Now is the time for reward! The developmental relationship between cognitive-motivational factors and adolescent substance use

Janssen, T.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (http://dare.uva.nl)
CHAPTER 8

GENERAL DISCUSSION
8.1 Summary

General aims for the current thesis were to investigate selected cognitive-motivational factors related to the development of substance use during adolescence. Adolescence has been described as a crucial and vulnerable developmental period marked by an increased tendency to engage in risky behavior. During this period, previous studies established that substance abuse is associated with atypical patterns of brain functioning, executive functioning, and other aspects of cognition. However, it was unclear whether these differences between substance abusing and non-abusing youth originated as a consequence of substance use, or served as pre-existing vulnerabilities originating before the onset of substance use (De Wit, 2009). Recent research has identified a number of key processes found to be associated with adolescent substance use and abuse. Strict parental alcohol-specific rules have been shown to reduce alcohol use during and beyond adolescence. Risk-associated externalizing and internalizing personality traits have been shown to influence onset of substance use. Both self-report and behavioral aspects of impulsivity and sensation seeking have previously been found to predict substance use. Deficits in executive functioning (defined as a set of cognitive abilities that allow us to control, regulate, inhibit and delay behavior) have been shown to be associated with relatively high levels of adolescent substance use (review: Peeters et al., 2014). Finally, cognitive biases that are activated by conditioned environmental cues and automatically trigger behavior in favor of substance use have been identified and associated with heavy substance use, addiction, and other cognitive traits such as impulsivity (Coskunpinar & Cyders, 2013; Field et al., 2007). Central to this thesis is the development of these processes and their co-development with related traits and early substance use. Empirical chapters in this thesis covered five specific research questions. We used data from a longitudinal online survey with assessments at four time waves over two years to address these research questions. At each wave, we assessed different cognitive processes, personality and environmental factors, and the amount of use of different substances including alcohol, tobacco and marijuana.

First, we examined the roles of an important environmental predictor, alcohol-specific parental rule-setting, and an important person-centered predictor, risk-associated personality traits, and their interaction, in the onset and escalation of alcohol use. We predicted lower odds of drinking, especially heavy drinking, as a main effect of parental rule-setting. We predicted higher odds of drinking, especially heavy drinking, as a main effect of risk-associated personality traits. We predicted that scoring high on risk-associated personality traits would be more predictive of drinking when a lack of parental rule-setting occurred. We concluded that
both high scores on risk-associated personality traits and lenient parental rule-setting each individually predicted onset and escalation of alcohol use, but no evidence was found that the impact of risk personality on adolescent drinking was moderated by parental rule-setting.

Second, we examined the role of self-reported and behaviorally assessed aspects of impulsivity and sensation seeking in relation to onset of substance use. We predicted that self-reported aspects of impulsivity and sensation seeking would predict the onset of all types of substance use. We also predicted that behavioral aspects of impulsivity and sensation seeking would additionally predict unique variance in onset after accounting for self-report measures. We found that when correcting for age and gender, self-report measures of sensation seeking prospectively predicted early onset of all types of substance use, but behavioral measures of impulsivity did not.

Third, we examined the role of aspects of executive functioning (working memory capacity and response inhibition) in relation to the onset of alcohol use. We predicted that weak working memory and response inhibition would each predict the onset of both drinking and binge drinking in a joint sample of adolescents enrolled in regular education and adolescents enrolled in special education. We found that low scores on two measures of executive functioning, namely working memory capacity and response inhibition, both predicted early onset of drinking. Furthermore, low scores on working memory capacity predicted early onset of binge drinking.

Fourth, we examined the prospective relationships between aspects of impulsivity and alcohol-specific cognitive biases, and the prospective relation between these biases and later onset and amount of alcohol use. We predicted that both self-report and behavioral impulsivity and sensation seeking would prospectively predict the presence of alcohol-specific cognitive biases. Also, we predicted that earlier substance use would additionally predict the presence of alcohol-specific cognitive biases when impulsivity was controlled for. Finally, we predicted that alcohol-specific cognitive biases would prospectively predict the amount of alcohol consumed, but not the onset of alcohol use. We found that high scores on attentional bias (assessed with a Visual Probe Task), but not differences in approach bias, predicted higher future alcohol use. However, there was no indication for the reverse relationship: that greater initial alcohol use or greater initial impulsivity, or their interaction, predicted changes in later cognitive biases.

Fifth, we examined the nature of the joint developmental relation between approach bias (the automatic tendency to approach and consume alcohol) and alcohol use. We predicted that the intercept of bias (or the basic level of bias displayed equally across time) would be
associated both to the intercept of alcohol use as to the growth of alcohol use. We also predicted that growth of bias would be associated both with the intercept of alcohol use and with the growth of alcohol use. We finally predicted that these relations would be stronger in adolescents with poor working memory capacity. We found that while the intercept of an approach bias was positively associated with the intercept of alcohol use, there were no significant associations between changes in either factor. Furthermore, there was no evidence of moderation of these associations by working memory capacity.

8.2 Reflection on the Main Findings

8.2.1 Findings regarding the Joint Role of Environmental and Cognitive Factors

Within the social environment of young adolescents, parents have previously been shown to play a vital role. It was found that parents may guide adolescent behavior by offering substance-specific rules (Van Der Vorst et al., 2005; Van Der Vorst et al., 2006). Such rules have been shown to be a strong influence on drinking behavior extending even into college (Wood, Read, Mitchell, & Brand, 2004). Equally, risk personality has been demonstrated to strongly influence onset and quantity of substance use behavior (Woicik et al., 2009). Within the context of joint environmental and cognitive factors, one might be interested to know whether parental rules work equally for different personality types. This interest led us to the hypotheses in Chapter 3.

Regarding risk personality, we demonstrated that both sensation seeking and hopelessness were both important predictors of drinking status. In both cases, sensation seeking and hopelessness predicted onset of alcohol use during the study period, while sensation seeking also predicted transitioning into heavy drinking for current drinkers. As with earlier studies using Dutch samples (Malmberg et al., 2010; Malmberg et al., 2012), higher trait impulsivity did not predict increased onset of alcohol and heavy drinking independently from sensation seeking. While the current study lacked cultural norm investigations, cultural differences in the acceptance of alcohol use among adolescents might explain these findings. Furthermore, we replicated earlier findings that suggest that although anxiety sensitivity later in life is associated with substance use behavior (Woicik et al., 2009), it appears to initially have the reverse relationship. Such a protective role from anxiety sensitivity was found earlier by Malmberg and colleagues (2010). Possibly, anxiety sensitive adolescents may fear the unfamiliar effects of alcohol use and worry about what a loss of control as a consequence of alcohol use may cause.
Regarding parental rules, we indicated in Chapter 3 that like in previous work involving Dutch adolescents, strict alcohol-specific rules strongly predicted delayed onset and reduced quantity of substance use. Worthy of comment is the increased overall rate of adolescents who indicated that their parents held strict alcohol-forbidding rules, compared to earlier work studying alcohol-specific rules (Van Der Vorst et al., 2006; Van Der Vorst et al., 2007). Despite dichotomizing parental rules as a predictor, effectively distinguishing only between alcohol-forbidding rules and alcohol-nuanced rules, we found that its influence was stronger than that of risk personality. The increased rate of strict parental rules appears to confirm the effectiveness of current Dutch national policy encouraging this strictness.

Currently, longitudinal experimental work testing the effectiveness of adolescent parental rules intervention on consumption during later adulthood would advance our knowledge on long-term effectiveness.

Perhaps surprisingly, we did not find the expected interactions between adolescent risk personality and parental rules in determining drinking status. While not examining the exact same traits as Van der Vorst and colleagues (2009), our conclusions largely match those from that work. There are two ways to look at our finding. Cast in a negative light, it would suggest that parental rules are no miracle cure for preventing at-risk adolescents from engaging in alcohol use. In other words, high scores on at-risk personality traits appear to influence the onset and escalation of alcohol use, regardless of whether parents apply strict alcohol-specific rules, although strict parental rules influence onset and escalation as well. However, cast in a positive light, it suggests that regardless of personality type, in line with previous findings (Van Der Vorst et al., 2007; Van Der Vorst et al., 2009), parents do consistently influence adolescent drinking behavior via alcohol-related rules. Perhaps it is the case that parents may prevent the worst or at least, supposedly, aid in instilling internalized norms in their adolescent child, the effects of which guide behavior even when the parents no longer supervise them. While risk personality does not appear to interact with parental rules, there is evidence in the literature that certain other cognitive factors may interact. One such example comes from Pieters and colleagues (2012) who demonstrated that approach bias did interact with parental rules, such that higher approach bias for alcohol more strongly predicted alcohol use in adolescent boys when parental rules were lenient. Finding interactions between environment- and person-centered variables in the prediction of substance use may continue to prove fertile soil for understanding adolescent cognitive processes specific to certain social situations or physical environments. Additionally, they are valuable in ensuring and improving the efficacy of
intervention strategies seeking to modify either at-risk personality or strictness of parental rules, or indeed a combination of the two. Data from the current sample underline that both strategies appear to be viable to influencing the onset and escalation of alcohol use.

8.2.2 Findings regarding Aspects of Impulsivity and Sensation Seeking

Recent research on cognitive predictors of substance use has used both behavioral and self-report assessments of impulsivity and sensation seeking. Based on previous work, there are indications that both types of assessments may play a separate and important role in predicting adolescent and adult substance use, and that sensation seeking’s role in predicting substance use may be mediated by cognitive biases (Ames, Sussman, Dent, & Stacy, 2005). We investigated the role of such aspects of impulsivity and sensation seeking in the onset of alcohol, smoking and marijuana use and studied their relation to cognitive biases.

Findings from Chapter 4 indicated that while previous research uniquely associated behavioral impulsivity, self-report impulsivity and self-report sensation seeking measures with substance use (Castellanos, 2009; Nees et al., 2011), such unique associations were not present in the current dataset. While self-reported sensation seeking was reliably associated with onset of substance use, no important role could be found for behavioral measures of impulsivity in the prospective prediction of onset of substance use. In our study, behavioral assessments were directly correlated with substance use only when predicting the amount of substance use, not when self-report assessments were controlled for. Prediction by sensation seeking is in line with earlier findings which suggest that adolescent risk behavior may be spurred by high scores on sensation seeking (Conrod et al., 2008; 2010), which is known to undergo a temporary increase in sensation seeking during adolescence (Steinberg, 2008). Overall, findings regarding sensation seeking’s role in predicting the onset of alcohol use were extended to include predicting onset of cigarette smoking and marijuana smoking. It is also worth noting that there was strong overlap between alcohol use, cigarette use and marijuana use in the current sample. For instance, all marijuana users also smoked. In this sense, sensation seeking’s prediction of these specific substances cannot be viewed independently from its role in predicting the onset of other substances.

Regarding behavioral assessments of impulsivity and sensation seeking, our findings deviate more strongly from previous works. We found in Chapter 4 that by and large, behavioral assessments did not uniquely predict the onset of substance use. There were, however, specific patterns of prediction when correlating behavioral assessment scores to
substance use prevalence. The Delay Discounting test significantly predicted smoking prevalence at baseline such that increased discounting of future reward predicted a greater likelihood of cigarette smoking at baseline. The same relation was present when prospectively predicting later cigarette smoking at trend significance level. The Passive Avoidance Learning Test also significantly predicted heavy drinking and marijuana prevalence prospectively, such that greater sensitivity to reward increased the likelihood of heavy drinking and marijuana use. Scores on the Balloon Analogue Risk Task (BART) were not significantly associated with any substance use prevalence, concurrent or prospective. Counter to an earlier study by Lejuez and colleagues (2007), the BART also did not correlate to sensation seeking in our study. However, it has been argued that behavioral measures of aspects of impulsivity often do not correlate with self-report measures and may capture unique variance in the prediction of substance use (Cyders & Coskunpinar, 2011). Indeed, a different study did not find a similar correlation between sensation seeking and the BART (Skeel et al., 2007), and other studies have found unique variance explained by behavioral measures over self-report ones (Nees et al., 2011), suggesting that correlation to self-report measures does not need to be considered a strict criterion of validity for behavioral measures assessing aspects of impulsivity. With regards to predicting substance use, however, earlier studies found that the BART predicted alcohol (Fernie et al., 2010; Fernie et al., 2013), smoking and marijuana use (Lejuez et al., 2003). Studies using adolescents also found that the Delay Discounting task predicted alcohol use (Fernie et al., 2013; Field et al., 2007), smoking (Reynolds et al., 2003), and marijuana use (Kollins, 2003) as well. Reward-related impulsivity measured by the Passive Avoidance Learning Task was found to predict heavy drinking in at-risk adolescents by Castellanos-Ryan and colleagues (2011). Few of these findings were replicated in the current study. In certain cases, like in the case of the BART, Chapter 4.2 details certain changes made to the task which may potentially explain why the behavioral assessment may lack in validity.

Samples in studies showing significant prediction of substance use by behavioral measures typically showed greater overall involvement in substance use and predicted the amount of substance use within these samples. This increase in variance may be required to provide sufficient resolution to predict individual differences in substance use onset. While the lack of resolution may be considered a weakness of our study, one could also argue that predicting the onset of substance use constitutes a separate, and theoretically quite interesting, case, by showing that these individual differences in aspects of impulsivity and sensation seeking preceded the onset of substance use. It furthers the notion that individual differences
in cognition precede the onset of substance use and influence this onset rather than the reverse, a notion that has seen much recent debate (Boelema, 2014; Wiers, Boelema, Nicolau, & Gladwin, in press). Of course, this finding does not exclude the possibility that alcohol use may exacerbate initial differences, which has similarly been argued (De Wit, 2009). Finally, data from the current study suggests individual differences that precede the onset of substance use may serve as potential targets for prevention efforts. Such prevention efforts targeting personality indeed exist, as a Canadian-British targeted prevention project (Preventure), selected adolescents with four high-risk personality profiles based on the SURPS and proved to be successful in creating adolescents’ awareness of their personality type in relation to risk behavior, and to encourage alternative coping strategies for their needs (e.g., adolescents high in sensation seeking were encouraged to seek other ways to fulfill this need than drinking alcohol, Conrod et al., 2008). This targeted form of prevention was shown to successfully delay the onset of alcohol use and of binge-drinking (Conrod, Castellanos-Ryan, & Strang, 2010), and it is currently being tested in the Netherlands (Lammers et al., 2011).

We further predicted that cognitive biases would be associated with aspects of impulsivity and sensation seeking, such that greater earlier impulsivity and sensation seeking would predict larger increases in cognitive biases. We expected this effect to be more pronounced when participants consumed greater amounts of alcohol. In Chapter 6, we showed that neither self-report nor behavioral aspects of impulsivity and sensation seeking predicted changes in cognitive biases. These findings are in contrast to earlier studies, including a review by Coskunpinar and Cyders (2013) suggesting that attentional bias is associated with aspects of impulsivity, especially if those aspects are assessed behaviorally. An earlier cross-sectional study had in fact shown that the predictive effects of sensation seeking were mediated by cognitive biases (Ames et al., 2005). Participants in the study of Ames and colleagues (2005) were at-risk adolescents, however, and the assessment of cognitive bias was by examining whether spontaneous word associations to ambiguous phrases were drug-related. As reported in Chapter 6, the computerized behavioral assessments of cognitive biases used in the current studies were typically unreliable, which may explain the lack of correlations and significant associations found. Given that adolescents from this sample were older and at-risk, dose-effect relations relating to the quantity of substance use during the study period may also have played a role. This potential issue is further elaborated upon in Chapter 7 and in Chapter 8.2.4.

Taken together, these findings were counter to our expectations and suggested that no great role for behavioral aspects of impulsivity exists among early adolescents. Furthermore,
they may indicate that there are differences in the role of aspects of impulsivity based on the samples examined. Our outcome measure, onset of substance use, differed from the outcome measure in previous studies examining the effect of aspects of impulsivity on substance use (Fernie et al., 2013; Lejuez et al., 2007; MacPherson et al., 2010; Nees et al., 2011), which were typically based on the relative amount of substance use exhibited. On the other hand, one could consider it a vital indication of support for the role of self-reported sensation seeking that it was able to prospectively predict the very limited amount of onset of marijuana use that occurred within the study timeframe. As concluded by Nees and colleagues (2011), the relative lack of role for behavioral or neurological factors in predicting adolescent substance use suggests that such factors do not carry as large a role during initial consumption as they do among heavy drinkers and addicted persons (as with heritability, cf. Ducci & Goldman, 2008). It is possible that when substance use becomes more automatic, more ingrained, or indeed more socially acceptable among this population, behavioral aspects of impulsivity may predict escalation in substance use.

8.2.3 Findings regarding Executive Functioning

Results from Chapter 5 concern a joint sample consisting of 1) the normative sample described in Chapter 2 and 2) the at-risk sample recruited in the sister project and described in more detail in Peeters and colleagues (2012; 2013). These results indicate that deficits in executive functioning prospectively predicted the onset of alcohol use and the onset of heavy drinking. Specifically, two measures of executive function, cognitive inhibition (assessed using the computerized classic Stroop task) and working memory (assessed using the computerized Self Ordered Pointing Test), both predicted the onset of alcohol use, while working memory but not cognitive inhibition predicted the onset of heavy alcohol use. These results were obtained by estimating odds of survival over time (informed by participant age at onset) and regressing both indices of executive functioning on this estimated curve. Results therefore imply that when scores on executive functioning indices were low, the relative odds of not experiencing onset of alcohol use during the study period decreased. Advantages of the joint sample creation include allowing for a broad range of divergent development trajectories, where cases of normative development are complemented by cases of potentially abnormal development.

Findings from the survival analysis thereby expanded on previous evidence indicating that deficits in executive functions predicted the emergence of substance use disorders. With
regards to predicting substance use, previous studies had focused either on the cross-sectional link between executive functions and substance use (Brown, Tapert, Granholm, & Delis, 2000; Townshend & Duka, 2005), or had been limited to longitudinal studies where subjects were not necessarily alcohol-naïve at baseline (Khurana et al., 2013). The current study eliminated those cases and showed that individual differences in executive functioning that existed before onset of alcohol use were predictive of that onset. Compared to Khurana and colleagues, our sample was slightly older on average, and the period of assessment was shorter. Nevertheless, our findings corresponded to those of Khurana and colleagues in the sense that they too confirmed that weaknesses in working memory predicted future substance use. Our study expanded upon those findings by examining whether cognitive disinhibition (earlier found to be cross-sectionally related to substance use by Grego et al., 2009; Squeglia et al., 2011) uniquely predicted alcohol use onset when working memory capacity differences were controlled for. Interestingly, this examination revealed that for binge drinking, working memory capacity, but not cognitive disinhibition, predicted onset of binge drinking. It is worth noting that from a bi-directional perspective, working memory capacity may predict onset of substance use while at the same time suffering deficits due to earlier substance abuse. Previous studies have suggested that binge drinking in particular might cause such deficits (Duka et al., 2004). Data from the at-risk sample mentioned in our study also showed that alcohol use did impair working memory at a 6-month follow-up (Peeters, Monshouwer, Janssen, Wiers, & Vollebergh, 2014). Other data from Dutch adolescents (Boelema, 2014) did not show that early adolescent alcohol use predicted later deficits, although it was suggested that cognitive measures used to establish in this sample were more basic and simple, possibly occluding a more subtle and specific influence of long-term alcohol use (Wiers et al., in press).

The relation between executive functions and substance use is thus described in terms of the deficit in executive functions and its impact, and vice versa (Hanson et al., 2011; Khurana et al., 2013; Squeglia et al., 2009; Tapert et al., 2002). In a second avenue, the moderating role of executive functions in the link between cognitive biases and substance use is examined (Grenard et al., 2008; Thush et al., 2008), finding that relations between cognitive biases and substance use are strongest when working memory capacity is low. However, these findings were found among at-risk or heavy young adult drinkers. Without replication of these findings among light or adolescent drinkers, it is difficult to establish whether these predictions are subject to dose-response relationships or whether they exist regardless of amount of substance use. Therefore, in Chapter 7, we examined whether the nature of the joint
development of approach bias and alcohol use differed due to individual differences in working memory. There, we expected that relations in the joint development of cognitive biases and alcohol use would be stronger when working memory capacity was poor. However, contrary to our expectations, there was no indication that working memory capacity moderated the relative strength of growth relations between approach bias and alcohol use. This finding seems to contrast an earlier study by Peeters and colleagues (2013) which found that approach bias was associated with changes in alcohol use only among members of the sample which had scored in the lower 50% of scores on inhibition skills. However, the study of Peeters and colleagues consisted of adolescents at risk for the development of substance use. The finding also contrasts earlier results among heavy drinkers (Grenard et al., 2008; Thush et al., 2008). This, together with the findings by Peeters and colleagues, suggest that there may be a dose-effect relationship associated with the possible influence of cognitive biases on substance use. Furthermore, unlike the previously referenced studies (Grenard et al., 2008; Peeters et al., 2012; Peeters et al., 2013; Thush et al., 2008), the current study featured online behavioral assessments of cognitive biases. There were no previous instances of the chosen measures for approach bias and attentional bias being used online in the literature. Potentially, scores on these tasks are affected by this measurement method, which in turn affected our ability to detect the moderation by working memory.

8.2.4 Findings regarding Cognitive Biases

Cognitive biases are commonly believed to result when earlier exposure to a previously rewarded substance evokes an automatically triggered response (See Chapter 1.3.2). As further discussed in Chapters 6.1 and 7.1, these automatic responses are believed to contribute to the maintenance of addiction because the automatic craving for the substance becomes dissociated from the hedonistic quality of the substance use experience (Robinson & Berridge, 2001).

In Chapter 6, we found that higher attentional bias prospectively predicted increases in the amount of substance use over a two-year period. However, higher approach bias did not, and the two aspects of cognitive bias did not correlate. Certain earlier studies have also failed to find a main effect of cognitive bias (van Hemel-Ruiter et al., 2011), while others have shown significant prediction by approach bias we did not find (Field et al., 2008; Field et al., 2011). The study population of Van Hemel-Ruiter and colleagues, like ours, consisted of light-drinking normative adolescents. Even a recent study by Pieters et al. (2014) which examined
the prospective prediction of adolescent alcohol use in an equally light drinking population found this moderating effect, although the main effects of cognitive bias and executive functions were not significant in this study. Findings from Chapters 6 further showed that counter to expectation, neither baseline impulsivity and alcohol use nor their interaction predicted later cognitive bias. Previous studies have typically found that impulsivity, especially behavioral impulsivity, correlates with attentional bias measures (Coskunpinar & Cyders, 2013). Results from Chapter 6 were the first to offer information on the prospective prediction of cognitive bias using impulsivity measures. The fact that the relation between impulsivity and cognitive bias was not confirmed there, and the fact that it did not prospectively predict use or escalation of use, implies that in the current sample measures of cognitive bias may not be as reliable as in previous studies.

In Chapter 7, the intercept of approach bias, but not the change in approach bias was associated with the intercept of alcohol use. This pattern of results appears to fit neither the theoretical assumptions regarding the relation between alcohol use and cognitive bias, nor the alternative explanation that cognitive biases do not have an important role in adolescent alcohol use yet. Instead, if anything, it appears as though there are pre-existing individual differences in the amount of bias which predict adolescent alcohol use. Such an account might make sense if cognitive bias was an alcohol-specific expression of an underlying general impulsivity-like trait. However, the complete absence of any relation to the included aspects of impulsivity suggests this is not the case either. Nevertheless, there are indications that among young adolescents, measures of non-drug specific attentional engagement predict substance use cross-sectionally (van Hemel-Ruiter et al., 2013). In this work, participants were stated to have higher attentional engagement when they were faster to respond to trials signaling an expected reward. The study was cross-sectional and carried out among non-alcohol-naïve subjects, implying that it is possible that previous alcohol use had had neurotoxic effects causing these individual differences. Nevertheless, it seems to suggest that some cognitive biases for reward may be non-substance-specific. Potentially, the finding that within our joint-development study, only intercepts of approach bias and alcohol use growth curves were related, may be explained by a general reward-sensitivity in these subjects. This view does not exclude the possibility that alcohol-specific biases may result from alcohol consumption, but it is possible that such changes do not occur unless alcohol use is strong and sustained. Indeed, studies that find neurotoxic effects of alcohol use typically report that this correlates to heavy alcohol use or binge drinking, which was relatively rare in the current sample. Taken together
and applied to the model suggested in Chapter 1.3.2, our findings suggest that rather than relying on previous exposure to levels of alcohol use in adolescence (as the model compared to assertions from Gladwin et al., 2011 suggests), a concurrent amount of nonspecific reward sensitivity may underlie the link between adolescent baseline approach bias and alcohol use. While the model by Wiers et al. (2007) is presented as a general heuristic and does not specifically reference influences during adolescence, current findings suggest that instead, (combinations with) factors other than previous alcohol use may underlie emotional evaluation and subsequent automatic approach tendencies.

These data, suggesting that cognitive biases do predict early substance use even if they are not influenced by them in turn, provide further evidence that a viable approach to preventing adolescent substance use might be to extend existing cognitive bias modifications. A variety of computer training techniques have been developed that aim to directly target cognitive biases that play a role in addictive behaviors (cognitive bias modification, review: Wiers et al., 2013). Such training programs are based on the notion that heavy drinkers, including adolescents, have cognitive biases that automatically trigger motivational processes to consume alcohol or other substances (Field & Eastwood, 2005; Peeters et al., 2012; Peeters et al., 2013). Although these computer training programs have been used successfully to aid recovering alcohol-dependent patients (Eberl et al., 2013; Wiers, Eberl, Rinck, Becker, & Lindenmeyer, 2011; Wiers et al., 2013), first attempts to apply this to adolescents in the Netherlands are currently undertaken, both for smoking in addition to cognitive behavior therapy (Krishnan-Sarin et al., 2013) and for alcohol and cannabis in a gamified variety (Boendermaker, Prins, & Wiers, 2015).

8.3 Discussion of Methodological and Measurement Limitations

8.3.1 Limitations due to Effect of Online Measurement and Reward Structure

The current online study included a strategy for rewarding participants that was based on previous research concluding superior effects for a mix of fixed and variable rewards. The implementation of this strategy included the awarding of lottery tickets that increased the relative chance that participants had to win prizes. Additionally, we made an effort to create a visually appealing, dynamic context for the online study that emphasized the use of appealing colors and rewarding, gamified indicators of participation progress. Despite this strategy, the study experienced heavy attrition. Tests included in the empirical chapters indicate that if anything, the attrition was focused on older adolescents, although this effect was not
significant when correcting for multiple testing. The attrition data from this study do not allow us to statistically test the effectiveness of our reward strategy, and therefore any conclusions drawn from this experience are mostly speculative. The attrition bias mentioned implies that our reward strategy that based around visually appealing, variably rewarding content did not appeal to older adolescents as much as it did to younger adolescents. However, feedback received from phone calls suggested that participants did not consider the reward strategy juvenile. When we requested feedback from unresponsive participants, they emphasized that the repetitiveness of many reaction time tasks as well as the overall length of the test battery was what discouraged them most from participating. Based on this feedback, we did shorten the test battery after the first wave of measurement, by excluding several notable lengthy tests (the intelligence test and the Probability Selection Task, most notably). Although attrition was relatively greatest after the first wave, it is impossible to causally ascribe the reduction in attrition to our changes based on this data. However, based on the above, I would tentatively suggest that scientists performing behavioral tests online take every care to limit the amount of tests required from their participants to a minimum in these circumstances. Aside from attrition, a lengthy test battery may also have consequences for the validity of individual tests within that battery (for more on this, see paragraph 8.3.2). Frustration with the length of the test battery may further compound threats to validity. Because we anticipated that adolescents might consider the test battery very long, we initially implemented restrictions intended to spread the participation per wave over several days. These restrictions, which automatically prevented the participant from continuing at the wave’s halfway point, were intended to limit the impact of the study’s length on test validity. However, given feedback from users, these restrictions themselves were considered highly frustrating by participants. As it turned out, participants felt that the restrictions meant they were not trusted to complete the full test and were annoyed that they could not get their participation over with in its entirety. Based on this feedback, we also removed these restrictions after the first wave and suggest that future researchers do not attempt this. It is a potential limitation of the current study that these differences between waves may have influenced participant behavior such that some tasks may have resulted in more reliable and valid assessments compared to the first wave. Findings from Chapter 6, however, suggest that no sweeping changes in reliability of cognitive bias measures occurred between waves.

8.3.2 Limitations due to Effects of Operationalization
Throughout the empirical chapters included in this thesis, there are marked differences in how substance use, the study sample, and behavioral measures are represented. This inconsistent representation is in part a consequence of measurement decisions, and in part is a consequence of what hypotheses were being tested.

With regard to the representation of substance use, different chapters have included the following operationalizations: a latent group representation that distinguished between non-drinkers, onsetters and heavy drinkers, a dichotomous representation of the onset or lack of onset for different substances, a representation of the onset of drinking in general, and binge drinking in specific, a zero-inflated Poisson representation, and a growth curve representation. The zero-inflated Poisson representation that was used, distinguishes between the odds of not drinking versus drinking on the one hand, and the amount of drinks consumed if a drinker on the other. The growth curve representation used distinguishes between differences in the consistent level of drinking shown throughout the study period, and the differences in development of drinking shown during the study period. In the case of substance use, these differences in operationalization were inspired by differences in research questions. We used dichotomous representations in instances where we were interested in whether the cognitive predictors pre-dated substance use, and whether each of these predictors had unique predictive validity. We used a group-based representation when we were also interested in predicting escalation post onset. Finally, we used continuous representation when we were interested in the association between increases on substance use relative to changes and increases in other predictors. These differences in representation have the unfortunate side effect that it becomes more difficult to directly compare results between studies. However, the overall distribution of substance use, in which zeroes are heavily overrepresented, precludes a more classical means/variances representation. Although a consistent operationalization of substance use is desirable, it remains necessary to adjust operationalization based on what one is theoretically interested in.

With regard to the study sample, different studies in this dissertation refer to differing numbers of participants included in these tests. This divergence is unfortunate, and only partly explained by differences in included samples (Chapter 5 refers to the joint samples from the main group and the at-risk group from the sister project). In general, we made use of 378 subjects included on the basis of finishing at least one full wave of data collection. Overall, to deal with missing data, we included measures associated with bias and use full information maximum likelihood. However, on top of this, Chapters 3 and 4 refer to samples of
respectively 252 participants and 284 participants. In both cases, we required that participants had completed at least two full waves of data collection. Furthermore, in Chapter 3, we excluded participants aged 12, 17 and 18. In the case of Chapter 3, this step was required to ensure that latent class models could successfully converge on class solutions and avoid age effects. We avoided this unfortunate limitation in all other chapters and ensured that age was represented differently in the models (generally as a covariate where appropriate). In all other chapters, we used full information maximum likelihood as it is deemed far preferable to exclusion of cases with missing data (Asparouhov & Muthén, 2010; Collins, Schafer, & Kam, 2001; Graham, 2003).

With regard to behavioral assessments, we generally committed to following standard computation methods described by the creators of that assessment method. In the case of bias measures, this typically meant computing some type of median reaction time difference between an alcohol- and a non-alcohol condition. In the case of reward-related measures (see Chapter 4) this typically meant comparing the number of points earned while performing a certain rewarded behavior. While reward-related measures were found to be quite reliable, measures of cognitive bias in the current study (see Chapters 6 and 7) suffered from very poor reliability with one notable exception. In most studies in this dissertation, one wave of data on a behavioral measure was used, which means it could be represented as a single observed value (and then used as a predictor or dependent variable; cf. Chapter 4, 5 and 6). However, when attempting to construct latent factors representing multiple waves of behavioral data, a lack of reliability of such behavioral assessments becomes an even more important limitation. We found that with one exception (the Stimulus-Response Compatibility Task), the lack of reliability prevented us from modeling the development of cognitive bias measures. When a measure shows such a strong lack of reliability, it becomes illogical to assume that a consistent trait was measured and that changes in this trait could be reliably predicted. The solution (and therefore limitation) in Chapter 7 of this dissertation was to examine changes only in measures reliable enough to be accurately represented in a growth curve model. Other studies have recently faced similar issues, and resolved issues of reliability either using parceling techniques (Peeters et al., 2013) or by using behavioral measures of at least moderate reliability (Peeters et al., 2014). Given that examining the bidirectionality of cognitive factors to substance use is currently considered a priority, resolving this lack of reliability is a pressing issue (Ataya et al., 2012). Novel ways to process existing data are being developed for certain measures of attentional bias, such as the variance-based bias score by Zvielli and colleagues (2014). This
type of bias score was developed to deal with potentially false assumptions regarding the stability of attentional bias for different exemplars used to assess it, and the supposed impossibility of being both motivated towards, and away from, certain environmental cues. Variance-based scores were shown to correlate more strongly to smoking rate than traditional scores (Zvielli et al., 2014). As a final note, reliability does not guarantee validity and is therefore not sacred. It is quite possible to reliably measure trivial things.

### 8.3.3 Limitations due to Environmental and Contextual factors

One relevant limitation that must not be overlooked is that with the exception of one study, this dissertation did not consistently account for the effects of environmental factors on the expression of different cognitive predictors. While the single study that did include environmental factors (Chapter 3) validates this decision somewhat by finding no indication of interaction, environmental factors remain clearly relevant. Unfortunately, even though we included parental rules as an environmental predictor, this fails to do justice to the full scope of social factors that can influence substance use behavior. Research on the role of peer influence suggests a vast array of social influences that can potentially impact adolescent substance use (Harakeh & Vollebergh, 2012; Larsen, Overbeek, Vermulst, Granic, & Engels, 2010; Larsen et al., 2009; Steinberg & Monahan, 2007; van der Zwaluw, Carmen S, Larsen, & Engels, 2012), and each of these social influences may potentially interact with cognitive predictors. Perhaps it is even more likely that the strength of social influences encouraging substance use may interact with behavioral measures of cognitive predictors, as behavioral measures are often believed to reflect aspects of individual cognitive differences of which people are unaware. For instance, while people might indicate they consider themselves quite controlled, at more unselfconscious moments they might find themselves responding quite uncontrolled when put under social pressure. The studies contained in this dissertation do not represent this potentiality sufficiently to comment on this possibility.

### 8.4 Implications for Future Research

Overall, we concluded that while there is evidence that individual differences in implicit and explicit substance-related cognitive processes, predict substance use, there is little evidence for the reverse relationship in the current sample of normative adolescent drinkers. Even cognitive biases, which are typically believed to be a consequence of early substance use, were predictive of, rather than being predicted by, early substance use. The current research’s
most surprising finding is the apparent lack of behavioral measures of impulsivity consistently predicting adolescent substance use. Instead, participants’ cognitive control and overt self-appraisal of their personality were the strongest predictors of onset of substance use along with what environmental predictors (parental rules) were included. Furthermore, the current research, on a measurement level, offers insights into the subtle skills that go into providing a reliable testing environment for adolescents.

Theoretical implications revolve mainly around a strong support for parental rules, self-reported risk personality and behavioral assessments of executive functions, a relative lack of support for behavioral measures of impulsivity within the current sample, along with support for a prospectively predictive role for cognitive biases within the study timeframe. Implications of this finding are twofold: they influence both our theoretical understanding of addictive behaviors, and the applications of what we believe are vital mechanisms of addictive behaviors to preventative efforts.

Regarding our understanding of theoretical implications on models detailing the role of impulsivity, automatic processes and social influences, it is relevant to dissociate early causal influences and potential later influences. Parent-related factors, self-reported sensation seeking and executive functioning were all shown to have differential effects on the initial onset of substance use. Factors implicated in the emergence of substance use need not necessarily be implicated in the maintenance of substance use despite adverse consequences. Hence, a lack of a role for certain aspects of cognition in the emergence of substance use, or even the amount of substance use in a sample of light drinking early adolescents, does not necessarily preclude these aspects from influencing addictive behaviors. Given this perspective, we would expect to see that aspects of cognition implicated in the maintenance of addiction emerge from earlier substance use. However, no such relations were evident in the current sample. Neither impulsivity nor earlier substance use contributed meaningfully to an increase in cognitive bias. Here, potentially, the limited temporal scope of the study determined a lack of results. Alternatively, issues with reliability prevented us from detecting such relations. However, it is not impossible to conceive that binge or coma drinking, rather than early light drinking, predicts the emergence of aspects of cognition responsible for the maintenance of addiction. Recent evidence (Boelema, 2014) supports this conclusion, suggesting that neurotoxic effects of alcohol use on aspects of cognition are not evident in a normative population of adolescents.
Implications for future research are cast by necessity in the light of addressing measurement issues with such factors. Both the dataset used in the current dissertation as in the work of Peeters et al. (2014) has a two-year timeframe and includes participants who had already drunk at baseline. This creates the unfortunate effect of not being able to prospectively predict the onset of the most at-risk portion of the population. If certain effects are exclusive to the most at-risk portion of the sample (who are also most likely to be the most active drinkers), the current study would not allow us to capture factors predicting the onset of that portion. Furthermore, a two-year window in most cases also fails to capture the vital transition of adolescent to young adult. The study would then have been potentially more sensitive to effects that may be specific to an older, more regularly drinking sample. The college period is well known as a period of high consumption of alcohol (O'Malley & Wagenaar, 1991). On top of this, it is the time in a young adult’s life when they are first faced with a great deal of independence (J. J. Arnett, 2005). Socially protective factors that may have initially prevented escalation of substance use may disappear at this time, leading to potentially increased self-determination and risk. After this period, there is also the well-documented period of transitioning out of heavy substance use (e.g. Jackson, O'Neill, & Sher, 2006). It is theoretically highly interesting to be able to track and associate (changes in) cognitive factors to alcohol use during each of these periods. This tracking could lead to discovering enhanced and theoretically informative developmental trajectories specified not only by changes in substance use, but also by changes in associated processes. Such developmental trajectories could then inform whether policies aimed at manipulating certain cognitive processes should expect to aid populations in general or should expect to aid specifically targeted individuals who may be at elevated risk within a certain part of their formative years. For instance, multiple studies have now demonstrated that anxiety sensitivity appears to not put adolescents at risk for substance use onset (Malmberg et al., 2010; Malmberg et al., 2012). Quite the opposite, it appears to play a protective role against substance use specifically, although anxiety sensitive adolescents may still be vulnerable to other risks. Certainly, studies have shown that it becomes a risk factor for substance use later in life (Woicik et al., 2009). If the time frame during which key cognitive processes become risk factors was well specified, this may enhance prevention efforts. All these aspects call for a wider time frame of measurement, and statistical methods that do not assume equality of relations over time. Alternatively, another approach is to apply more fine-toothed measurement techniques such as ecological momentary assessment (Moskowitz & Young, 2006) to determine whether internalizing personality aspects as momentary states...
(mood changes) predict substance use. This may be the case even when general personality traits do not predict substance use.

Aside from addressing the time frame of longitudinal studies, the measures used in these observational studies bear further examination as well. Though this dissertation contains notable failures to replicate earlier results which may be theoretically informative, it must also be considered that parts of these non-replications may be traced to circumstances in which these tasks had never before been attempted. The online setting in which these tasks were used typically involved participants in their home setting, where they are potentially easily distracted. Some tasks used in the current study had previously only been attempted in laboratory settings. Typically, these tasks were then used to predict differences in the amount of substances consumed, rather than predicting the onset of substance use. However, previous larger, well controlled studies also failed to find large relations between behavioral assessments and substance use (Boelema, 2014; Nees et al., 2011). To resolve these potential differences in validity between online and lab-based assessment, it may be necessary to conduct further primary research confirming the measurement properties of tasks used in an online setting. Alternatively, results from the current study could be confirmed using a similar sample measured in more traditional lab-based conditions. Furthermore, there remains always the creative challenge of imagining new tasks that offer novel and reliable ways of implicitly capturing such processes. For example, researchers may seek to inspire themselves by what adolescents themselves consider the most thrilling aspect of what performance tasks they face on the Internet, in the form of gaming. Many games, especially real-time strategy games, have been shown to require a large amount of cognitive control and planning (Lewis, Trinh, & Kirsh, 2011; Synnaeve & Bessiere, 2011). Simultaneously, such games are typically found to be far more engaging than behavioral assessments. While the multidimensionality of aspects involved with performance during video games obviously makes them unsuited for extracting measurements, it bears considering that time constraints may drive adolescents to further engagement.

8.5 Final conclusion

In conclusion, the current work has furthered knowledge on the role of implicit and explicit cognitive-motivational traits by examining whether they were also predictive of the onset of substance use, thereby examining whether such traits preceded substance use or may have arisen as a consequence of it. We demonstrated that self-reported risk personality (with
sensation seeking foremost among those personality traits) and behavioral assessments of executive functioning were predictive of the onset of substance use in general and onset of alcohol use specifically. As such, while it is still possible that such traits also further develop as a consequence of alcohol use, they are shown to be pre-existing vulnerabilities in the current samples. Such pre-existing differences are potentially informative to current debate, showing that such individual differences do not necessarily arise from substance use and that as such, substance use may not affect behavior as easily as sometimes believed. Knowledge of pre-existing differences are also informative as potential targets for prevention, as delaying the onset of substance use is recommended due to high rates of adverse consequences related to substance use during adolescence.

Regarding study characteristics, it is suggested that further studies carefully limit the extent of their test battery to ensure participants remain motivated, and to closely examine the validity of available behavioral assessments and their interpretations. It is also suggested that further study into potential moderation of other factors by substance-specific biases be explored. Finally, it is suggested to extend the timeframe of measurement to include young adulthood when substance use may become more habit-driven and therefore less influenced by environmental restrictions or encouragement. Potentially, cognitive-motivational mechanisms that influence behavior have a stronger influence on substance use during those times.