue (which then will be moderated by the strength of their executive control). In substance-abusing adolescents, attention will be strongly attracted and engaged to substance stimuli, which heightens the possibility that their attention is maintained and they will start using. The actual maintenance of attention then could determine the strength of their substance abuse. Thus, the results of the current project suggest that reward-related (appetitive) bias and attentional bias are involved in the development of adolescent substance use, and provide mixed evidence for a (moderating) role of executive control. Due to the mostly cross-sectional nature of our studies we do not know the direction of these relationships. Some questions that remain to be answered are therefore: does attentional bias for substance cues precede substance use escalation, and what exactly is the role of cognitive control in the development of adolescent substance (ab)use? A longitudinal approach is therefore recommended for future research in order to shed light at these questions. Another question that arose from this dissertation is whether the roles of attentional processes and executive control are different in the development of alcohol, cannabis or illicit drug use. Research using different samples of substance abusing adolescents might provide answers to this question. Finally, research investigating the effect of attentional bias modification might reveal whether attentional biases are indeed causally involved in the development of substance use behavior.

LIMITATIONS

Some methodological considerations need to be discussed. First of all, an important limitation is the correlational nature of most of the studies that were presented in this dissertation. It is therefore not possible to draw conclusions about the causal status of relationships. Second, it should be acknowledged that the effect size of the relationships between substance use and variables that were measured behaviorally (i.e., approach tendencies, attentional bias, executive control) were very small. However, since these kinds of measures provide only rough indications of the targeted behavioral processes, small effects can still be relevant, especially given the considerable risk for negative health and societal consequences related to substance use behavior. Next, the reliability of the attentional bias measures is subject of discussion based on findings indicating relatively low internal consistency (see Ataya et al., 2012). However, several authors (e.g., Huntjens et al., 2014) have argued that internal consistency might not be an adequate index of reliability in performance measures especially when the target stimuli (here drinks) are task-irrelevant and participants' performance profits most from ignoring the target stimuli and to focus on the task at hand (here probe identification). Moreover, its current ability to differentiate between patients and controls, together with its stable pattern over time within the patient group seem to speak to its reliability and validity. Importantly, new algorithms are being developed to more reliably assess attentional bias (e.g., Zvielli, Bernstein & Koster, 2014). One last consideration is the use of a self-report measure for substance use. Participants might not have been entirely honest in reporting their alcohol use, because most of them had not yet reached the legal age of sixteen to use alcohol (Brener et al., 2003; note that currently in the Netherlands the legal age to drink alcohol is eighteen, but at the time of the assessments this was still sixteen). However, self-report measures of substance use have been found to be valid and reliable as long as confidentiality and anonymity is guaranteed (Del Boca & Darkes, 2003).

CLINICAL IMPLICATIONS

The finding that attentional bias is already involved with substance use in (young) adolescents contributes to the available literature regarding the role of alcohol attentional bias in adolescents (Field et al., 2007a; Pieters, et al., 2011; Zetteler et al., 2006). It has been suggested that by repeated use of alcohol (or drugs) related brain circuitry become sensitized, by which substance-related attentional bias will be reinforced (e.g., Wiers et al., 2007). This stresses the importance to develop interventions that are aimed at adolescent substance abusers, in order to prevent escalation of substance use problems. One way to alter attentional biases is by means of computerized Attention Bias Modification (ABM) procedures (MacLeod et al., 2002). Although initial studies in the field of anxiety yielded promising results, recent meta-analyses do not provide consistent conclusions regarding the effect of ABM on psychiatric symptoms (e.g., Beard et al., 2012; Cristea, Kok & Cuijpers, 2015; Cristea, Mogoașe, David & Cuijpers, in press; Linetzky, Pergamin-Hight, Pine & Bar-Haim, 2015), which emphasizes the need for more thorough research in this area. In the field of addiction, recent laboratory studies found that attentional bias for alcohol or smoking stimuli changed after one ABM session, but that this change did not generalize to new pictures, and was not related to a change in substance use symptoms (smokers: Attwood, O'Sullivan, Leonards, Mackintosh & Munafò, 2008; Field, Munafò & Franken, 2009; McHugh, Murray, Hearon, Calkins & Otto, 2010; drinkers: Field, Duka, Eastwood, Child, Santarcangelo & Gayton, 2007; Schoenmakers, Wiers, Jones, Bruce & Jansen, 2007). More recently, promising results were generated using multiple-session ABM in (sub)clinical groups of alcohol drinkers (Fadardi & Cox, 2009; McGeary et al., 2014; Schoenmakers et al., 2010) and smokers (Kerst & Waters, 2014; Lopes, Pires & Bizarro, 2014). One of the major advantages of ABM is that it can be delivered via the Internet, and that interventions can be developed with some game-like character, which makes this kind of intervention especially suited for young individuals. It is therefore recommended to test attentional bias modification procedures in samples of heavy substance-using and/or substance-dependent adolescents. If ABM would turn out to be an effective intervention for modifying attentional bias and reducing substance use and problems, this would also provide evidence for a causal relationship between attentional bias and the maintenance of adolescent substance use.

Further, although the findings regarding the possible role of executive control were mixed, it would still be recommended to test the effects of interventions aimed at increasing executive functioning. Results of such cognitive control training would provide insight in whether an increase in executive control would have a decreasing effect on substance use. This would then not only provide evidence for the efficacy of such training, but also indicate a causal relationship between cognitive control and substance use. Preliminary results of a study using a working memory training showed that indeed heightened working memory capacity was associated with a decrease in alcohol intake for more than one month after the training (Houben, Wiers & Jansen, 2011).

CONCLUSION

Together the findings of this dissertation indicate that relatively high reward sensitivity, appetitive valence, and attentional bias, together with relatively low executive control might help explain the early development of adolescent substance (ab)use, whereas approach bias seems not involved in early substance use. First, heavy substance using adolescents were characterized by a relatively strong attentional bias towards reward, and relatively high self-reported reward sensitivity. Second, early adolescent alcohol use was related to relatively strong appetitive valence of alcohol stimuli and to maintained attention toward alcohol stimuli, especially in low cognitive control adolescents. Third, casting some doubt on the relevance of impaired executive control in the development of substance abuse problems, treatment-seeking adolescents showed similar executive control abilities as non-abusing controls. Fourth, underlining the relevance of attentional processes in substance abuse problems, also treatment-seeking adolescents showed engagement and maintained attention for substance cues, whereas the strength of this latter tendency was related to the level of substance use problems. Finally, both the level of problems and the strength of maintained attention remained unaffected by 6-month conventional treatment. Perhaps, then, current addiction treatments might benefit from adding attentional bias modification interventions to treatment as usual.

To return to the major aims that were mentioned in the introductory chapter of this dissertation, it can be concluded that adolescents who are highly sensitive for rewards, evaluate substances as positive and maintain their attention toward substances strongly might be at risk for developing excessive substance use.

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SAMENVATTING

Wat maakt dat jonge mensen gevaar lopen om problematisch middelen te gaan gebruiken, en welke cognitieve processen zijn betrokken bij de ontwikkeling van experimenteel naar problematisch middelengebruik? Deze vragen staan centraal in dit proefschrift.

Achtergrond

Middelengebruik en –afhankelijkheid vormen een groot probleem onder jonge mensen, niet alleen voor het individu zelf maar ook voor de maatschappij. Het gebruik van middelen zoals alcohol en drugs neemt toe met de leeftijd en kent een piek in de jonge volwassenheid. Sinds 2007 daalt het gebruik van alcohol en drugs in de vroege adolescentie (10-16 jaar), maar het gebruik in de late adolescentie blijft zorgwekkend hoog (16-21 jaar). Ter illustratie: terwijl slechts 1% van de twaalfjarigen in Nederland aangeeft ooit dronken te zijn geweest, is dit onder zestienjarigen 45%. Verder geeft 72% van de alcoholdrinkende middelbare scholieren aan, de laatste maand weleens vijf of meer drankjes tijdens één gelegenheid te hebben gedronken. Onder de twaalfjaren heeft bijna niemand ooit cannabis gebruikt, maar onder de zestienjarigen heeft meer dan een kwart al ervaring met cannabis, van wie 13% dit ook de afgelopen maand heeft gebruikt (zie de Looze, et al., 2014). Het grootste deel van de adolescenten die in behandeling gaan voor middelengebruik heeft een probleem met cannabis- of alcoholgebruik. Ter illustratie: In Nederland is 51% van de adolescenten die zich aanmelden voor een behandeling bij een verslavingsinstelling misbruiker van cannabis, gevolgd door 19% alcoholmisbruikers (zie Wisselink, Kuijpers & Mol, 2013).

Waarom beginnen jongeren met het gebruik van alcohol en drugs, en hoe komt het dat sommige jongeren excessief gaan gebruiken en anderen het houden bij ‘af en toe een glaasje’? Om dit soort verschillen in gedrag te verklaren maakt de psychologie gebruik van zogenoemde duale procesmodellen. Dit soort modellen gaat ervan uit dat alle gedrag gestuurd wordt door twee verschillende typen processen, namelijk gecontroleerde, regulerende processen en automatische, impulsieve processen. Automatische processen gebeuren snel en spontaan, en worden gestuurd door de affectieve of emotionele waarde van informatie in de omgeving. Het herhaaldelijk gebruik van een verslavend middel zorgt ervoor dat de affectieve waarde van het middel groter wordt, waardoor de aandacht en het gedrag automatisch in de richting van dit middel gaan. Gecontroleerde, regulerende processen vinden langzaam en bewust plaats en worden beïnvloed door rationele overwegingen. Door het gebruik van middelen worden de automatische processen steeds sterker, en de controlerende processen steeds zwakker. De automatische processen sturen dus steeds meer aan op het gebruik van middelen, terwijl de controlerende processen dit gedrag steeds minder goed kunnen reguleren (zie bijv. Wiers et al., 2007).

Automatische en controlerende processen bij verslaving

Eén van de automatische processen die een belangrijke rol krijgt toebedeeld bij verslavingsgedrag is *aandachtsbias*: De aandacht van zware gebruikers van verslavende middelen (zoals alcohol, cannabis, heroïne) wordt automatisch en snel getrokken naar informatie (cues) in de omgeving die met het gebruik van 'hun' middel te maken heeft. Een alcoholverslaafde zal bijvoorbeeld tijdens een rondwandeling door een stad alle uithangborden van Heineken en Grolsch opvallen, terwijl een medicijnverslaafde juist alle apotheken zal opmerken. De sterkte van deze aandachtsbias is in verband gebracht met de ernst van het gebruik/misbruik, met escalatie van gebruik en risico op terugval (zie voor een overzicht Field & Cox, 2008).

Een ander automatisch proces dat een rol lijkt te spelen bij verslaving is *toenaderingsbias*: Dezelfde informatie die de aandacht grijpt, zorgt er bij zware gebruikers en verslaafden voor dat zij automatisch de neiging krijgen het middel tot zich te nemen. Deze toenaderingsbias zorgt voor een toename in gebruik (zie Wiers et al., 2007).

De controlerende processen kunnen ervoor zorgen dat het gedrag wordt gereguleerd. Iemand van wie de executieve of controlerende functies sterker zijn, zal dit beter kunnen. Zijn of haar gedrag zal dan minder gestuurd worden door automatische processen zoals aandachtsbias of toenaderingsbias. Iemand met suboptimale executieve functies zal daarentegen juist kwetsbaar zijn voor het ontwikkelen van verslavingsgedrag (zie Wiers et al., 2007).

Onderzoek bij (jong) volwassenen heeft laten zien dat stevige gebruikers en misbruikers van alcohol en drugs zich kenmerken door een automatische aandachtsbias voor cues die gerelateerd zijn aan het middel dat ze gebruiken en een automatische naderneiging in de richting van dit middel. Er is echter nog relatief weinig bekend over hoe automatische en controlerende processen een rol spelen bij het middelengebruik onder (jonge) adolescenten. Het is belangrijk om hier meer over te weten te komen, vanwege het feit dat verslavingsproblematiek vaak al begint in de jeugd, en middelengebruik in de adolescentie een belangrijke voorspeller is voor later gebruik en misbruik. Slechts een paar studies hebben onderzoek gedaan naar aandachtsbias en toenaderingsbias bij jongeren, en deze studies richtten zich bijna allemaal op alcoholgebruikende jongeren. Het doel van dit proefschrift is daarom om meer zicht te krijgen op de rol van automatische en gecontroleerde processen bij alcohol en drugsgebruik en –misbruik in de vroege en midden adolescentie.

Aandacht voor beloning

Door de herhaaldelijke ervaring van het belonende effect van het gebruik van verslavende middelen raken cues die te maken hebben met het verslavende middel gelinkt aan dit belonende effect en zullen ze de aandacht grijpen, waardoor iemand steeds meer gaat gebruiken (zie bijv. Robinson & Berridge, 2003). Een logische gevolgtrekking is dat juist jongeren die extra gevoelig zijn voor beloning en van wie de aandacht automatisch meer gericht is op belonende informatie in de omgeving, degenen zijn die eerder en heviger starten met het gebruik van alcohol of drugs. Hierdoor zal naar verwachting ook hun automatische aandacht voor alcohol of drugsgerelateerde cues versterken. In hoofdstuk 2 en 3 is daarom onderzocht of adolescenten die een sterkere automatische aandacht hadden voor mogelijke beloning een hoger middelengebruik (alcohol, sigaretten en drugs) rapporteerden. In hoofdstuk 5 is onderzocht of jongeren die een hogere beloningsgevoeligheid rapporteerden op een vragenlijst, ook meer alcohol dronken.

Voor de studies in hoofdstuk 2 en 3 is gebruik gemaakt van gegevens die zijn verzameld in de TRacking Adolescents' Individual Lives Survey studie (TRAILS; zie www.trails.nl). Binnen deze grootschalige studie worden vanaf 2001 ruim 2500 jongeren door de tijd heen gevolgd. Toen de deelnemende jongeren ongeveer 16 jaar waren, is in deze studie ook een computertaak afgenomen, als maat voor belonings-gerelateerde aandacht. Dit betrof een soort spel waarbij de deelnemers in een deel van het spel punten konden winnen als ze snel genoeg op een bepaalde cue reageerden en in een ander deel van het spel punten konden verliezen als ze niet snel genoeg reageerden op een bepaalde cue. Daarnaast zijn op hetzelfde meetmoment en drie jaar later vragenlijsten afgenomen om het gebruik van alcohol, tabak, cannabis en harddrugs te meten. Het bleek dat jongeren die hun aandacht sneller richtten op plekken waar een beloning (winst van punten) werd verwacht, of waar zij verwachtten vrij te blijven van straf (verlies van punten) degenen waren die een hoger gebruik van alcohol, cannabis en tabak rapporteerden, zowel op hetzelfde meetmoment alsook drie jaar later. Deze aandacht voor beloning kon echter niet voorspellen bij welke jongeren het gebruik tussen hun 16^{e} en 19^{e} het sterkst was toegenomen. Daarentegen bleek het wel een voorspellende waarde te hebben voor de mate van gebruik van harddrugs binnen de subgroep die in deze periode begon met het gebruik hiervan: jongeren die begonnen met gebruik gingen vrij snel veel gebruiken als ze zich kenmerkten door hoge beloningsgevoeligheid.

Een andere manier om beloningsgevoeligheid te meten is door deelnemers zelf een vragenlijst te laten invullen waarin zij aangeven of de items wel of niet op hen van toepassing zijn (bijvoorbeeld ‘Doe je vaak iets om geprezen te worden?’ of ‘Motiveert het vooruitzicht om geld te krijgen je erg om bepaalde dingen te doen?’). In de studie in hoofdstuk 5 is daarom een beloningsgevoeligheid vragenlijst afgenomen bij 86 jongeren tussen de 12 en 18 jaar en is de score hierop gerelateerd aan het zelfgerapporteerde alcoholgebruik. Dit onderzoek liet zien dat jongeren die hoger scoorden op de vragenlijst voor beloningsgevoeligheid ook een hoger alcoholgebruik rapporteerden. Dit onderzoek liet dus zien dat jongeren die meer gevoelig zijn voor beloning, ook meer alcohol drinken.

Samengevat lieten deze onderzoeken zien dat jongeren die hun aandacht richtten op of gevoelig waren voor beloning relatief veel verslavende middelen gebruikten of gingen gebruiken. De onderzoeken gaven geen aanwijzing dat beloningsgevoeligheid ook gerelateerd was aan een escalatie van gebruik bij jongeren die al gebruiken.

Middelgerelateerde toenaderingsneiging

Eén manier waarop beloningsgerelateerde processen het middelengebruik bij jongeren zou kunnen beïnvloeden is via automatische toenaderingsneiging. In hoofdstuk 4 is onderzocht of jongeren die een sterkere neiging hadden tot het benaderen van alcoholplaatjes in een computertaak, ook meer alcohol gebruikten. In dit onderzoek participeerden 43 jongeren tussen 13 en 17 jaar. Naast het doen van een computertaak, vulden zij ook een vragenlijst in over hun alcoholgebruik. Tijdens de computertaak zagen zij steeds een plaatje van een alcoholische drank of een frisdrank op een computerscherm. Zij kregen de taak om dit plaatje met behulp van een joystick weg te duwen (duw joystick naar voren) of naar zich toe te trekken (trek joystick naar je toe) op basis van de positie van het plaatje. Voor de helft van de deelnemers was de instructie: “Is het plaatje in landschapsformaat (dus liggend) gefotografeerd, dan moet je het plaatje wegduwen. Is het plaatje in portretformaat (dus staand) gefotografeerd, dan moet je het plaatje naar je toe trekken.” Deze instructie was precies andersom voor de andere helft van de deelnemers. De toenaderingsneiging werd berekend door de snelheid waarmee alcoholplaatjes werden aangetrokken af te trekken van de snelheid waarmee ze werden weggeduwd. Een hoge score betekende dus dat iemand een sterke neiging had alcoholplaatjes naar zich toe te trekken (te naderen). Dit onderzoek liet echter het verwachte verband niet zien: jongeren die een relatief hoog alcoholgebruik rapporteerden hadden geen sterkere neiging om alcoholplaatjes naar zich toe te trekken. Sterker nog, zij hadden juist een sterkere neiging alcoholplaatjes van zich weg te duwen. Ook andere recente studies bij jongeren hebben niet allen de verwachte resultaten gevonden. Er is alleen consequent een verband gevonden tussen automatische naderneiging en alcoholgebruik in groepen adolescente zware gebruikers of adolescentgroepen met een verhoogd risico om excessief te gaan drinken (hoogrisico adolescenten; bijvoorbeeld jongeren in speciaal onderwijs, of jongeren met een genetische aanleg) maar niet in groepen jongeren met een normaal risico (laagrisico adolescenten). Mogelijk speelt automatische alcohol naderneiging vooral een rol bij verdere escalatie van al bestaand excessief drinken, en niet zozeer bij het eerste experimentele gebruik ervan.

Naast de automatische neiging om alcohol te benaderen, zal ook de meer bewuste (positieve) evaluatie van alcohol gerelateerd kunnen zijn aan alcoholgebruik. In ditzelfde onderzoek is daarom ook gemeten met behulp van een computertaak hoe lekker de deelnemers alcoholplaatjes eruit vonden zien. De deelnemers zagen op een computerscherm één voor één de alcoholplaatjes die gebruikt waren in de voorgaande taak voorbijkomen, en zij kregen de instructie ieder plaatje te scoren op een schaal die liep van "dat ziet er lekker uit" naar "dat ziet er niet lekker uit". De resultaten lieten inderdaad zien dat jongeren die de plaatjes positiever waardeerden ook meer alcohol consumeerden. Dit verband was vooral sterk bij jongeren die slecht scoorden op een werkgeheugentest als maat voor cognitieve controle. Het lijkt er dus op dat positieve kenmerken van alcoholische dranken drinkgedrag zou kunnen aanmoedigen, en dan vooral in jongeren met zwakke cognitieve controle.

Aandachtsbias voor middelen

Gerelateerd aan automatische naderneiging is automatische aandachtsbias. In de studie beschreven in hoofdstuk 5 is daarom onderzocht of jongeren die een verhoogde aandachtsbias voor alcohol lieten zien ook een hogere alcoholconsumptie rapporteerden. Aan dit onderzoek deden 86 jongeren mee tussen 12 en 18 jaar. Alcoholgebruik werd gemeten met behulp van een vragenlijst. Aandachtsbias werd gemeten met behulp van een computertaak waarbij zij aan zij steeds twee plaatjes op het scherm werden aangeboden. Het ene plaatje vertoonde een alcoholische drank en het andere plaatje een frisdrank. De plaatjes bleven kort in beeld (500 ms) of wat langer (1250 ms) en als ze verdwenen verscheen er op de plek van één van de twee plaatjes een pijltje dat omhoog of naar beneden wees. Deelnemers kregen de instructie zo snel mogelijk met behulp van een knoppenkast de corresponderende toets in te drukken (dus pijltje naar boven of pijltje naar beneden). Aandachtsbias voor alcoholplaatjes werd berekend door de reactietijd op trials waarbij het pijltje verscheen op de plek waar eerst het alcoholplaatje stond af te trekken van de reactietijd op trials waarbij de pijltjes verschenen op de frisdranklocatie. Een hogere score betekende dus een sterkere aandachtsbias voor de alcoholische drank.

De resultaten lieten zien dat jongeren die meer alcohol dronken dan anderen hun aandacht relatief lang bleven richten op alcoholplaatjes, maar niet dat hun aandacht ook relatief snel getrokken werd door deze plaatjes. De neiging om de aandacht te blijven richten op de alcoholplaatjes bleek vooral sterk te zijn bij jongeren die slecht scoorden op een algemene aandachtstest als maat voor cognitieve controle.

Voortbouwend op deze bevindingen is bij een klinische groep middelafhankelijke jongeren tijdens de intake-fase van de behandeling onderzocht of zij een aandachtsbias lieten zien voor het middel waaraan ze verslaafd waren. In de studie participeerden 72 jonge cliënten van een verslavingszorginstelling (12-25 jaar), en 61 gezonde jongeren. Om aandachtsbias te meten werd gebruik gemaakt van dezelfde taak als eerder beschreven. Deze studie liet zien dat de middelafhankelijke jongeren een aandachtsbias vertoonden in zowel de vroege als meer late aandachtsprocessen, dus dat zij hun aandacht sneller richtten op middelplaatjes en dat hun aandacht daar ook langer op gericht bleef. Verder hing de volgehouden aandacht samen met de ernst van de verslaving. Hoe ernstiger de verslavingsproblematiek, des te sterker de aandachtsbias. De cliëntengroep liet echter geen verminderde executieve controle zien ten opzichte van de controlegroep, en ook hield executieve controle geen verband met de mate van middelengebruik of ernst van de verslaving. Tijdens een vervolgmeting zes maanden na de intake bleek de aandachtsbias niet verminderd; dit was echter in overeenstemming met de bevinding dat er evenmin verandering was opgetreden in middelengebruik en de ernst van de verslaving.

Deze twee onderzoeken zijn in lijn met ander recent onderzoek onder adolescenten dat een verband liet zien tussen aandachtsbias en alcoholgebruik bij hoogrisico jongeren, maar is afwijkend van studies in laagrisico groepen jongeren. Het lijkt erop dat aandachtsbias vooral een rol speelt bij de ontwikkeling van drinkgedrag van jongeren die al (veel) drinken. Daarnaast is het een aanvulling op eerder onderzoek door de klinische aard van de laatste studie. De bevinding dat aandachtsbias gerelateerd was aan de ernst van de verslaving laat zien dat aandachtsbias voor middelen hand in hand gaat met middelengebruik en –problemen. Dat de aandachtsbias maar ook het gebruik en de ernst van de verslaving niet verminderd waren na zes maanden onderstreept het weerbarstige karakter van verslaving. Een interventie gericht op het manipuleren van de aandachtsbias zou daarom een goede aanvulling kunnen zijn op traditionele verslavingsbehandeling. Onderzoek heeft laten zien dat het mogelijk is om met behulp van een soort computerspel mensen te trainen om hun aandacht automatisch te herrichten, weg van het verslavende middel. Een recente klinische studie onder abstinente alcoholisten die een variant van de aandachtsbias meettaak heeft gebruikt om de aandacht te manipuleren, liet zien dat aandachtsbias effectief gereduceerd kan worden en dat hierdoor ook de kans op terugval kleiner werd (Schoenmakers et al., 2010).

Hoewel de studies in hoofdstuk 4 en 5 lieten zien dat jongeren met zwakke cognitieve functies mogelijk kwetsbaarder zijn om meer middelen te gaan gebruiken, wees de klinische studie niet in die richting. Ook eerdere onderzoeken onder verschillende middelen gebruikende doelgroepen waarbij executieve controle gemeten werd door middel van een variatie aan taken hebben wisselende resultaten laten zien. Vooralsnog is het dus niet precies duidelijk of en hoe executieve controle een rol speelt bij middelengebruik en –misbruik.

Conclusie

Samenvattend laten de resultaten van dit proefschrift zien dat relatief hoge beloningsgevoeligheid, evaluatieve waardering en aandachtsbias, samen met zwakke executieve controle zou kunnen helpen om de vroege ontwikkeling van middelen gebruik/misbruik bij jongeren te verklaren. Ten eerste, jongeren die relatief veel middelen gebruikten, vertoonden een verhoogde aandachtsbias voor beloning en relatief hoge zelfgerapporteerde beloningsgevoeligheid. Ten tweede, alcoholgebruik bij jonge adolescenten was gerelateerd aan relatief sterke evaluatieve waardering van, en aan volgehouden aandacht voor alcoholplaatjes, en dit gold voornamelijk voor jongeren met een zwakke cognitieve controle. Ten derde, middelafhankelijke jongeren vertoonden een vergelijkbare executieve controle als een gezonde controlegroep. Deze bevinding roept enige twijfel op ten aanzien van een mogelijke relevantie van verminderde executieve controle in de ontwikkeling van problematisch middelengebruik. Ten vierde, middelafhankelijke jongeren richtten hun aandacht sneller naar, en hielden hun aandacht langer gericht op afbeeldingen van de verslavende middelen, en de sterkte van de volgehouden aandacht bleek gerelateerd aan de ernst van de verslavingsproblemen. Dit onderstreept de relevantie van aandachtsbias in problematisch middelengebruik. Ten slotte, zowel het niveau van de verslavingsproblemen als de aandachtsbias bleven onveranderd na een half jaar waarin een conventionele behandeling werd aangeboden. Mogelijk zouden huidige verslavingsbehandelingen kunnen profiteren van een toegevoegde interventie om aandachtsbias "weg te trainen". Op basis van een gecomputeriseerde oefening zouden cliënten kunnen leren hun aandacht weg te richten van de verslavende middelen, waardoor het effect van een reguliere behandeling mogelijk vergroot kan worden.

Om terug te komen op het doel van dit proefschrift, kan geconcludeerd worden dat jongeren die sterk beloningsgevoelig zijn, middelen positief evalueren, en hun aandacht sterker richten naar en gericht houden op verslavende middelen, een groter risico lijken te lopen om excessief middelengebruik te ontwikkelen.

DANKWOORD

En dan is daar eindelijk, maar toch ook wel plotseling de finale van de grote reis van mijn promotie. Wat zijn er veel mensen belangrijk geweest tijdens de afgelopen jaren. Mensen die me gesteund en aangemoedigd hebben, de pieken met me mee hebben gevierd, en me uit de dalen hebben gesleept. Mensen die mij van feedback hebben voorzien, en met me hebben meegedacht. Bedankt daarvoor! Een aantal van hen wil ik graag persoonlijk bedanken.

Peter, wat een geluk dat jij mijn begeleider was tijdens mijn masterthese. Want dat was het begin van een hele prettige samenwerking. Dankjewel voor je vertrouwen in mij toen ik je zeven jaar geleden vroeg me te helpen met het schrijven van onze subsidieaanvraag voor ZonMw. Deze subsidie maakte de weg vrij voor mijn promotieonderzoek onder jouw begeleiding. Ik had geen betere promotor kunnen hebben! Met jouw passie voor onderzoek, je enorme kennis en interesse, en je enthousiasme wist je mij steeds te inspireren. Het pingpongen met stukken tekst gaf me energie en zorgde voor een flow in het schrijven. Wat heb ik de afgelopen jaren verschrikkelijk veel van je geleerd. En wat fijn is het dat we ook nu vanuit mijn onderzoeksfunctie bij VNN met elkaar blijven samenwerken.

Reinout, ik weet nog goed hoe ik jaren geleden achter mijn laptop zat en jouw oratie las over verslavingsgedrag bij jongeren. Het was een grote bron van herkenning en inspiratie, en de aanzet voor het onderzoek dat ik nu nog met zoveel passie doe. Wat ben ik blij dat ik destijds de stoute schoenen heb aangetrokken, en dat mailtje aan jou heb geschreven. Wat geweldig dat het niet alleen bij een masterthese bleef, maar dat je ook daarna als mijn tweede promotor nauw betrokken bent geweest bij mijn entree in dit onderzoeksveld. Het was fijn dat ik altijd een beroep mocht doen op jouw expertise. Dank je voor de prettige samenwerking de afgelopen jaren, je onomwonden feedback en de discussies. Ik kijk uit naar de komende tijd waarin we alweer in een volgend project blijven samenwerken.

Brian, I am so happy that you came over from the US and started working at our department. Thus far I was the only one besides Peter that was doing addiction research. So it was really great to finally have a ‘partner in crime’ ;). Thank you for the always inspiring conversations and discussions. I appreciate the time and energy that you spent on the papers, and our discussions. It was and it still is a real pleasure to work with you.

Ook dank aan de leden van de beoordelingscommissie: Prof. Wilma Vollebergh, Prof. Ingmar Franken en Prof. Ritske de Jong voor het kritisch doorlezen van mijn proefschrift.

Het eerste deel van mijn project was in samenwerking met TRAILS. Tineke, jij was vanuit TRAILS betrokken bij mijn onderzoek. Ondanks je overvolle agenda reageerde je altijd snel op mijn mailtjes. Ik heb je eerlijke, kritische, maar ook opbouwende feedback als zeer waardevol ervaren. Bedankt voor je betrokkenheid en de fijne samenwerking!

Mijn laatste onderzoek (dat overigens de meeste tijd in beslag heeft genomen) was in samenwerking met en bij VNN. Jannet, jij hebt me geïntroduceerd bij je collega's, en meegedacht over de onderzoeksopzet. Dankjewel voor je input in deze fase. Frank, ik herinner me heel wat keren dat wij de planning weer eens moesten bijstellen. Wat ging dit project soms moeizaam! Dank dat je me steeds weer in contact bracht met collega's die me verder zouden kunnen helpen. Zo kwamen we stapje voor stapje in de richting van het einddoel. Dank voor jouw inzet voor dit project, en wat bijzonder dat ik in VNN het stokje van je mocht overnemen vorig jaar. Behandelaren jeugd van VNN, zonder jullie was het nooit gelukt om de studie rond te krijgen. Heel veel dank voor jullie hulp bij het werven van cliënten voor dit onderzoek! Bettina, jij was vanaf het eerste begin betrokken bij dit onderzoek. Dankjewel voor je enthousiasme, je betrokkenheid en je enorme inzet om dit project te laten slagen!

Een speciaal dank en een woord van bewondering voor alle cliënten en niet-cliënten die hebben deelgenomen aan de onderzoeken. Jullie hebben tijd geïnvesteerd voor iets waar je zelf niet direct belang bij had. Dank ook voor de ouders die hun toestemming gegeven hebben zodat hun kind kon deelnemen aan het onderzoek. Daarnaast wil ik de scholen bedanken waar wij jonge deelnemers mochten werven. Wat fijn dat jullie ons het vertrouwen, de gelegenheid en de ruimte gaven!

Van onschatbare waarde zijn ook de masterthese studenten die mij hebben geholpen bij het werven en meten van deelnemers. Dank ook jullie vrienden en familie van wie veel als proefpersoon hebben meegedaan om de controlegroep vol te krijgen. Yvette, wat geweldig dat je na je masterthese als student-assistent de data-inclusie verder hebt weten rond te breien. Leonie, dank ook voor jouw inzet in de eindspurt. Esther S, het was fijn dat jij tijdens mijn zwangerschapsverlof de studie bij VNN draaiend hebt gehouden.

Collega's van Klinische: Misschien besef ik het achteraf nog wel meer, maar wat heb ik een geweldige tijd gehad met jullie op de gang. Ik denk nog vaak met wat weemoed terug – en wat is het dan fijn om heel af en toe nog even langs te komen. Heel erg bedankt voor alle support en gezelligheid! Esther V, jij was de eerste periode van mijn AIO-zijn mijn kamergenoot. Het was erg fijn dat jij me kon introduceren in de gebruiken van onze afdeling. Dank voor de gezellige tijd! Charmaine, we had so many special conversations, thanks for being a really wonderful colleague. Gemma, mijn 'roomie' ☺. Dankjewel voor je altijd luisterende oor, je opbeurende woorden, je gezelligheid en je humor. Ik kijk met heel veel plezier terug op onze gesprekken, koffietjes en theetjes, en wandeltjes naar de supermarkt**.** Gemma en Charmaine: wat fijn dat jullie mijn paranimfen zijn! Met jullie aan mijn zijde durf ik alles aan! Ook een woord van dank voor de vaste staf. Voor jullie input, de mogelijkheid om met jullie te sparren, en het bieden van een stimulerende werkomgeving. Dankjewel ook Bert (voor alle technische ondersteuning en Mark (het bespreken van statistische vraagstukken onder het genot van een kopje koffie. Goeie combi!). Een speciaal woord van dank voor de dames van de secretariaten. Want naast de praktische ondersteuning, zorgden jullie ook voor een gezellige sfeer. Jullie waren er als ik behoefte had aan een luisterend oor, een opbeurend woord, of een grap en een grol. En Hendri, als jij beneden achter de balie zat, begon mijn dag goed en liep ik meestal met een grote glimlach de trap op naar boven.

Collega's van VNN: Wat ben ik blij met mijn nieuwe werkplek, en mijn nieuwe collega's! Wat is er een prettige sfeer van belangstelling en gezelligheid. Margreet en Eric, dank voor jullie belangstelling en aanmoediging in de laatste fase van het schrijven van mijn proefschrift. En wat is het geweldig dat ik de ruimte heb gekregen om bij VNN een vervolg te geven aan mijn onderzoekslijn!

Lieve vrienden en lieve (schoon)familie: Wat is het heerlijk om nu eindelijk tegen jullie te kunnen zeggen: het is klaar, af, done, finito! :) Papa en mama, wat was het fijn dat jullie tijdelijk wat vaker op de jongetjes konden passen, zodat ik aan mijn proefschrift kon werken. Dank voor jullie onvoorwaardelijke steun, belangstelling en liefde! Pa en ma, hoe lastig het ook was om te begrijpen wat ik nu precies deed, het weerhield jullie er niet van om er steeds met interesse naar te vragen. Dank voor jullie betrokkenheid. Lieve broers, schoonzussen en zwagers, neven en nichten (Matijs en Foekje, Sander en Fenja, Teun en Tineke en (schoon)kinderen, Adriaan en Carla en kinderen), dank jullie wel voor al jullie steun en belangstelling voor dat wat ik doe. Matijs, wat geweldig dat jij de omslag van mijn proefschrift wilde ontwerpen. Wat is het mooi geworden! Sander, af en toe even een belletje of appje om te horen hoe het ging. Het was fijn te weten dat jullie op afstand meeleefden. Sandra, steeds als ik je vertelde dat ik een belangrijke deadline had, of een praatje moest houden, vroeg je me later hoe het geweest was. Dank voor je warme vriendschap en betrokkenheid! Wendy, jij was erbij toen ik begon aan dit grote avontuur. En wat is er veel in onze levens gebeurd in de tussentijd. Dank voor je lieve vriendschap door de tijd heen.

Maarten en Michiel, het is toch wat dat je als tiener opeens een 'boze stiefmoeder' krijgt die zich bezighoudt met onderzoek naar alcohol en drugsgebruik bij jongeren. Dank dat ik jullie af en toe mocht 'gebruiken' als testpersoon - helaas dan niet voor het testen van de drankjes, maar voor saaie computertaken ;). Er zijn vast niet veel leeftijdsgenoten die zoveel weten van (de gevaren van) alcohol en drugs als jullie. Des te meer dank voor jullie belangstelling door de tijd heen!

Benjamin en Jonathan, mijn lieve, grappige, stoere ventjes :) Wat was het soms ingewikkeld: de combi werk, gezin, en proefschrift. Maar wat zorgden jullie ook steeds weer voor een welkome afleiding met jullie grappen en ontelbare knuffels en kusjes. Wat ben ik dankbaar dat jullie in mijn leven zijn gekomen!

Nico Jan, mijn allerliefste man, mijn grote liefde. Je hebt me steeds onvoorwaardelijk gesteund. Me opgepept als ik het niet meer zag zitten, en mij opgetild bij ieder succes. Het lukt jou gewoon altijd om mij aan het lachen te maken. Dankjewel voor het heerlijke leven dat we samen hebben. Het is zo fijn om bij jou thuis te komen! Dankjewel voor jou.

Voor jullie allemaal, en ook voor al die lieve mensen in mijn leven die ik hier niet genoemd heb: dankjewel dat je er voor me was!

CURRICULUM VITAE

Madelon van Hemel-Ruiter was born on June 27th 1978 in Leeuwarden, the Netherlands. After completing Grammar School in 1996 she had the wish to work with adolescents and started studying Social Work (BSc) at the CHN college of higher education in Leeuwarden. In the last year of the study she did an internship as a social worker at a residential setting for youth care, which was followed by a temporary job at the same setting. She moved to Groningen in 2001 where she started working as a youth welfare worker in Drenthe. Needing a more cognitive challenge alongside her job as a social worker Madelon started studying Psychology (BSc) in 2003. Working with adolescents and experiencing the effects of the use of alcohol and drugs in this age group laid the foundation for her interest in the development of adolescent alcohol and drug use. In the final year of her study Madelon performed her Master thesis aimed at examining the role of automatic alcohol approach tendencies in young adolescent drinkers (Chapter 4 of this thesis) supervised by Prof. Dr. Peter de Jong and Prof. Dr. Reinout Wiers. Madelon finished her MSc. Psychology in 2007 and got the opportunity to get a temporary part-time job at the University of Groningen as a research assistant and teacher. Her dream was to work as a researcher, and she therefore decided to that quit her job as a social worker, and focus on career opportunities at the University of Groningen. In 2008 Madelon worked on a grant proposal "Attentional processes in the development and maintenance of substance abuse and dependence" together with Prof. Dr. Peter de Jong. The grant proposal was awarded by ZonMw in 2009 and became the funding of her PhD studies under supervision of Prof. Dr. Peter de Jong, Prof. Dr. Reinout Wiers and Dr. Brian Ostafin. Since May 2014 Madelon works as a senior researcher at VNN addiction care center in Groningen. In 2015 she earned a ZonMw grant for a research proposal "Internet-based attentional bias modification training as add-on to regular treatment in alcohol or cannabis dependent outpatients". Madelon lives in Assen together with her husband Nico Jan, stepsons Maarten (1994) and Michiel (1998) and sons Benjamin (2012) and Jonathan (2014).

LIST OF PUBLICATIONS

Van Hemel-Ruiter, M. E., Wiers, R.W., Brook, F. G., & de Jong, P. J. Attentional bias and executive control in treatment-seeking substance-dependent adolescents: a cross-sectional and follow-up study. *Submitted for publication.*

Van Hemel-Ruiter, M. E., de Jong, P. J., Ostafin, B. D., & Oldehinkel, A. J. (2015). Reward-Related Attentional Bias and Adolescent Substance Use: A Prognostic Relationship? *PLoS ONE 10(3): e0121058.*

Van Hemel-Ruiter, M. E., de Jong, P. J., Ostafin, B. D., & Wiers, R. W. (2015). Reward sensitivity, attentional bias, and executive control in early adolescent alcohol use. *Addictive Behaviors, 40*, 84-90.

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Ostafin, B. D., Kassman, K. T., de Jong, P. J., & van Hemel-Ruiter, M. E. (2014). Predicting dyscontrolled drinking with implicit and explicit measures of alcohol attitude. *Drug and alcohol dependence,, 141*, 149-52.

Van Hemel-Ruiter, M. E., de Jong, P. J., Oldehinkel, A. J., & Ostafin, B. D. (2013). Reward-related attentional biases and adolescent substance use: The TRAILS study. *Psychology of Addictive Behaviors, 27*, 142-150.

Van Hemel-Ruiter, M. E., de Jong, P. J., & Wiers, R. W. (2011). Appetitive and regulatory processes in young adolescent drinkers. *Addictive Behaviors, 36,* 18-26.

Ruiter, M. E. (2008). Het nieuwe onbewuste*. Gedragstherapie, 41*, 199 - 208.

What makes young individuals more likely to develop problematic substance use, and which cognitive processes underlie the development from experimental or recreational to harmful substance use? These two questions were the starting point for the current project.

This dissertation presents five studies that investigated several factors that may be involved in adolescent substance (ab)use, including proneness to detect signals of reward, selective attention for substance cues, automatic approach tendencies, and low executive control. Adolescents with high levels of substance (ab)use showed a relatively high sensitivity for signals of reward, a difficulty to redirect their attention away from substance cues, and a relatively positive affective judgment of substances. An important next step is to experimentally manipulate these factors (e.g., via Attentional Bias Modification) in order to ascertain their causal status, and to investigate their relevance as targets for preventive and therapeutic interventions.

ISBN 978-90-367-8262-3