Rethink your drink...

The bidirectional relationship between automatic and controlled processes and the development of drinking behavior in at-risk adolescents

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De bidirectionele relatie tussen automatische en gecontroleerde processen en de ontwikkeling van drinkgedrag bij at-risk adolescenten.

(met een samenvatting in het Nederlands)

Proefschrift

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Content:

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Introduction

Introduction

Experimenting with risky behaviors, such as alcohol use, is considered to be a part of the normal development of adolescents. Therefore it is not surprising that the engagement in risk behavior peaks at the age of 15-16 years (Steinberg, 2007). More than 50 percent of the 15-16 year olds indicate that they have consumed alcohol in the past month (Hibell, 2012), and the mean age of drinking onset is 13-14 years in Europe (Hibell et al., 2012), and 14-15 in North-America (Kosterman et al., 2000; Vega et al., 2002). These numbers suggest that alcohol use is common among adolescents. Nevertheless, several drinking patterns such as an early onset of alcohol use and consistent heavy drinking have been associated with later problems like escalation of use (De Wit et al., 2000), intoxication (Morean et al., 2012) and cognitive impairments (Tapert et al., 2002). The use of alcohol during adolescence may be normative; however that is not to say that it is without risks. Drinking alcohol is tempting, -and often (immediate) rewarding, particularly for adolescents (Crone and Dahl, 2012), and once initiated, it increases craving. Behavioral control is essential to avoid frequent alcohol use, and precisely this ability is developing in rapid pace in adolescence and only reaches mature levels in young adulthood (18-21 years, Blackemore and Choudhurry, 2006). In combination with a shift from self-oriented behavior towards more other-oriented behavior, and the inclination to attach greater importance to peer admiration (Crone and Dahl, 2012), it makes adolescence a particularly vulnerable period for the development of problematic drinking patterns (Bava and Tapert, 2010). In addition, individual differences in the capacity of behavioral control for instance, result in even more difficulties for some adolescents to resist involvement in tempting risky behaviors such as alcohol use (Verdejo-Garcia et al., 2008). It has been well documented that particularly adolescents with behavioral control problems (e.g. impulsivity, relatively weak executive functions) drink more heavily compared to their peers without such problems (Nigg et al., 2006; Tarter et al., 2003; White et al., 2011; Whelan et al., 2012). These findings sketch a picture of adolescent risk behavior, which, appears to be part of the normal development on one hand, while on the other hand, might result in serious problems later in life, to which some adolescents are more prone compared to others. In the present thesis we will analyze the relationship between cognitive functioning, impulsive behavior, and (problematic) alcohol use among adolescents, with a special focus on the hypothesized bidirectional nature of these relationships. More specificaly, we will examine the influence of automatic and controlled processes involved in adolescents' drinking behavior, and evaluate the role of related interacting variables such as temperament, personality and the social context. The present thesis examines both high-risk adolescents (e.g. adolescents with behavioral control problems), who show an increased risk for early onset of drinking and heavy alcohol use (Kepper et al., 2011), and adolescents from community samples.

The bidirectional relationship between alcohol use and cognitive functioning

Recent studies have suggested that the neurotoxic effects of alcohol use might be more adverse for adolescents than for adults, because the brain is rapidly developing during adolescence (Crews and Hodge, 2007; DeBellis et al., 2000). The adolescent brain would be more vulnerable to delayed development and impairments in cognitive functioning caused by heavy alcohol use. Although several studies seem to support this assumption (DeBellis et al., 2000; Medina et al., 2008; Tapert et al., 2002), both the level at which the effects are found (e.g. brain volume versus cognition) as well as the research design (e.g. sample size, clinical vs. community) vary strongly across studies, making it difficult to connect the results and draw conclusions concerning general populations. In addition, several other studies have found indications for pre-existing impairments in cognitive functioning before the onset of alcohol use (Khurana et al., 2012; Nigg et al., 2006) suggesting that some weaknesses are already present before drinking alcohol is initiated. This raises the question of directionality in the relationship between adolescent alcohol use and cognitive functioning.

An important maturing part of the brain is the prefrontal cortex, which undergoes changes until late adolescence (Casey et al., 2008; Galvan et al., 2006; Luna et al., 2004). This area of the brain plays an important role in cognitive functions involved in the organization and regulation of behavior. Response inhibition, attention shifting and working memory are examples of such functions, and a commonly used umbrella term to describe them is executive functions (Gazzaniga et al., 2002). Response inhibition refers to the ability to overrule impulses and control behavioral responses and plays a significant role, particularly for the inhibition and interference of fast and automatic responses (Nigg, 2000). Attention shifting is necessary for switching between multiple tasks or mental sets (Miyake et al., 2000). For the completion of tasks, it is often necessary to ignore irrelevant stimuli and pay attention to relevant stimuli. Working memory is responsible for keeping information active in memory and shielding it from distracting information, which is crucial in the attainment of goals. Goal directed behavior requires cognitive capacity to keep relevant information active in memory, which is the primary task of working memory (Baddeley, 1983).

Although it is clear that there is a relationship between executive functions and alcohol use in adolescence, many studies fall short, either in design (e.g. cross-sectional studies) or sample characteristics (e.g. samples where the problems are already evident, lack of alcohol-naïve adolescents, lack of variation in alcohol use) to draw conclusions about the direction of the relationship. The present thesis attempts to resolve this gap by examining adolescents' alcohol use from a longitudinal perspective and by focusing on the bidirectional relationship between executive functioning and alcohol use in different adolescent samples.

The bidirectional relationship between alcohol use and automatic processes

Dual process theories of addiction assume that addictive behavior is a result of an imbalance between strong automatic processes and relatively weak reflective processes (Deutsch and Strack, 2006). These reflective processes, which are intentional and deliberated, are controlled by executive functions such as working memory and response inhibition (e.g. cognitive control). The automatic processes are driven by fast and impulsive cognitive processes (e.g. something attractive draws attention and "pulls"), and typically take place without conscious awareness (Fazio and Towles-Schwen, 1999). Reflective processing involves cognitive load and time and in circumstances in which one or both factors are limited, automatic processes are more likely to guide behavioral responses (Gladwin et al., 2011). Recently it has been argued that the insertion of higher order reflective processing is not a matter of available resource (e.g. ego depletion, Baumeister et al., 2007) instead, it can be understood as a motivational process, that makes a distinction between so called "have to" tasks and more rewarding "want to" tasks (Inzlicht et al., 2014). Individuals appear to strive for a balance between these two tasks. Inzlicht and colleagues suggested that individuals are less motivated to exert control after "have to" tasks, and more likely to shift attention towards "want to" tasks. Anyhow, behavior is likely to be guided by automatic processes when higher order cognitive control processes, are in any way diminished.

Depending on experience (e.g. conditional learning as introduced by Pavlov, 1927) individuals are either inclined to approach or avoid certain stimuli (e.g. spiders, alcohol; Robinson and Berridge, 2008). With respect to alcohol use, previous results have shown that individuals with a strong automatic approach orientation towards alcohol are more likely to drink heavily comapred to individuals with a weaker approach orientation (Ostafin and Palfai, 2006; Palfai and Ostafin, 2003; Wiers et al., 2009a). In addition, it is hypothesized that this automatic approach behavior is further strengthened by the repeated use of alcohol (i.e. conditional learning, Gladwin et al., 2011; Robinson and Berridge, 2008; Wiers et al., 2007).

The repeated use of alcohol during adolescence, and the positive (or negative) associations with drinking alcohol could reinforce orientation towards (or away from) alcohol. Note that positive effects typically precede negative consequences, which results in stronger positive associations. Consequently, young adolescents might develop a certain drinking pattern which becomes more difficult to change as they mature and this drinking pattern might lead to problematic alcohol use in (young) adulthood. A strong approach orientation towards alcohol in adolescents could therefore be an escalating factor in the development of problematic alcohol use. However, until now, most research has focused on (young) adult drinking behavior (Field et al., 2008a; Palfai and Ostafin 2003) or examined automatic processes and alcohol use in adolescence using a cross-sectional design (Grenard et al., 2008; Thush et al., 2008). To the best of our knowledge, only one study examined the prospective relation between automatic processes and alcohol use in adolescents, however, the bidirectional relationship was not examined (Thush and Wiers, 2007).

Automatic processes can be examined and assessed in different manners. Attentional bias, approach bias and implicit associations are most commonly examined processes in relation to alcohol use (Rooke et al., 2008). The first process refers to selective attention that is given to certain stimuli. It appears that heavy drinkers show stronger selective attention to alcohol related cues than to non-alcohol cues (Field et al., 2004). This results in an attentional bias, in which alcohol stimuli are processed faster than non-alcohol stimuli, and behavior may be more likely oriented towards alcohol. Several behavioral measures have been used in previous studies to assess this attentional bias, for instance the emotional Stroop and the visual probe task (Rooke et al., 2008). The second process, approach bias, refers to the tendency to approach stimuli that are liked (and wanted), and avoid stimuli that are disliked (Robinson and Berridge, 2008). Recent studies have found that drinkers reveal a stronger approach tendency towards alcohol than non-drinkers (Field et al., 2008a). This motivational orientation can be assessed with the Alcohol-Approach Avoidance Task (A-AAT, Wiers et al., 2009a) or the Stimulus Response Compatibility Task (SRC task, Field et al., 2005). Probably most familiar, are implicit associations, referring to connections between a target or stimuli and a attribute, which are stored in memory. The most commonly used instrument to assess the strength of these associations, is the Implicit Association Test (IAT, Greenwald et al., 1998).

Although many studies have been conducted in heavy adult drinkers, only few studies on the relation between automatic processes and alcohol use, have been conducted in young adolescents (Rooke et al., 2008). Moreover, most studies among adolescents have examined implicit associations (Ames et al., 2007; Grenard et al., 2008; Stacy et al., 1996), while less is known about automatic approach tendencies. Finally, only one study examined the prospective relation (Thush and Wiers, 2007). The results of these studies indicated that stronger implicit associations predict heavier drinking among adolescents. Nevertheless, none of these studies examined the bidirectional relationship between alcohol approach tendencies and alcohol use. Therefore, the present thesis examined the cross-sectional and bidirectional relationship (longitudinally) between alcohol use and alcohol approach tendencies in adolescence.

In addition, we looked at the moderating role of reflective processing in the relationship between automatic processes and adolescent alcohol use. Dual process theories (Fazio and Towless-Schwen, 1999; Hofmann et al., 2009; Strack and Deutsch, 2004; Wiers et al., 2007) assume that relatively weak cognitive control increases the likelihood of automatic processing in the execution of behavioral responses. For instance, recent studies have revealed that working memory functioning is an important moderator in the relation between alcohol use and implicit associations in adolescents (Grenard et al., 2008; Thush et al., 2008). Adolescents with relatively strong implicit alcohol associations and weak working memory functioning, drank more heavily compared to adolescents with good working memory functioning. In line with these results (Grenard et al., 2008; Thush et al., 2008) and general dual process theories (Strack and Deutsch, 2004), it is likely that individuals who have difficulties to inhibit behavioral responses, elicit stronger behavioral responses which are automatically activated. Response inhibition has not yet been examined as a moderator in the relationship between alcohol approach tendencies and adolescent alcohol use. Besides the main effects of alcohol approach tendencies on adolescent alcohol use, we therefore examined the moderating effect of response inhibition in the relation between alcohol approach tendencies and alcohol use in high-risk adolescents.

Social context as moderator

The environment and setting in which automatic and reflective processes take place are relevant to the extent to which both of these processes are involved in behavioral decisions. Reflective processing for instance, requires time and cognitive effort (Gladwin et al., 2011; Inzlicht et al., 2014), and in situations in which time is limited, for instance someone offers you a glass of beer in a bar, the interference of deliberated processing in the decision whether or not to accept the beer is less likely to occur compared to situations in which time is indeterminate, such as deciding which drink to order while waiting on the waitress. Similarly, the environment and setting in which the behavioral decisions take place affect alcohol cognitions (e.g. cognitions that direct automatic processes). The context in which a stimulus is presented affects the accessibility of associations (important for retrieval and storage in memory) and the predictive influence of automatic processes (Krank and Goldstein, 2006). For example, individuals primed with alcohol in a bar setting appear to drink more heavily compared to the control group, who are primed with alcohol in a neutral setting. In addition, children exposed to alcohol commercials are more likely to activate positive alcohol associations compared to children not exposed to these commercials (Dunn and Yniguez, 1999). In line with this reasoning, we hypothesized that the home context might be an important moderator in the relation ship between alcohol use and implicit associations. That is, alcohol availability at home might activate and trigger positive associations with alcohol which subsequently influences the drinking behavior of adolescents.

Outline Thesis

In the present thesis we examined both controlled and automatic processes in relation to adolescent alcohol use. It is assumed that executive functions such as working memory and response inhibition, play an important role in the drinking behavior of young adolescents. However, the direction of the relationship between executive functions and alcohol use is not yet fully understood. Therefore, the first aim of the present thesis was to examine the hypothesized bidirectional relation between executive functioning and alcohol use in adolescence. Our second aim was to study the hypothesized bidirectional association between automatic processes and alcohol use in adolescence, and to examine the moderating role of response inhibition within this relationship. The third aim of this thesis was to explore the moderating role of the social context in the relationship between automatic processes and adolescent alcohol use.

Chapter 2 presents an overview and state of affairs of the recent literature on the relationship between executive functioning and alcohol use in adolescence. Chapter 3 describes the prospective bidirectional relationship between working memory and alcohol use among adolescents. It has been suggested that impairments in working memory capacity are a result of heavy drinking and binge drinking (Stephens and Duka, 2008), and we therefore examined this relationship in a sample of heavy drinking adolescents (i.e. Dutch high-risk sample). Chapter 4 addresses the longitudinal and bidirectional relationship between alcohol use and three measures of impulsivity in an English community sample of young adolescents. Response inhibition, delay discounting and risk-taking behavior were examined as possible predictors of, as well as cognitive processes affected by adolescent alcohol use. In some circumstances, motivational and affective processes (e.g. hot cognitions) play a greater role compared to other circumstances (for instance drinking with peers). Particularly when behavior is rewarding, behavioral choices are influenced by the degree to which someone is more or less sensitive to reward and is willing to make risky decisions. Therefore, this study not only examined measures of executive functioning (e.g. response inhibition) but also so called "hot cognitions" (e.g. risk behavior, delay discounting). Chapter 5 reports on the predictive effect of response inhibition and working memory on the onset of drinking and binge drinking in Dutch high-risk adolescents and community sample of adolescents. Both functions (e.g. inhibition and working memory) have been related to adolescent alcohol use (Khurana et al., 2012; Nigg et al., 2006; Verdejo-Garcia et al., 2008), however, none of these studies examined the prospective effect of these functions in alcohol naïve adolescents. Chapter 6 discusses the results of a cross-sectional study examining the association of automatic approach tendencies and alcohol use among high-risk adolescents as well as the moderating effect of response inhibition on this relationship. Response inhibition was not previously examined as a possible moderator in the relationship between alcohol approach tendencies and alcohol use in adolescents. Chapter 7 replicates the latter study, examining the same relationship in a longitudinal design. Chapter 8 reports on the hypothesized moderating effect of the social context (alcohol availability at home) on the relationship between implicit alcohol cognitions and alcohol use in high-risk adolescents. Chapter 9 describes the predictive effect of undercontrolled and overcontrolled personality factors on the onset of drinking and the use of other substances in high-risk adolescents. Recent studies revealed that specific behavioral traits are also associated with impulsive decision-making. Undercontrolled personality styles, such as impulsivity and sensation seeking, have been related to risk behavior in general (Horvath and Zuckerman, 1993) and specifically to alcohol use (Woicik et al., 2009). Chapter 10 describes the methodological issues, such as high amount of missingness, associated with studying high-risk samples. A simulation study was carried out to determine the most efficient and optimal method to handle missing data in high-risk groups. Finally, chapter 11 provides an overview and discussion of the results.

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Psychological changes and cognitive impairments in adolescent heavy drinkers

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Abstract

Adolescence is a developmental period characterized by increased risk-taking behavior, including the initiation of alcohol and other substance use. In this brief review paper we describe psychological and cognitive constructs that are associated with heavy drinking during adolescence. These associations raise the question of causality: is alcohol somehow neurotoxic, or can we identify specific psychological and cognitive variables that serve as risk-factors for the escalation of heavy drinking? This narrative review summarizes results of recent prospective studies that focus on causal relationships between adolescents' alcohol use, psychological changes and cognitive impairments.Psychological constructs such as elevated impulsivity and poor executive function are risk-factors for alcohol involvement in youth. Furthermore heavy drinking during adolescence, particularly in a binge pattern, may exert neurotoxic effects and produce corresponding changes in executive function, perhaps setting the stage for the development of alcohol use disorders later on in life. Although the findings of the discussed studies shed light on the nature of the relationships between alcohol involvement and cognitive deficits, the question of cause and effect remains unanswered. The limitations of existing research and the need for well-powered prospective studies are highlighted.

Introduction

During adolescence many youngsters begin to engage in risky behaviors such as the use of alcohol and other drugs. Across Europe, 50-70% of 16 year olds have consumed alcohol once in their lives, and more than 35-70% of adolescents who have ever drunk report at least one heavy drinking episode in the previous month (Danielsson et al., 2011). In the same developmental period major physical, social and cognitive changes occur. The neuro-developmental changes that occur during adolescence have been well characterized (Blakemore and Choudhury, 2006; Giedd et al., 1999), and these neurobiological alterations have been mapped to changes in motivated behaviour and self-control (see Bava and Tapert, 2010 for an overview). The psychological changes that occur mean that adolescents are more likely to engage in heavy drinking (Crone and Dahl, 2012), but doing so during adolescence may confer neurotoxic effects (Crews et al., 2007). Recent debate has centered around the relationships between cognitive function and alcohol use: It has been suggested that some cognitive deficits observed in drinking adolescents may precede the onset of alcohol use (Khurana et al., 2012), whereas others may reflect neurotoxic effects of alcohol if consumed in large quantities during this sensitive developmental period (Hanson et al., 2011). In the current review we discuss some recent findings relevant to this issue, and we specifically focus on the bidirectional relationships between alcohol use and psychological functioning in adolescents.

Brain maturation during adolescence: risk and reward

Why do adolescents take risks? Some argue that adolescents are not aware of the potential hazards of risky behavior (Cohn et al., 1995), while others suggest that slow maturation of self-control skills is responsible for increased risky behavior during adolescence (Steinberg, 2007; Casey et al., 2008). Indeed, it seems that that several brain regions associated with self-control continue to mature into young adulthood (Blakemore and Choudhury, 2006; Giedd et al., 1999). Two important networks that undergo changes during adolescence are the limbic system and the prefrontal cortex (Spear, 2000a; Steinberg, 2007). The prefrontal cortex is involved in executive control and plays a significant role in regulating, organizing and controlling behaviour. Executive functions include response inhibition (e.g. impulse control), working memory and attention (Blakemore and Choudhury, 2006; Gazzaniga et al., 2002).

The mesolimbic system is involved in social and emotional processing (Gazzaniga et al., 2002) and is important for reward processing (Gazzaniga and Heatherton, 2005). The alterations in these brain regions are visualized by Magnetic Resonance Imaging (MRI) studies, which have identified decreases and increases in gray and white matter, respectively caused by synaptic pruning and myelination (Giedd et al., 1999). Myelination is a process whereby neuronal axons are covered with myelin, a white greasy substance that enhances communication between neurons (Gazzaniga et al., 2002). In many regions of the brain, synaptic pruning - the loss of infrequently used neuronal connections and the strengthening of frequently used connections - is an ongoing process that is generally complete by the end of childhood (around 11 years of age). In the prefrontal cortex and the limbic system however, synaptic pruning continues during adolescence (Blakemore and Choudhury, 2006; Giedd et al., 1999; Spear, 2013) meaning that executive functions and reward related circuits tend to mature relatively late.

It has been suggested that increased risk-taking behaviour during adolescence is related to synaptic remodeling in reward circuits combined with delayed maturation of the prefrontal cortex (Crews et al., 2007; Spear, 2000b). With respect to reward and decision-making, Galvan and colleagues (2006) found differences in brain activation between adults and adolescents in regions associated with reward (e.g. nucleus accumbens and the orbitofrontal cortex) during performance of a decision-making task. Brain activation in these regions was more pronounced in adolescents compared to adults, which might reflect an increased response to rewards in adolescents. Studies such as this have led investigators to suggest that when making decisions, adolescents exhibit increased involvement of appetitive motivational systems, but blunted recruitment of executive control systems (Casy et al., 2008; Galvan et al., 2006, 2007; Steinberg, 2007). In other words, there is an imbalance (or 'maturity gap') between responsiveness to rewards on the one hand, and control over impulses on the other hand, and the neurobiological substrate of this is fairly well understood (Crews et al., 2007; Somerville and Casey, 2010; Steinberg, 2007).

Crone and Dahl (2012) argue that this imbalance is reflected in changes in social and affective processing during adolescence. They suggest that these neuro-developmental changes mean that adolescents' behaviour is particularly flexible, and well suited to adapting to different situations. This flexibility manifests itself as rapid decision making which can be very useful in the rapidly changing environment in which adolescents grow up. The motivational context in which adolescents' risk behaviour occurs might be different from that of adults.

That is, peer relations (including romantic relations) and social status become increasingly important during adolescence, and risky behaviors may be spurred on by motivations such as receiving peer approval and acceptance (see also Spear, 2000a,b). The rewarding value of risky behaviors might outweigh the negative long-term outcomes, leading to reduced involvement of controlled processes in behavioral decisions (Gladwin et al., 2011). This suggests that risk behavior in adolescence is not a matter of immature self-control, but might be based on different evaluation of potentially rewarding outcomes.

Characteristics of adolescents who drink heavily versus those who do not

As previously noted, many people begin to use alcohol during their adolescent years. Before attempting to explain the causes and consequences of drinking in adolescents, it is important to note that cross-sectional studies have revealed robust differences between adolescents who regularly drink, and those who do not, in terms of brain structure and function (De Bellis et al., 2000; Medina et al., 2007), cognitive function (Brown et al., 2000; Townshend and Duka, 2005) and personality traits (De Wit, 2009; Woicik et al., 2009; White et al., 2011). Personality traits such as impulsivity and sensation seeking are elevated in heavy drinking adolescents (Castellanos-Ryan et al., 2011; Clark et al., 2008). Moreover, several studies have shown cognitive impairments in heavy drinking adolescents and young adults, that are not seen in non-drinking adolescents. Cognitive impairments for instance were found amongst adolescents with alcohol use disorder (AUD) (Brown et al., 2000; Sher et al., 1997), non-dependent heavy drinkers (Mahmood et al., 2010) and young female binge drinkers (Scaife and Duka, 2009). Brain imaging studies reveal that adolescent drinkers exhibit reduced activity in the orbitofrontal cortex compared to adolescent non-drinkers (Whelan et al., 2012). Moreover, differences in hippocampal brain volume were found between drinking and non-drinking adolescents (Medina et al., 2007). Volume differences in the prefrontal cortex were found between adolescents with an AUD and adolescents with limited experience with alcohol use (Medina et al., 2008). Both studies found reduced brain volume in (heavy) drinking adolescents, which might indicate cell death or adjusted synaptic pruning (Medina et al., 2007, 2008). In sum, psychological and cognitive differences between adolescents who drink heavily and those who do not can be related to differences in brain structure and function.

However, the question remains if these differences are a consequence of alcohol use or if they precede the onset of alcohol use in adolescents. The assumption that alcohol use, particularly during adolescence, has adverse effects on the brain (Squeglia et al., 2009; Nixon and McClain, 2010) has led to increased awareness about adolescent alcohol misuse, not only among researchers (see for an overview Zeigler et al., 2005) but also among health workers and parents. In the following sections we will review some recent findings that shed light on the nature of the relationships between alcohol use and adolescent brain function. Prospective studies have examined differences in cognition and brain structure and function between drinking and non-drinking adolescents (Norman et al., 2011; Squeglia et al., 2012), or young adults (Goudriaan et al., 2011). However, it is beyond the scope of this review to comprehensively review all of the evidence linking alcohol use during adolescence to brain damage (see other papers in this special issue). Our focus is on the prospective relationships between alcohol use and cognitive functioning in adolescents.

The chicken and the egg: what causes what?

Tapert et al., (2002), Hanson et al., (2011), and Squeglia et al., (2009) prospectively examined the relation between alcohol use and cognitive performance in adolescents. Tapert and colleagues (2002) found that in adolescents with a substance use disorder (SUD) (13-17 years) prolonged alcohol use and withdrawal predicted impaired cognitive functioning (attention, visuospatial functioning, verbal learning and memory functioning) eight years later. The authors excluded recently intoxicated adolescents and controlled for baseline age and cognitive functioning, which indicates that alcohol use caused the cognitive deficits. Nevertheless, it is difficult to exclude a reversed causal effect because the study sample was clinically diagnosed with SUD at the beginning of the study. Moreover, because these participants also used other drugs it is difficult to attribute the cognitive deficits to alcohol alone. Even though the authors examined each substance separately, it is possible that a combination of cannabis and alcohol use caused the impairment, rather than a direct effect of alcohol in isolation. This criticism also applies to a study by Hanson et al., (2011), who examined adolescents with an alcohol or substance use disorder (some of whom were still using the substance) and compared them to adolescents without an AUD or other SUD on various cognitive tasks. Recently intoxicated adolescents were excluded from analysis and the authors controlled for age and education. Participants were followed-up over a period of 10 years and it was found that adolescents with an AUD or SUD showed more decline in visuospatial functioning and verbal learning and memory functioning compared to control adolescents when assessed 10 years later, after controlling for cognitive performance at baseline. Although baseline similarities suggested no differences between the three adolescent drinking groups, it is possible that cognitive deficits preceded the onset of AUD in the first place (non-drinking adolescents were not included in this study).

Squeglia and colleagues (2009) examined neurotoxic effects in non-dependent adolescents who consumed minimal amounts of alcohol at baseline. The authors used drinking days in the past year, quantity of alcohol consumed in the past 3 months and hangover symptoms as predictors of changes in tests of neuropsychological function. Results revealed that for girls, drinking days in the previous year and the quantity of alcohol consumed over the previous 3 months predicted poorer visuospatial functioning between baseline and 3 year follow-up. These relationships were not seen in boys, although increase in hangover symptoms was associated with poorer attention functioning one year later (relative to baseline performance). Therefore, for boys, the relationship between cognitive impairment and self-reported alcohol use was unclear, because hangover symptoms are obviously a consequence of alcohol use but they do not reveal anything about the quantity that was consumed. Nevertheless, for girls, frequency and quantity of alcohol use preceded impaired cognitive functioning. Moreover, the majority of the adolescents initiated alcohol use after the baseline assessment of cognitive function which points to the direction of cause (i.e. alcohol) preceding effect (i.e. cognitive functioning). It is also important to note that these results were based on small sample sizes, and there were large between-subject differences.

Although the study designs do not rule out reversed effects, these findings indicate that alcohol use can have negative consequences on cognitive functioning in some adolescents. Visuospatial functioning and attention appear to be particularly affected by alcohol use during adolescence, particularly if drinking is heavy and is accompanied by hangovers. Repeated experience of alcohol withdrawal has been associated with impairments in cognitive functioning (Crews et al., 2004; Duka et al., 2002, 2004) and it is suggested that repeated cycles of binge-withdrawal might lead to deficits in cognition as a consequence of glutamatergic adaptations, which are analogous to those seen in repeatedly detoxified alcoholics (see Duka et al., 2004; Stephens and Duka, 2008; Scaife and Duka, 2009). However, at present it is unclear if adolescents who drink moderate amounts of alcohol also experience cognitive deficits as a consequence of their drinking. Additional prospective studies are required to investigate this issue.

Recent studies have identified relatively weak executive functioning as premorbid to the onset of alcohol involvement, including binge drinking and chronic heavy drinking. Nigg and colleagues (2006) found that relatively poor response inhibition in early adolescence (12-14 years) prospectively predicted the escalation of alcohol use in late adolescence (15-17 years), after controlling for confounding variables such as parental alcoholism, age, IQ, and baseline problem drinking. Nevertheless, the findings do not exclude the possibility that variations in baseline response inhibition were a consequence of previous alcohol use, and any further alterations are a knock-on consequence of those previous impairments. Comparable findings were reported by Wong and colleagues (2006). Q-sort ratings of clinicians were used to assess behavioural control and resiliency from childhood (2-5 years) to early adolescence (14 years). Relatively slow development of behavioural control during childhood predicted early onset of alcohol use, after controlling for age, parental alcoholism and externalizing problems. However, the analyses reported make it difficult to establish whether slow development of behavioural control predicts the initiation of 'first contact' with alcohol, or the development of heavy drinking.

Khurana et al., (2012) found that working memory was cross-sectionally associated with the frequency of alcohol use, and it also predicted the rate of increase in frequency of drinking over a period of 4 years in young adolescents (mean age 11 at the start of the study). This prospective relationship was mediated by two forms of impulsivity, delay discounting (behavioural measure) and acting without thinking (self-report), which suggests that relatively poor working memory might manifest itself through impulsive behavior which in turn predicts alcohol use. Therefore, this study suggests that (poor) working memory predicts an increase in the frequency of drinking, an effect that is mediated by increased impulsivity, but the study is silent regarding the predictive relationships between working memory and the quantity of alcohol consumed, or alcohol problems (these were not measured).

In another study, Fernie and colleagues (2013) found that three components of impulsivity, namely response inhibition, risk-taking and delay discounting each prospectively predicted adolescent alcohol involvement (a composite index of frequency of drinking, the number of binges, and the severity of alcohol problems). Individual differences in these three components of impulsivity predicted change in alcohol involvement 6 months later in young adolescents (12-13 years at baseline), and these relationships were consistent over a two-year period. These authors were able to exclude reverse causation by the use of a cross-lagged model: Only cross-lagged relationships from impulsivity to future alcohol involvement were significant, whereas relationships between alcohol involvement and future impulsivity were not. Nevertheless, many of the participants in this study were already consuming alcohol at the first assessment, so this study does not inform us about the influence of different components of impulsivity on the initiation of alcohol involvement.

When we consider these results together, it appears that deficits in working memory, disinhibition and other aspects of executive function and impulsivity are risk-factors for heavy drinking among adolescents. However, no individual study has so far provided a definitive answer to this particular 'chicken and egg' issue. Given the differences between studies, it is possible that different aspects of cognition are predictive of different aspects of alcohol use (e.g. age of onset of drinking, frequency of binges) in adolescents (see Wiers et al., 2010a), and further studies are required to investigate this.

Conclusion

Although these findings shed light on the nature of the relationships between alcohol involvement and cognitive deficits, the question of cause and effect remains unanswered (Macleod et al., 2004). Our review of recent literature mainly reveals "indication for" rather than definitive evidence of causal influences. A weakness in the majority of the studies discussed was in the quantification of alcohol consumption: if this is not measured reliably, it is not possible to establish dose-response relationships between alcohol intake and cognitive deficits. Findings from some studies may have been contaminated by the use of other substances (e.g. cannabis) alongside alcohol, which makes it difficult to attribute any cognitive deficits to alcohol alone. Furthermore, very few studies included participants of a sufficiently young age that they had not yet started drinking occasionally at study enrolment. Although some types of statistical models (e.g. cross-lagged analyses) can overcome these difficulties, prospective studies in which alcohol-naïve participants are followed up for many years are needed to provide more definitive data on the cognitive causes and cognitive consequences of heavy drinking during adolescence.

Nevertheless, we can cautiously conclude that elevated impulsivity and poor executive functioning precede the onset of alcohol involvement, and they place the individual at increased risk for the development of alcohol or other substance problems later on in life. Other cognitive deficits such as attention and visuospatial functioning can be attributed to the effects of chronic heavy drinking during adolescence (Hanson et al., 2011; Squeglia et al., 2009; Tapert et al., 2002). The volume of alcohol consumed appears to be an important determinant of neurotoxicity, which is apparent in adolescents who drink in a binge pattern or who have a history of extreme alcohol use. However, in community samples increased impulsivity seems to be a risk factor for (future) alcohol involvement, but not a consequence of it (Fernie et al., 2013; Khurana et al., 2012; Wong et al., 2006). Overall, although it seems that heavy drinking during adolescence might be neurotoxic, these effects are certainly not seen in all adolescents who drink, particularly not those who drink small amounts. It is possible that alcohol itself is not neurotoxic, but the effects associated with heavy alcohol use (e.g. repeated cycles of bingeing followed by hangover) are responsible for neurotoxicity and accompanying cognitive deficits.

3

Working memory and alcohol use in at risk adolescents: A two year follow-up.

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Abstract

Previous research has identified low working memory as possible risk factor for problem drinking in adolescence. At the same time results suggest that working memory functioning is negatively influenced by the use of alcohol. To get a better understanding of the nature of this relationship, the present study examined the prospective bidirectional association between alcohol use and working memory in a sample of young adolescents high risk for problem drinking. Adolescents were all 8th graders from 17 different Special Education Schools (for youth with externalizing behavior problems). At the beginning of the study, 374 adolescents participated (mean age of 13.6 years). Approximately every six months adolescents completed a questionnaire to establish alcohol use and a Self-Ordered Pointing Task (SOPT) to assess working memory. Cross-lagged analyses revealed that alcohol use at T1 negatively predicted working memory functioning six months later ($p < .001$). Working memory functioning at T2 and at T3 predicted alcohol use six months later ($p < .01$). Working memory functioning has been identified as both risk factor for and as function negatively influenced by alcohol use. Findings indicate that early alcohol use in high risk adolescents negatively influences the development of subsequent working memory functioning, which in turn constitutes as a risk factor for later alcohol use problems. Implications for early interventions are discussed.

Introduction

Adolescence is a period in which risk-taking behaviors such as substance use, risky sexual behavior and drunk driving reach their peak (Arnett, 1992; Gardner and Steinberg, 2005). Arnett (1992) suggests that changes in sensation seeking, sense of responsibility, and cognitive maturation may underlie this peak in reckless behavior in adolescence and eventually the decrease of reckless behavior in young adulthood. Important executive functions, such as working memory functioning and behavioral inhibition, mature in middle and late adolescence (Bava and Tapert, 2010). Working memory in particular, is not fully developed until young adulthood (Luna et al., 2004). It is suggested that immature executive functioning may promote reckless behavior such as substance use (Steinberg, 2005), but it is also possible that some of these risky behaviors affect the development of important executive functions (Wiers et al., 2007; Windle et al., 2008). Although many studies have examined the relationship between cognitive functioning and alcohol use (Mahmood et al., 2010; Nigg et al., 2006; Sher et al., 1997; Squeglia et al., 2012) and marijuana use (Meier et al., 2012), only few studies have examined this relationship prospectively. Results of longitudinal studies reveal neurotoxic effects of alcohol use on cognitive functions such as memory and visuospatial functions (Hanson et al., 2011; Tapert et al., 2002), however no effects were found for executive functions such as working memory. To the contrary, predictive effects of executive functioning on alcohol use have been found for inhibition (Nigg et al., 2006) and working memory (Khurana et al., 2012). It has been suggested that binge drinking and heavy alcohol use are related to impaired working memory and impulsivity (Stephens and Duka, 2008) and this could explain why in community samples (see for instance Khurana et al., 2012), deficits in executive functioning are not found. The amount of alcohol might be too low in this group to negatively influence the development of executive functions. We therefore explored the nature of the prospective relation between alcohol use and working memory in a heavy drinking sample of young adolescents (Kepper et al., 2011).

Previous research has examined cognitive functioning both as predictor and outcome variable in relation to adolescent alcohol use. Romer and colleagues (2011) found that relatively poor working memory (spatial and verbal) prospectively predicted risk-taking behavior in young adolescents. Moreover, in another study it was found that a composite score of verbal and spatial working memory functioning prospectively predicted alcohol use in adolescents (Khurana et al., 2012). Working memory functioning has also indirectly been associated with alcohol use, in such a way that working memory in combination with strong alcohol-related cognitions predicts alcohol use in high risk adolescents (Grenard et al., 2008; Thush et al., 2008). In addition, Squeglia and colleagues (2012) found that brain activity associated with visual working memory predicted alcohol use. Differences in working memory brain activity were found before the onset of drinking between adolescents who abstained from drinking and adolescents who drank heavily later on. These results indicate that at least on a neurofunctional level, differences between drinkers and non-drinkers exist even before the onset of drinking. In sum, different studies have identified working memory as possible predictor of future alcohol use. Poorer working memory functioning might place adolescents at risk for either the onset or escalation of alcohol use.

Another line of research has found that the use of alcohol and other substances predicts impairment of cognitive functions. Tapert and colleagues (2002) for instance, found that substance use prospectively predicted impaired visuospatial functioning in adolescents with an alcohol use disorder (AUD). Similar results were found over a period of ten years (Hanson et al., 2011). That is, alcohol use predicted impaired visuospatial and memory functioning in adolescents diagnosed with AUD. Cross-sectional results indicate that poorer memory functioning is associated with chronic substance use (Bava et al., 2010) and alcohol use (Mahmood et al., 2010) in adolescents. Squeglia and colleagues (2009) found that in adolescents, moderate drinking in girls and hangovers in boys were associated with decreased visuospatial functioning and attention functioning 3 years later. In sum, these results suggest that alcohol use might impair cognitive functioning in adolescents. However, the majority of the studies found impairment in visuospatial and memory functioning, and less is known about the effect of alcohol on working memory. Working memory continues to mature in adolescence (Luna et al., 2004) and it is assumed to be an important cognitive function in relation to the negative effect of heavy drinking on the developing brain (Stephens and Duka, 2008). In addition, it appears that binge drinking and problematic alcohol use are risk factors for impaired cognitive functions. In the present study we therefore selected a group of adolescents assumed to be at risk for heavy drinking and problematic alcohol use. Previous results indicate that the chance of heavy weekly drinking is twice as high in this group of young adolescents (12-14 years) compared to peers from community samples (Kepper et al., 2011).

This specific group of adolescents is characterized by behavioral problems such as attention-deficit hyperactivity disorder (ADHD) and conduct disorder (not necessarily diagnosed). These externalizing behavioral problems are associated with relatively weak working memory functioning (Barkley, 1997, Pihl et al., 1990), and might place adolescents at risk for problematic alcohol use and later alcohol dependence. At the same time, heavy alcohol use might interfere with development of working memory. This bidirectional relationship particularly appears to be present in high risk adolescents (Thush et al., 2008). Cognitive dysfunction and hyperactivity have been described as characteristics of a specific high risk group with respect to problematic alcohol use, namely sons of male alcoholics, indicating that these behavioral characteristics are associated with a heightened risk for alcohol problems (Nigg et al., 2004; Pihl et al., 1992). Moreover, Finn (2002) suggested that adolescents with inhibition problems in particular, who have an attention bias toward rewarding stimuli relative to punishment stimuli, and thus experience rewarding stimuli as more salient, will have more difficulties to keep the less salient punishment stimuli active in memory. It is therefore less likely that negative consequences of drinking will be processed in memory of adolescents who have problems with inhibition and working memory functioning.

To get a better understanding of the cause and effect of alcohol use and working memory we examined the influence of heavy alcohol use and working memory functioning over a period of two years in a cross-lagged panel model; a model particularly suitable for examining reciprocal effects and change in behavior. Contrary to what has been found in community samples (Khurana et al., 2012, Romer et al., 2011) we expected to find bidirectional effects of working memory and alcohol use in this high risk sample. We hypothesized that poor working memory would predict an increase in alcohol use and alcohol use would predict a decrease in working memory functioning.

Methods

Participants

Participants in the current study took part in a longitudinal study consisting of four data waves. At baseline, the sample included 374 adolescents (330 males, 44 females) with a mean age of 13.55 (SD = 0.87, range = 12-16). Wave two, three and four were conducted at intervals of approximately 6 months, with respectively 279 adolescents (236 boys, mean age; 14.11 (SD = 0.85, range = 12-16) participating in the second wave (75 % response), 230 adolescents (198 boys, mean age; 14.60 (SD = 0.87, range = 13-17)) in the third wave (61 % response) and 196 adolescents (176 boys, mean age; M = 14.95 (SD = 0.85, range = 13-17) in the fourth wave (52 % response).

Participants were recruited from seventeen secondary special education schools in the Netherlands. Adolescents attend these school to receive education appropriate to the needs of the student, which deviate from the standard (e.g. smaller classes, more individual attention, professional counseling). This type of special education includes adolescents who are characterized by externalizing behavioral problems such as aggression, attention problems and/or hyperactivity but are not necessarily diagnosed with a behavioral disorder. Adolescent were mainly boys (> 85%) which is distinctive for this population, and predominantly 8th graders at the beginning of the study. Few students (< 5%) were 7th graders at the beginning of the study due to mixed classes. Passive parental permission was obtained by an informative letter sent to all parents and caregivers. Adolescents were informed about the anonymous and voluntary nature of the study. Fifteen parents (3.8%) and seven students (1.7%) declined participation. In total 381 adolescents participated in at least one wave. Full information maximum likelihood (FIML) was used to deal with missing data. Therefore the total analytical sample consisted of 381 adolescents (note that the total amount of participants is higher than the starting sample (i.e. 374) as adolescents could participate in the study even if they had missed the first wave). Many participants skipped school without notice, were suspended, moved to another school, or had to go to court or juvenile institution, so attrition rates were relatively high. Therefore study variables and other possible predictors of drop out were examined in relation to missingness; age, gender, alcohol use, smoking, illicit drug use, family composition (e.g. divorced), externalizing behavioral problems, (assessed with the Strength and Difficulties Questionnaire, Goodman, 1997), and working memory. Each possible predictor was first analyzed separately and significant predictors (i.e. alcohol use, smoking and age) where then analyzed jointly. Only age remained a significant predictor of missingness, indicating that those who were older more likely dropped out. FIML is an appropriate method to deal with larger amounts of missing data under the condition of missing at random (MAR, Neworking memoryan, 2003) and was therefore selected.

At each measurement wave, participants completed both a questionnaire and a computer task under the guidance of a trained research assistant. Some adolescents were absent or ill during assessment and completed the questionnaire at a later point under the guidance of a teacher instead. The computer task required trained guidance and was therefore only administered in the presence of a research assistant.

Measures

Alcohol use and Problems. Alcohol use was assessed by three alcohol measures, namely frequency of use, quantity of use and problematic use. Information on frequency of alcohol use was obtained by asking participants to rate their use of alcohol in the past month on a 14-point rating scale (ranging from “never” to “ten times”, and three ratings consisting of aggregate scores; “11-19”, “21-39”, “forty times or more”, O’Malley et al., 1983). Adolescents were asked to indicate on how many weekend days (Friday till Sunday) and on how many weekdays (Monday till Thursday) they consumed alcohol (Engels and Knibbe, 2000). Adolescents were also asked to indicate the number of glasses of alcohol consumed on a regular drinking day, separately for weekend and weekdays (0, 1, 2, 3, 4, 5, 6 , 7-10 glasses, 11-14 glasses, 15-19 glasses and 20 glasses or more, Engels et al., 1999). A quantity measure of alcohol was calculated by multiplying drinking days by glasses. For range ratings, integer values representing the mean of the range were used. Standard glasses in the Netherlands contain approximately 12.5 ml alcohol. Problem drinking was measured by the CRAFFT (mnemonic for the six items of the scale; **C**ar, **R**elax, **A**lone, **F**orget, **F**riends, **T**rouble), a problem drinking screening instrument used in clinical settings to diagnose problematic alcohol use and alcohol dependence in adolescents. An example of one of the items is “Do you drink alcohol when you are by yourself”? (Knight et al., 1999). The internal consistency of the scale in the present study was acceptable (Cronbach’s Alpha = .74).

Working memory. Working memory was assessed by the Self Ordered Pointing Task (SOPT) (Petrides and Milner, 1982), a task that has successfully been used in previous studies in adults (Petrides et al., 1993) and adolescents (Grenard et al., 2008; Thush et al., 2008). The SOPT is a non-spatial working memory task (Cragg and Nation, 2007). In the present study, we used a non-verbal version of the task with representational drawings of everyday objects. Depending on the amount of pictures in each trial, pictures were presented in a square or rectangle. Participants received the following instructions; (1) select each picture one time, and (2) do not select the same location of the picture twice in succession. Adolescents were encouraged to complete the task without any errors. However, irrespective of the errors made, all participants received the feedback “well done” after each trial. With respect to the second instruction, the task was programmed not to allow selecting the same location twice in a row. The total task included five trials with one practice trial and four assessment trials. The practice trial consisted of four unique pictures. The test trials consisted of respectively six, eight, ten and twelve unique pictures. For each test trial a proportion error score was computed by dividing the number of errors by the number of pictures. The total SOPT score was calculated by taking the mean of the proportion error scores over the four trials. Higher scores indicated more errors and therefore poorer working memory functioning.

Strategy for analysis

Descriptive statistics (Table 1) and Pearson correlations (Table 2) of the four measures on four different measurement waves were provided. To test if there was an underlying dimension for the three alcohol indicators, a confirmatory factor analysis (CFA) using Mplus version 6.0 (Muthén and Muthén, 1998-2010) was performed. Factor loadings and measurement invariance assumptions were discussed. Next, the relationship between alcohol use and working memory was investigated in a cross-lagged model. Because the three indicators for alcohol use revealed a non-normal distribution (i.e. left skewed), maximum likelihood estimation with robust standard errors (MLR) was used. This estimator is robust for non-normal data (Muthén and Muthén, 2002). FIML was used to cope with the missing data. FIML uses all available information instead of deleting cases with missing variables. That is, in case of missing values, parameter estimation is based on “borrowed” information of other correlated observed values. Compared to traditional approaches (e.g. listwise/pairwise deletion) FIML has been found to be a reliable and efficient approach (Enders and Bandalos, 2001).

In addition, the influence of confounding variables was examined. Previous studies (Hanson et al., 2011; Tapert et al., 2002) suggest that the use of other substances (cannabis, ecstasy and cocaine), which are related to the use of alcohol, might cause deficits in cognitive functioning.

Results

Descriptives

The descriptive statistics of alcohol use and working memory errors are presented in Table 1. Table 2 includes Pearson correlations of the three alcohol measures and the working memory task. All alcohol measures over a period of two years were significantly correlated with each other. Only working memory at wave 2 correlated significantly with alcohol use at wave 1 and wave 2 (i.e. not with problem drinking). All alcohol measures (i.e. alcohol frequency, alcohol quantity, and problem drinking) increased over the two years of study. Working memory errors decreased (indicating better performance) between wave 1 and wave 2, followed by stabilization on the subsequent measurements.

Table 1. Descriptive statistics for four measurement waves (N = 381).

	Wave 1 M (SD)	Wave 2 M (SD)	Wave 3 M (SD)	Wave 4 M (SD)
Percentage drinkers*	47.0%	51.2%	51.3%	55.6%
Alcohol frequency	1.45 (2.95)	1.59 (3.13)	2.57 (5.92)	2.85 (6.45)
Alcohol quantity	3.36 (7.99)	3.71 (8.64)	4.12 (9.01)	5.59 (10.97)
Problem drinking	0.81 (1.35)	0.85 (1.31)	0.86 (1.39)	0.95 (1.38)

** percentages are calculated relative to participants at each wave*

Factor analysis

The CFA revealed good factor loadings for all three indicators (alcohol frequency; .74, alcohol quantity; 81, problem drinking; .62 for the first measurement and ranging between .57 and .86 for the subsequent waves). To examine if there was a similar underlying factor of "alcohol use and problems" for each measurement wave, we assumed measurement invariance (further referred to as "alcohol use"). We compared the constrained model, in which variances and factor loadings of all alcohol use indicators were constrained to be equal over time, to the unconstrained model in which no constraints were imposed. The Bayesian Information Criteria (BIC) slightly favored the constrained model (BIC; 15616, 45) over the unconstrained model (BIC; 15619, 54), indicating that measurement invariance of alcohol use between the four measurement waves was justified. One of the advances of using a latent factor is the

Table 2. Bivariate Correlations Between Study Variables

		2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1	Alcohol frequency 1	.57**	.45**	.52**	.32**	.40**	.42**	.23*	.30**	.30**	.18*	.43**	-.01	.17*	-.05	-.08
2	Alcohol quantity 1		.57**	.46**	.34**	.48**	.58**	.37**	.39**	.27**	.28**	.39**	.02	.30**	-.01	-.04
3	Problem drinking 1			.40**	.41**	.61**	.48**	.37**	.59**	.21**	.34**	.48**	-.04	.18*	-.02	-.09
4	Alcohol frequency 2				.52**	.54**	.49**	.40**	.46**	.28**	.41**	.59**	.01	.20**	.04	.05
5	Alcohol quantity 2					.49**	.61**	.76**	.45*	.22**	.63**	.50**	-.01	.22**	.00	.09
6	Problem drinking 2						.44**	.38**	.58**	.28**	.40**	.64**	-.02	.13	-.05	-.08
7	Alcohol frequency 3							.69**	.57**	.40**	.62**	.54**	-.05	.09	-.03	.04
8	Alcohol quantity 3								.65**	.34**	.81**	.62**	.01	.08	-.01	.13
9	Problem drinking 3									.42**	.65**	.74**	.06	.04	.02	-.05
10	Alcohol frequency 4										.63**	.43**	-.03	.04	-.08	.00
11	Alcohol quantity 4											.60**	-.02	.01	-.01	.05
12	Problem drinking 4												.06	.05	-.08	-.01
13	Working Memory 1													.27**	.13	.14
14	Working Memory 2														.32**	.32**
15	Working Memory 3															.48**
16	Working Memory 4															

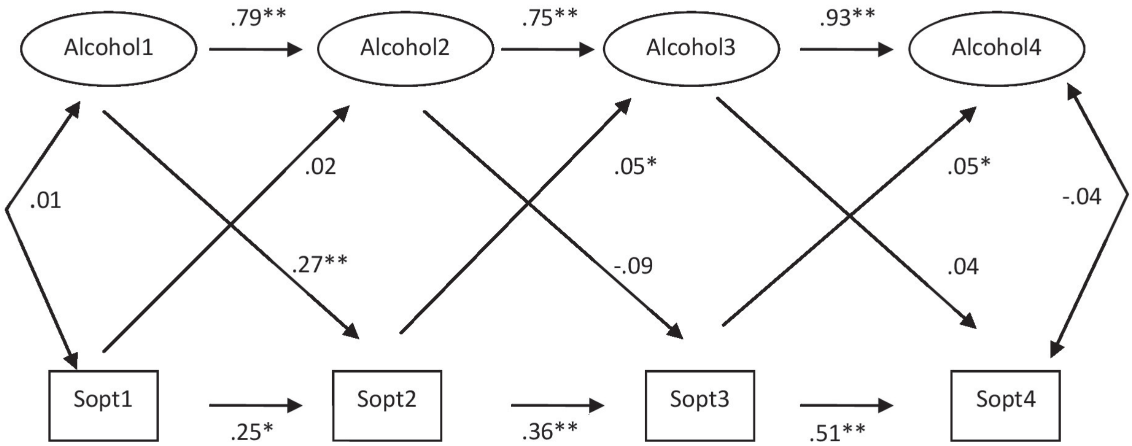
** = p < .05, ** = p < .01*

explicit definition of measurement error (Hoyle and Smith, 1994). This allows to correlate the measurement error associated with each indicator to the corresponding measurement error on the subsequent measurements (e.g. alcohol quantity at wave 1 with alcohol quantity at wave 2, problem drinking at wave 2 with problem drinking at wave 4 etc., Hoyle and Smith, 1994). The model fit measures of the CFA model were good (CFI = .99, RMSEA = .02).

Cross-lagged model

The cross-lagged model for alcohol use and working memory showed acceptable model fit (CFI = .94, RMSEA = .04, Fig. 1). Stability paths for alcohol use and problems and working memory were all significant ($p < 0.01$ and $p < 0.001$ two-tailed), with increasing stability for working memory. Cross-sectional correlations between alcohol use and working memory were all non-significant. Three out of six cross-lagged paths were significant. Alcohol use at T1 predicted working memory six months later ($\beta = .27$, $p < .001$ two tailed). Working memory at T2 ($\beta = .05$, $p < .01$ two tailed) and T3 ($\beta = .05$, $p < .01$ two tailed) both predicted alcohol use six months later.

Figure 1. Cross-lagged model with prospective effects of alcohol use and working memory performance over four waves (N = 381). Cross-sectional correlations only presented for the first and last wave, other correlations were included in the model but not illustrated. All cross-sectional correlations were non-significant.



*CFI: .94, RMSEA: .04, * = p < .01, ** = p < .001*

Confounding variables

Percentage of cannabis users at baseline was 12%, the percentage ecstasy users as well as cocaine users at baseline was 4 %. Since adding substance use as confounding variable would complicate the model (i.e. 24 additional paths), we first examined Pearson correlations between working memory and three measures of drug use (past 6 month prevalence cannabis, life prevalence ecstasy and cocaine) to determine the influence of other substance use variables. No significant correlations were found suggesting that in the present study, substance use is not a confounding variable. This was confirmed by post-hoc analyses focusing on the first two waves, which revealed that alcohol use at T1 predicted working memory functioning six months later (T2) also when drug use (cannabis, ecstasy, cocaine) was taken into account (β = .33, $p < .001$).

Discussion

In this study we examined the prospective bidirectional relationships between alcohol use and problems on the one hand and working memory functioning on the other hand, over a period of two years in a sample of young adolescents with externalizing behavior problems. Although the participating adolescents were very young (mean age = 13.55 at wave 1) alcohol use was already rather stable, indicating that early use of alcohol is a strong predictor of later alcohol use at this young age in the present sample. Working memory functioning became more stable as adolescents grew older (as indicated by the increasing stability paths), which is partly in agreement with cognitive developmental theories indicating that particularly working memory continues to mature in adolescence (Blakemore and Choudhury, 2006; Luna et al., 2004). On a group level, the stabilization of working memory between wave 3 and wave 4 (as indicated by the stabilization of mean performance scores) was an unexpected finding. Cognitive development theories suggest a continuous maturation of working memory until late adolescence instead of stabilization around the age of 15 years (Blakemore and Choudhury, 2006). Even though maturation is not observed between wave 3 and wave 4 on a group level it is possible that working memory continued to improve after the last wave was completed. The results from the cross-lagged model suggest that alcohol use and working memory mutually influence each other longitudinally. More specifically, it was found that alcohol use at T1 negatively predicted working memory six months later (T2). Working memory functioning at T2 and T3 predicted alcohol use respectively at T3 and T4, with increasing alcohol use when working memory functioning was lower at the previous wave. Previous alcohol use already explained a large proportion of the variance in current alcohol use, leaving only a small amount of variance to be explained by other factors. This explains the lower cross-lagged regression coefficients from working memory to alcohol use at T2 and T3. In a model where there is not much change, it will be harder to predict change in behavior. Nevertheless, the path coefficients were both significant ($p < .01$). Moreover, since the predictive effect of working memory on alcohol use was found at two waves, the results appear to be fairly consistent. Interestingly, no cross-sectional relations between working memory and alcohol use were found (Fig. 1), suggesting that working memory predicts change in alcohol use but is concurrently not related to alcohol use. This finding is in line with results of Khurana and colleagues (2012), who found that the effect of working memory on alcohol use was mediated by impulsivity. Poor working memory functioning might reinforce impulsive behavior which in turn might increase alcohol use among adolescents. Working memory might therefore be a potential risk factor in the escalation of alcohol use. The results support previous findings indicating that working memory functioning is prospectively associated with risk-taking behavior such as alcohol use (Romer et al., 2011). Moreover, results are consistent with previous research that assign an important role to working memory (Grenard et al., 2008; Thush et al., 2008) and other executive functions (Peeters et al., 2012) in relation to alcohol use in high risk adolescents. Particularly in this high risk group, improving working memory functioning (Houben et al., 2011a) might be an interesting means in preventing problematic alcohol use in young adolescents.

Prediction of working memory functioning by alcohol-related outcomes was only found between waves 1 and 2, with a strong effect ($\beta = .27$, $p < .001$ two tailed). This result suggests that alcohol use at is a negative predictor for later working memory functioning but only at the youngest age of our investigation (mean age between 13.6 and 14.1) and not on subsequent measurements. During early adolescence, when the brain is still developing and maturing, working memory functioning might be particularly sensitive to the neurotoxic effects of alcohol. Yet, one would expect to find influences of alcohol on working memory over an extended period (i.e. over the two years of investigation) as working memory continues to develop until late adolescence. It is possible that particularly when there is large variability in working memory functioning (i.e. between the first two waves) alcohol use has a negative impact on working memory in such a way that adolescents who consume more alcohol show a delay in improving working memory. When working memory reveals a more stable pattern (i.e. between wave 2 and 4), the influence of alcohol on working memory decreases. An anonymous reviewer suggested that this finding may be related to acquiring a learning strategy. It is possible that drinking adolescents might be slower in obtaining a strategy or select less efficient strategies to solve the task. As the study proceeded, the difference between drinkers and non-drinkers became smaller as (improved) strategies were acquired. This might imply that the higher working memory error at wave 2 (i.e. the slower improvement) reflects delayed strategy learning, however, still affects working memory performance. Previous results indeed suggest that the use of strategies increases working memory performance (McNamara and Scott, 2001). Though, we found no prolonged effect of alcohol use on working memory, a slower development of strategy use is still undesirable for drinking adolescents because these strategies might also be important for memorizing, reading and mathematical skills.

The results of this study should be interpreted with some caution. First, adolescents from this specific high risk sample may already have a lower level of executive functioning, related to their externalizing problems (e.g. conduct disorder, ADHD), which makes it difficult to generalize the results to other adolescent samples (also because of the unequal gender distribution). Nevertheless, the findings are relevant for this specific group of adolescents who are at risk for problem drinking (Groenman et al., 2013; Peterson et al., 1990; Pihl et al., 1990) and it might be this specific characteristic (i.e. relatively poor working memory functioning) which is responsible for the increased risk of problem drinking later in life (cf. Finn, 2002). These findings may help identify individuals best suited for interventions aimed at preventing (escalation of) alcohol use in this high risk group. Second, a limitation directly related to this risk sample is the high amount of drop-out. In this specific high risk group, it is difficult to follow adolescents and retain them in the study. Nevertheless, we used an appropriate method to handle the missing data (Enders and Bandalos, 2001; Neworking memoryan, 2003). In addition, when there is not enough information to analyze a model, the model will not converge (Graham, 2012). In our case the model did converge, which suggests that there was enough information available to deal with the missing data (which also can be deduced from the high stability paths of alcohol, Fig. 1). Third, alcohol use was assessed using self-report measures only. It would be preferable to rely on multi-informant or multi-method procedures. Nevertheless self-reported alcohol use has been found to provide reliable information on the alcohol use of young adolescents (Koning et al., 2010). Fourth, since working memory is not fully developed until young adulthood (Luna et al., 2004), results with respect to the relation between working memory functioning and alcohol use could differ in later adolescence compared to early adolescence, particularly because alcohol use increases throughout adolescence (Chassin et al., 2002). For future research it could be useful to extend the two-year follow-up period and include older adolescents in the study. Related to this, it is conceivable that other working memory-tasks (e.g., n-back, complex-span) may be better suited to identify the negative effects of alcohol and drug use during mid- and late adolescence. Finally, it is suggested that IQ might be a confounding variable in the relation between working memory and alcohol use (cf. Finn et al., 2002; Nigg et al., 2004). Unfortunately, due to limited examination time, we were unable to assess IQ in our study.

Despite these limitations the present study suggests that the use of alcohol in early adolescence may have harmful effects on working memory functioning in externalizing youth. Moreover, working memory deficits increase the risk of escalation of alcohol use in young adolescents at risk for alcohol misuse. Interventions aimed at delaying the onset of drinking (Koning et al., 2009; Koning et al., 2011) might be desirable and perhaps particularly effective in reducing working memory deficits. Furthermore, interventions aimed at increasing working memory functioning (Houben et al., 2011a) might decrease the use of alcohol in young adolescents, especially when combined with motivational interventions (both motivation and the ability to self-regulate alcohol consumption are important, Wiers et al., 2013). The present study indicates that working memory might be a potential risk factor underlying the escalation of alcohol use in high risk youth. Early prevention in high-risk groups might be especially beneficial because of the interacting nature of early alcohol use and working memory development.

4

Multiple behavioural impulsivity tasks predict prospective alcohol involvement in adolescents

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Abstract

We investigated reciprocal prospective relationships between multiple behavioural impulsivity tasks (assessing delay discounting, risk-taking, and disinhibition) and alcohol involvement (consumption, drunkenness, and problems) among adolescents. We hypothesised that performance on the tasks would predict subsequent alcohol involvement, and that alcohol involvement would lead to increases in behavioural impulsivity over time. Design: Cross-lagged prospective design in which impulsivity and alcohol involvement were assessed five times over two years (once every six months, on average). Two hundred and eighty seven adolescents (51% Male) who were aged 12 or 13 at study enrolment. Participants reported their alcohol involvement and completed computerized tasks of disinhibition, delay discounting, and risk-taking at each assessment. Cross-sectional and prospective relationships between the variables of interest were investigated using cross-lagged analyses. All behavioural impulsivity tasks predicted a composite index of alcohol involvement six months later (all ps < .01), and these prospective relationships were reliable across the majority of time points. Importantly, we did not observe the converse relationship across time: alcohol involvement did not predict performance on behavioural impulsivity tasks at any subsequent time point. Multiple behavioural impulsivity tasks predicted escalations in alcohol involvement in young adolescents, but we did not see any evidence to suggest that alcohol use increased behavioural impulsivity in our sample.

Introduction

There are several distinct facets of behavioural impulsivity, many of which overlap with sub-components of executive (dys)function (Bickel et al., 2012). For example, impulsive decision-making can be assessed with delay discounting procedures, in which participants make choices between small rewards that are available immediately versus larger rewards that are available after a delay (Bivkel and Marsch, 2001). Disinhibition is assessed with computerized tasks such as the stop-signal (Logan et al., 1997) and go/no-go tasks, both of which establish a dominant motor response that participants are required to occasionally inhibit. Risk-taking can be assessed with tasks such as the Balloon Analogue Risk Task (BART (Lejuez et al., 2002) in which participants attempt to win rewards by risking what they have accumulated up to that point. Dependent measures obtained from these tasks reflect distinct underlying concepts (Cyders and Coskunpinar, 2012), which suggests that impulsivity is not a unitary construct (De Wit, 2009). Nonetheless, performance on each of these measures is associated with heavy drinking and alcoholism (Dick et al., 2010; Fernie et al., 2010; Weafer et al., 2011) and with other substance use disorders (Verdejo-Garcia et al., 2008).

Initial experimentation with alcohol begins during adolescence. For example, in the United Kingdom approximately 24% of 12 year olds report at least one episode of alcohol consumption, rising to 77% of 15 year olds (Fuller, 2011). Individual differences in behavioural impulsivity are associated with drinking behaviour and alcohol problems in adolescents (Field et al., 2007). Theoretically, elevated impulsivity may pre-date alcohol involvement and serve as a risk factor for the development of heavy drinking and alcohol problems once individuals begin to experiment with alcohol (Dawe et al., 2004). Consistent with this, longitudinal studies demonstrate that high levels of disinhibition are predictive of the development of heavy drinking and alcohol problems several years later (Nigg et al., 2006; Wong et al., 2006; Zucker et al., 2011). Regarding other behavioural impulsivity measures, individual differences in the rate of increase in risk-taking during early adolescence (but not absolute levels of risk-taking) are predictive of subsequent alcohol involvement (MacPherson et al., 2010). Furthermore, individual differences in delay discounting predict the likelihood of starting smoking (Audrain-McGovern et al., 2009), although the relationship between delay discounting and subsequent heavy drinking in adolescents has not been investigated.

Adolescence is a critical stage of brain development, and the maturational changes that occur may render adolescents particularly sensitive to neuroadaptations that underlie development of alcohol dependence. For example, developmental brain changes that influence reward processing and impulse control are essential to the long-term development of self-regulation and adaptive decision-making (Spear, 2011; Steinberg, 2005). Neuroimaging studies have shown that adolescents, relative to adults and young children, show a heightened neural response to rewards in the nucleus accumbens (Ernst et al., 2005; Galvan et al., 2006). This heightened sensitivity occurs within the context of immature processing of reward and risk within the orbitofrontal cortex, a key region involved in inhibitory control (Eshel et al., 2006; Galvan et al., 2006). These features of brain development may render adolescents vulnerable to increased disinhibition, impulsive decision-making and risk-taking as consequences of heavy drinking. Consistent with this, studies with rodents demonstrate that the extent of neuronal loss following binge alcohol exposure is more pronounced in adolescents than in adults (Crews et al., 2000), as is increased probability discounting caused by heavy drinking (Nasrallah et al., 2009). There is also some preliminary evidence for neurocognitive deficits arising from alcohol exposure in human adolescents (McQueeny et al., 2009; Squeglia et al., 2009). However, there is no direct evidence that heavy drinking during adolescence leads to increased impulsivity.

Our goal in the present study, was to investigate the relationships between alcohol involvement and performance on behavioural impulsivity tasks among adolescents. We performed a cross-lagged prospective study involving a large sample of adolescents who were aged 12 or 13 at the beginning of the study and tested each participant five times over two years (every six months). We recruited participants in this age range as UK government data (Fuller, 2011) indicate that alcohol consumption in British adolescents tends to increase rapidly between the ages of 12 and 15. We hypothesised reciprocal prospective relationships between alcohol involvement and impulsivity. Specifically, we predicted that (a) individual differences in impulsivity would predict alcohol involvement at subsequent time points, and (b) individual differences in alcohol involvement would predict impulsivity at subsequent time points.

Methods

Participants

Two hundred and eighty-seven participants (51.2% male) were initially recruited from a total of five mixed-sex secondary schools across the Merseyside region of North West England. Each school allowed us to recruit pupils from year nine, in which all pupils were aged either 12 or 13 (mean age at enrolment was 13.33 years (SD = 0.33). All participants provided informed assent, and the parents or guardians of each participant provided either opt-in or opt-out consent depending on the preference of the individual school. The University of Liverpool Research Ethics Committee approved the study.

We initially contacted 105 schools to request their participation in the study. Of these, head teachers from nine schools expressed an interest in taking part, and we selected five of these schools for inclusion. We were successful in targeting schools that spanned the range of educational achievement (based on average exam results) and social deprivation (based on Government data), both at the initial recruitment stage and when selecting the final five schools for inclusion in the study. Each school was asked to provide a random selection of around 60 pupils, although the number actually recruited from each school ranged from 15 to 82. Four schools selected classes of pupils at random, and one school selected an entire academic year of pupils (i.e. multiple classes).

Self-report measures

Alcohol Use Questionnaire. This questionnaire measured the frequency and quantity of alcohol consumption. Participants were first asked whether they had ever had a proper alcoholic drink ("a whole drink, not just a sip", Fuller, 2011). If they answered 'yes', participants indicated how often they had consumed alcohol over the previous six months, using a question taken from the Adolescent Alcohol Involvement Scale (Mayer and Filstead, 1979), and they also estimated the number of times they 'got drunk' during this period. Participants also completed a retrospective diary in which they recorded all alcoholic beverages consumed over the previous two weeks.

Alcohol Problems Index (API, Magar et al., 2008). Participants indicated if any of six possible adverse consequences of drinking had happened to them in the previous 6 months (e.g. 'I lost money or other items'). All affirmative responses are scored 1, therefore the range of possible scores is 0-6.

Demographics and socio-economic status (SES). Participants indicated their sex and date of birth before completing the three-item Family Affluence Scale (Currie et al., 1997), a well-validated measure of socioeconomic status (Torsheim et al., 2004). Scores ranged from 0 to 6 (higher scores indicate higher SES). The mean value in our sample was 3.89 (SD = 1.46).

Behavioural Measures

Delay discounting task (DD, Du et al., 2002). This version of the task has been used with adolescent substance abusers to predict treatment outcome (Stanger et al., 2012). We simplified the interface and reduced the amounts of hypothetical rewards that were on offer. The resulting task was similar to one administered to children (mean age of 12 years) with ADHD and a healthy control group (Demurie et al., 2012). In this task, participants made hypothetical choices between a relatively small sum of money that was available immediately versus a fixed larger sum which was available after a delay. The value of the immediate reward and the length of the delay were adjusted on successive trials. We used the adjusting immediate amount procedure, as this is preferable to other versions of the task (Holt et al, 2012). The first trial presented the choice between £50 available immediately versus £100 available after a delay of one day. On subsequent trials the magnitude of the immediate reward was adjusted based on the decreasing adjustment algorithm (Du et al., 2002). In brief, if participants chose the immediate reward on a given trial, the magnitude of the immediate reward was decreased on the next trial, but if they had chosen the delayed reward, the magnitude of the immediate reward was increased on the subsequent trial. Participants made six choices at each of five delays (one day, one week, two weeks, one month, six months). Delay discounting was calculated using area under the curve (AUC; Meyerson et al., 2001). AUC values were inverted so that larger values indicated higher rates of delay discounting (i.e. high impulsivity). The internal reliability of the task was good: Cronbach's α values (calculated from indifference points at the different delays) ranged between .84 and .87 (mean α = .86).

Balloon Analogue Risk Task (BART, Lejuez et al., 2002). This task was initially validated in adults (Lejuez et al., 2002), although a modified version where participants win points rather than money has been validated in children with a mean age of 15 years (Lejuez et al., 2007). The version used in the present study was identical to that used in a previous study which revealed that risk-tasking was cross-sectionally associated with alcohol use in college students (Fernie et al., 2010). On each trial of the task, participants used the mouse to inflate an on-screen balloon in order to add hypothetical money to a temporary bank. Participants were instructed that at some point the balloon would burst and if this happened all the money in the temporary bank would be lost. Participants could collect from the temporary bank at any point before the balloon burst by clicking on a button marked “Collect”. The task comprised 30 trials, with a new balloon on each trial. On each trial, the balloon was randomly set to burst after between one and 128 pumps (Lejuez et al., 2002). The adjusted number of pumps (average number of pumps on trials when the participant banked their temporary funds before the balloon burst) provides the measure of risk-taking. The internal reliability of the task was good: Cronbach’s α values (calculated from adjusted pumps in blocks of 10 trials) ranged between .77 and .85 (mean α = .82).

Stop-Signal Task (Bitsakou et al., 2008). This version of the task was identical to one used in a previous study (Bitsakou et al., 2008) in which participants were children with ADHD and healthy controls, with a mean age of 12 years (range 6-17). In the task, participants manually categorised visual ‘go’ stimuli as quickly as possible. On 25% of trials, an auditory ‘stop’ tone was presented; this tone signalled that participants should refrain from responding. At the start of each block of trials, the stop signal delay (SSD), that is, the delay between onset of the ‘go’ stimulus and onset of the ‘stop’ stimulus was set at 250ms. On subsequent trials, SSD was altered in response to participants’ performance: if participants had successfully inhibited on the previous ‘stop’ trial, SSD on the next stop trial was increased by 50ms (making inhibition more difficult). If participants failed to inhibit on the previous trial, SSD was reduced by 50ms (making inhibition easier). There were six blocks of 32 trials, with eight stop-signal trials per block. The use of this ‘tracking procedure’ to manipulate SSD results in an SSD on which participants are able to inhibit on approximately 50% of trials, in which case Stop Signal Reaction Time (SSRT), can be computed as the average ‘Go’ reaction time minus the average SSD (Band et al., 2003).

The internal reliability of the task was good: Cronbach's α values (calculated from SSRT in each block) ranged between .66 and .96 (mean α = .85). High SSRTs indicate high levels of disinhibition.

Procedure

Participants completed five identical testing sessions, each lasting no more than one hour, spread over a two-year period. We aimed for a six-month interval between testing sessions. The interval between sessions was between four and seven months in 96% of cases, although in a minority of instances the delay was shorter (but no less than three months) or longer (but no more than nine months). All participants were tested at their school, in groups ranging in size between four and eight. On rare occasions, participants were absent from school on the date of the original planned testing session; in these cases the researcher returned at a later date and the participant was tested individually. All participants provided written informed assent before enrolling in the study and at the beginning of each individual testing session. Participants sat at individual desks facing a laptop computer. We arranged the seating to minimise interaction between participants and to ensure that individuals could not see the laptop screens of others. Participants initially completed the self-report measures, before a battery of computerized tasks in one of five predetermined counterbalanced sequences. At the initial testing session, the experimenter demonstrated how to complete all self-report measures and computerized tasks. In subsequent sessions these instructions were briefly re-iterated, with more detailed explanations or demonstrations if necessary. Participants wore headphones during all tasks. Experimenters were present throughout experimental sessions in order to ensure that participants were focused on the tasks.

At the end of each session, participants received a £5 voucher that they could spend in a national chain of music stores. Participants also received an additional £25 voucher at the end of the final (fifth) testing session if they had completed all testing sessions up to that point. At the end of the study, participants and teachers at the schools attended a debriefing presentation given by the lead researcher (GF).

Counterbalancing of task order

Participants completed the battery of five computerized tasks in one of five predetermined counterbalanced sequences. The within-session sequence remained the same across all of the testing sessions. Following the first wave of data collection we noted that some participants were very slow to complete the BART, although there was minimal variation in the time taken to complete the other tasks. As this presented an obstacle to successful data collection (all testing sessions had to be completed in under one hour in order to allow participants to get to their next lesson), we took the decision to modify the order of task presentation so that the BART was always completed last during waves 2-5 of data collection, so that it could be omitted if there was insufficient time. However, we always had sufficient time to administer all tasks, including the BART.

Missing data

Some data were missing from the BART (8 cases in session 1 and 1 case in session 3) and the delay discounting task (1 case in session 2, 5 cases in session 3, 1 case in session 4 and 2 cases in session 5) due to technical problems. Considering all missing data (that is, data which was genuinely missing data plus data excluded due to excessive errors or outlying reaction times on the stop-signal task), no more than 10% of data were missing from any individual task or self-report measure at any one session. Despite missing 5-10% of data in sessions 2-4, less than 3.3% of data was missing from the fifth and final session. Little's MCAR (missing completely at random) test was used to see if the data from each behavioural task were missing at random. Importantly, none of the alcohol use or behavioural task variables predicted missing data at the final session.

Data reduction and analysis

On the stop-signal task, trials with errors and reaction time outliers (defined as reaction times faster than 200ms, slower than 2000ms, and then if they were more than 3 standard deviations above the participants' mean RT) were removed. Participants' stop-signal data were excluded from analysis if they had an outlying high rate of missing data (errors and outliers), determined by visual inspection of box and whisker plots.

To test if there was a latent factor for alcohol involvement, we performed a confirmatory factor analysis (CFA) using Mplus version 7.0 (Muthen and Muthen, 1998-2010) on three observed measures: frequency of drinking in previous six months, frequency of getting drunk in previous six months, and the Alcohol Problems Index (for mean values, see Table 1). We checked for measurement invariance of the latent factor "alcohol involvement" between the five time points. We compared the constrained model, in which variances and factor loadings for alcohol involvement were constrained to be equal across the different time points, with an unconstrained model in which no constraints were imposed. The Bayesian Information Criteria (BIC) slightly favored the unconstrained model (BIC_constrained = 30011 (86) BIC_unconstrained = 29995 (106) indicating that measurement invariance was not ensured across all waves. Additional analysis revealed that 'got drunk' frequency at wave 4 was the cause of measurement deviation of the latent factor. The BIC dropped down (from 29975 (94) to 29970 (88) when the equality constraining of the factor loading of 'got drunk' frequency at wave 4 was released. If we did not constrain the factor loading of 'got drunk' frequency at wave 4, this increased the model fit (CFI = .93, RMSEA = .06 versus CFI = .90, RMSEA = .07 when constrained). However, since the overall model fit of the cross-lagged model was acceptable, at least weak measurement invariance was assumed (Conroy et al., 2003). Correlations between the measurement error of the latent indicators were defined (e.g. API1 with API2, API1 with API3, etc). All factor loadings were significant, ranging between .63 and .86. The overall fit of the model, assessed by the Comparative Fit Index, was good (Figure 1, CFI = .97, RMSEA = .05, $\chi 2$ / df = 1.85).

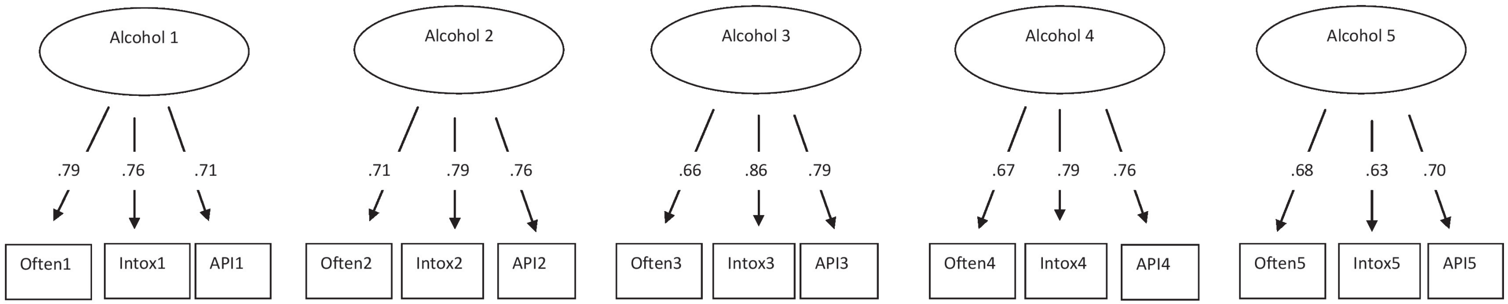
Table 1. Descriptive statistics. Values are means (standard deviation)

Session	1	2	3	4	5
Alc. cons freq.	1.01 (1.37)	1.29 (1.48)	1.45 (1.42)	1.72 (1.45)	1.80 (1.42)
'Got drunk' freq.	1.67 (4.96)	1.71 (4.61)	1.74 (3.93)	3.44 (7.80)	3.44 (8.26)
API	0.36 (0.92)	0.54 (1.24)	0.55 (1.09)	0.58 (1.07)	0.78 (1.23)
Disinhibition	273.23 (73.98)	268.67 (74.23)	259.59 (120.89)	277.08 (142.05)	274.75 (127.71)
Risk-taking	25.20 (10.70)	29.55 (11.80)	33.43 (11.96)	34.26 (12.03)	34.55 (11.02)
Delay discounting	0.51 (0.25)	0.52 (0.25)	0.50 (0.27)	0.49 (0.26)	0.48 (0.26)

Notes: Alc. cons. freq. = self-reported frequency of consuming alcohol in previous six months, coded 0 = never, 1 = a few times per year, 2 = once per month, 3= once per fortnight, 4 = once per week, 5 = several times per week, 6 = almost every day.

For all impulsivity measures, higher values indicate higher impulsivity.

Figure 1. Latent factor for alcohol involvement at each time point.



CFI = .97, RMSEA = .05, χ2 / df = 1.85, factor loadings are all significant at $p < .001$

Often = how often alcohol consumed
Intox = frequency of drinking to intoxication in last six months
API = Alcohol Problem Index

Delay discounting, disinhibition and risk-taking were not consistently inter-related at any time point. Indeed, when we performed an additional CFA in an attempt to create a latent impulsivity factor based on the three outcome measures from the impulsivity tasks (i.e. SSRT, BART adjusted pumps, and delay discounting AUC), this model did not converge, which suggests no latent factor of 'impulsivity'.

Data were analyzed using separate latent autoregressive cross-lagged models (Figure 2), to examine prospective relationships between the alcohol involvement variable and each impulsivity measure in isolation. These models permit investigation of the relationships between variable X (e.g. delay discounting) at time 1 and variable Y (e.g. alcohol involvement) at time 2, after controlling for cross-sectional relationships between X and Y at both time points, and for the stability paths of variables X and Y (Geiser, 2013). Maximum Likelihood Robust (MLR) Standard Errors was used as the estimation method for all analyses. This method was chosen because the alcohol involvement measures were skewed, and MLR is robust to non-normality of data distributions (Muthen and Muthen, 2002).

To account for the clustering effect of school we considered a multi-level modelling. However, in preliminary analyses we examined the intra class correlations (ICC). ICCs for the majority of study variables were low (.01 - .1), indicating that any clustering effect of school was too small to have significantly affected the accuracy of Standard Errors (Hox, 2002). Consequently, we proceeded with models that ignored any school effect.

Results

Study dropouts and missing data

Of the 287 participants who initially enrolled in the study and completed the first session, 16 participants dropped out of the study across the two-year period, resulting in a retention rate of 94.4%. There were no significant differences between study dropouts and study completers on any of the demographic or alcohol use measures, or on performance on any of the cognitive tasks at the first session (data not shown). An additional 18 participants missed at least one of the second, third or fourth sessions (of these, only one participant missed two sessions). We used Full Information Maximum Likelihood estimation (FIML, Graham, 2009) to handle missing values for these participants.

Descriptive statistics

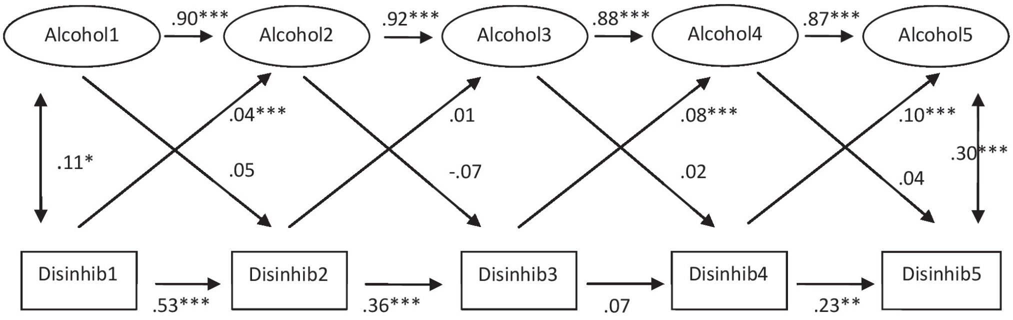
In the first session, 64% of participants stated they had ever consumed an alcoholic drink. This percentage increased over subsequent sessions to 99% at the fifth and final session. Table 1 shows data from alcohol use and behavioural impulsivity tasks from all participants at each session: scores on the API, the frequency of alcohol consumption, and the 'got drunk' frequency all increased over time. Risk-taking increased over the first three waves, but disinhibition and delay discounting showed no reliable changes over time.

Cross-lagged models

In the first model, we investigated the bidirectional relationships between disinhibition (inferred from stop-signal reaction time, SSRT), and alcohol involvement (see Figure 2a). The overall model fit was acceptable (CFI = .93, RMSEA = .06, TLI = .91, $\chi2$ / df = 1.96, $p < .01$), and the stability paths between the five waves for the latent alcohol involvement factor were high, indicating that alcohol involvement across the five measurements was very stable. Stability paths for disinhibition were significant across all waves, apart from between waves 3 and 4 (there was a trend towards significance, p = .07). Cross-sectional relationships between alcohol involvement and disinhibition were only significant at wave 1 and wave 5. Most importantly, cross-lagged paths from disinhibition to alcohol involvement six months later were all significant with the exception of disinhibition at wave 2 and alcohol involvement at wave 3, where the relationship fell short of significance (β =.01, p = .06). However, cross-lagged paths from alcohol involvement to disinhibition six months later were all non-significant. This suggests no prospective effects of alcohol involvement on disinhibition.

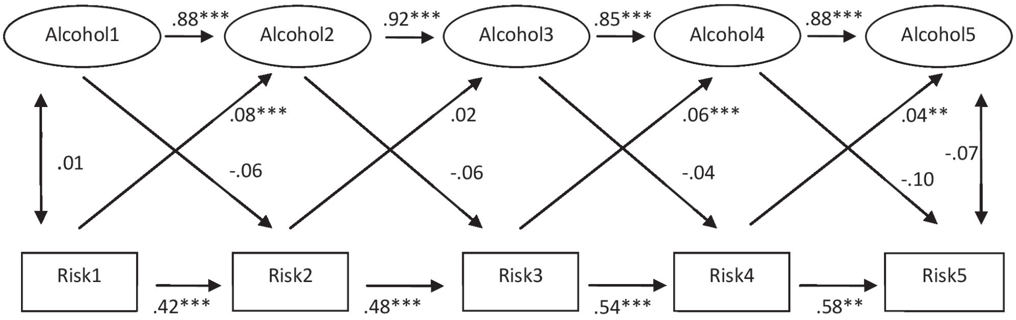
The analysis was repeated using risk-taking (based on the BART; Figure 2b) and delay discounting (Figure 2c). Model fit for risk-taking was acceptable (CFI = .91, RMSEA = .07, TLI = .88, $\chi2$ / df = 2.33, $p < .01$), although it was just below acceptable for delay discounting (CFI = .89, RMSEA = .08, TLI = .85, $\chi2$ / df = 2.77, $p < .01$). The stability paths for alcohol involvement, risk-taking and delay discounting were high. For both risk-taking and delay discounting, the cross-lagged paths from the impulsivity measure predicting alcohol involvement six months later were significant: risk-taking and delay discounting assessed at waves 1, 3 and 4 predicted alcohol involvement six months later. Neither risk-taking nor delay discounting at wave 2 predicted alcohol involvement at wave 3, the same pattern that was seen for the stop-signal task. Importantly, the reverse paths (cross-lagged paths from alcohol involvement to risk-taking

Figure 2a.



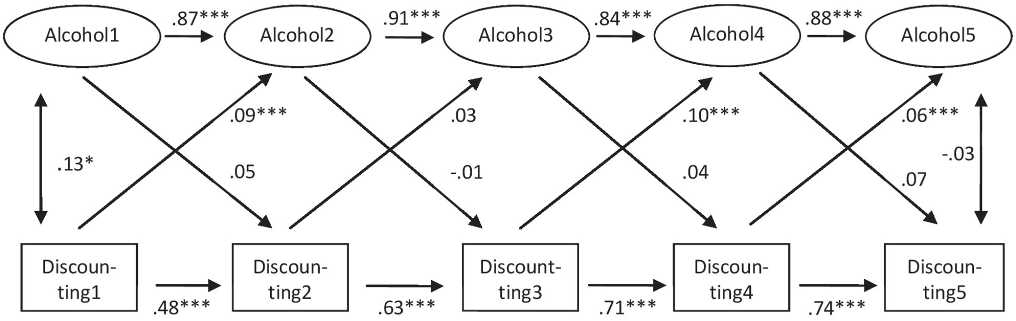
*CFI = .93, RMSEA = .06, TLI = .91, χ2 / df = 1.96, p < .01, * = p < .05, ** = p < .01, *** = p < .001*

Figure 2b.



*CFI = .91, RMSEA = .07, TLI = .88, χ2 / df = 2.33, p < .01, * = p < .05, ** = p < .01, *** = p < .001*

Figure 2c.



*CFI = .89, RMSEA = .08, TLI = .85, χ2 / df = 2.77, p < .01, * = p < .05, ** = p < .01, *** = p < .001*

Figure 2. Cross-lagged models showing the reciprocal relationships between alcohol involvement ('Alcohol') and disinhibition (a), risk-taking (b) and delay discounting (c). Cross-sectional correlations are only presented for the first and last session, other correlations were included in the model but not illustrated.

and delay discounting six months later) were all non-significant. As with the disinhibition data, we detected no prospective effects of alcohol involvement on risk-taking or delay discounting six months later.

Discussion

Our cross-lagged models indicated that individual differences in performance on three behavioural impulsivity tasks each predicted a composite index of alcohol involvement six months later. These prospective relationships were consistent, as they were evident at three of the four six-month intervals that we tested. However, we found no evidence for hypothesised alcohol-induced increases in behavioural impulsivity: individual differences in alcohol involvement did not predict subsequent impulsivity at any time point.

As hypothesised, individual differences in disinhibition (as assessed with the stop-signal task) at the baseline assessment predicted alcohol involvement six months later. This finding is consistent with previous reports (Nigg et al., 2006; Zucker et al., 2011) and to our knowledge it is the first demonstration of this relationship in an adolescent sample from outside North America. Equally important, our study is the first to demonstrate that delay discounting and risk-taking also predict alcohol involvement after fairly short-follow-up periods of six months. Although previous studies have demonstrated cross-sectional associations between alcohol involvement and delay discounting in adolescents (Field et al., 2007), no previous studies have investigated whether individual differences in delay discounting are associated with subsequent changes in alcohol consumption and problems, and so our study contributes important new data. Regarding risk-taking, a previous report (MacPherson et al., 2010) found that the rate of increase in risk-taking predicted a very small increase in the likelihood of alcohol involvement at subsequent assessment points (OR = 1.02), in a sample of adolescents who were slightly younger (9-12 years of age) than our own sample at the beginning of the study. Our results show that the absolute level of risk-taking predicted alcohol involvement only six months later, a relationship that was seen across multiple timepoints.

We did not detect any evidence of changes in behavioural impulsivity as a consequence of heavy drinking during adolescence. Our study was the first to directly investigate this issue, and this is an important finding. However, it is possible that a longer follow-up period, or a focus on adolescents ‘at risk’ for development of substance use disorders (Nigg et al., 2006) rather than a random sample as in the present study may have yielded a different outcome. On a related note, while the frequency of drinking alcohol increased over time, the majority of our participants were drinking infrequently even at the end of the study. These are limitations of our study and an important avenue for future research, but we highlight the high financial costs associated with conducting longitudinal research over such long periods of time. The model fit for our cross-lagged models were not exceptional (ideally, both CFI and TLI should be .95 or above, and RMSEA should be .05 or below). However, our fit indices can be described as acceptable (Kline, 2010). While our sample size was large, model fit may have been better with an even larger sample. In the delay discounting and risk-taking tasks, participants were responding for hypothetical rather than real financial rewards. We opted to use hypothetical rewards for ethical and practical reasons, and on the basis of previous studies that obtained comparable results from delay discounting tasks when real versus hypothetical rewards were used (Lagorio and Madden, 2003; MacKillop et al., 2011; Madden et al., 2004). In addition, other studies have shown that discounting rates for hypothetical monetary rewards are associated with alcohol use (Field et al., 2007) and addictive behaviors more generally (MacKillop et al., 2011). Regarding the BART, although no previous studies have directly contrasted risk-taking behavior when participants are responding for real versus hypothetical rewards, it is notable that risk-taking as measured by the BART is cross-sectionally associated with alcohol use regardless of whether hypothetical (Fernie et al., 2010) or real (Weafer et al., 2011) monetary rewards are used. However, one recent study suggests that the predictive validity of discounting tasks is superior when real rather than hypothetical rewards are used (Melanko and Larkin, 2013) and therefore it is important to replicate our findings using real financial rewards in the delay discounting and BART tasks.

Other limitations are our failure to record participant ethnicity, other drug use, and trait (self-reported) impulsivity, so we were unable to evaluate the relative importance of behavioural measures of impulsivity after controlling for these other variables. Finally, we note some strengths of our study: the dropout rate was low, as was the percentage of missing data, thereby ensuring a high level of statistical power for all of our primary analyses. No previous studies have tracked changes in performance on behavioural impulsivity tasks in relation to alcohol involvement over such an extended period of time, and we believe that the current study makes a very important contribution in this regard.

In summary, in the present study we explored bidirectional and longitudinal relationships between various indices of alcohol involvement and performance on behavioural impulsivity tasks. Across multiple time points we found that disinhibition, delay discounting and risk-taking predicted alcohol involvement only six months later. Importantly, we found no evidence to suggest that heavy drinking had an impact on performance on any of these behavioural measures.

5

Weaknesses in executive functioning predict the onset of adolescents' alcohol use.

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Submitted

Abstract

Recently, it has been suggested that impairments in executive functioning might be risk factors for the onset of alcohol use rather than a result of heavy alcohol use. To test this assumption, we examined whether two aspects of executive functioning, working memory and cognitive control, predicted the onset of drinking and binge drinking in young adolescents. Participants were 534 adolescents between 12-14 years at baseline. Executive functioning and alcohol use were assessed four times over a period of two years. Discrete survival analyses were used to evaluate the predictive effect of executive functioning on the onset of drinking and binge drinking. Working memory uniquely predicted the onset of both drinking and binge drinking while cognitive control only uniquely predicted the onset of drinking. These results suggest that the association of executive functioning and alcohol use found in former studies cannot simply be interpreted as an effect of alcohol use, as weaknesses in executive functions appear to precede the onset of drinking in adolescents.

Introduction

Recent studies have demonstrated associations between cognitive impairments and (heavy) drinking in adolescents (Fernie et al, 2013; Hanson et al., 2011; Khurana et al., 2012; Nigg et al., 2006; Squeglia et al., 2009; Tapert et al., 2002; Tarter et al., 2003). Especially binge drinking seems to be associated with cognitive impairments in adolescents and young adults (Hermens et al., 2013; Peeters et al., 2014a; Stephens and Duka, 2008). An important question that arises from these findings is whether these impairments are present prior to and predict the onset of drinking or whether the (heavy) use of alcohol induces these impairments. Although this relationship has been investigated in several studies (Fernie et al., 2013; Khurana et al., 2012; Squeglia et al., 2009; Tapert et al., 2002), none of these studies have included alcohol-naïve adolescents at baseline, which clearly limits the interpretation of the associations found. In the present study we therefore examined whether the relative weaknesses in executive functions predicted the initiation of alcohol use and the onset of binge drinking in young adolescents.

During adolescence several important cognitive functions mature and develop. Executive functions such as working memory and response inhibition, continue to mature until late adolescence (Blakemore and Choudhury, 2006). These functions are important for the planning, organization and coordination of other cognitive processes (e.g. cognitive control, Baddeley 1983; Miyake et al., 2000), and involve neural networks including different areas in the prefrontal cortex. In contrast to other brain regions (e.g. the visual cortex), the prefrontal cortex undergoes changes until late adolescence (Blakemore and Choudhury, 2006). It has been argued that the slower maturation of the prefrontal cortex, and the accompanying gradual development of cognitive control, might underlie the often observed increases in risky behaviors during adolescence, including binge drinking (Casey et al., 2008; Steinberg, 2007). A different line of research has suggested that the increase in risk-taking behavior is primarily a motivational issue (Crone and Dahl, 2012). It is more rewarding for adolescents than it is for adults to engage in risky behaviors (because of factors such as peer acceptance or popularity), which might explain the increased risk-taking behavior during adolescence (Crone and Dahl 2012). In this line of reasoning, the delayed development of the prefrontal cortex is not seen as immature functioning, but rather as more flexible functioning (for a detailed description see Crone and Dahl, 2012). Nevertheless, in both lines of research, cognitive control plays an important role in risk-taking behaviors. Namely, a lack of control has been associated with increased risk behavior in adolescence.

Regarding alcohol use, several longitudinal studies have suggested that relatively poor executive functioning predicts drinking behavior in adolescence. Nigg and colleagues (2006), for instance, found that poor inhibition skills in early adolescence (12-14 years) predicted later (15-17 years) problematic alcohol. Although not specifically found for alcohol use, Tarter and colleagues (2003) found that disinhibition at age 10-12 predicted substance use disorders at age 19 in boys (both in the high-risk and control group). Moreover, Khurana and colleagues (2012) found that relatively poor working memory predicted growth in the frequency of alcohol use in a community sample of adolescents. Moreover, the authors found that the effect of working memory on alcohol use was mediated by impulsivity suggesting that poor working memory functioning might increase impulsive behavior which subsequently increases alcohol use among adolescents. In addition, Fernie and colleagues (2013) found that several measures of impulsivity (i.e. delay discounting, risk-taking and response inhibition) predicted increase in alcohol use among young adolescents (12-13 years). The question remains, however, whether these impairments precede and predict the onset of adolescents' drinking, since previous studies have examined executive functioning after adolescents already consumed their first drink thus leaving open the possibility that the impaired executive functioning was already the result of earlier drinking.

In the present study we examined the predictive effect of two executive functions, namely working memory and cognitive control, on the onset of drinking in a sample of young adolescents (12-15 years, before the legal age for alcohol buying of 16 – in the Netherlands). Binge drinking is a common drinking pattern among young adolescents, and it has been linked to several (health) risk behaviors (Miller et al., 2007). We therefore also examined the predictive effect of executive functioning on the onset of binge drinking (i.e. five or more glasses on one day). We hypothesized that relatively weak working memory and cognitive control would predict the onset of both drinking and binge drinking in this sample. Although cognition involves many more aspects than executive functions, we decided to focus on these two cognitions, since particularly these functions are assumed to play a vital role in adolescent alcohol use as they continue to mature in adolescence (Verdejo-Garcia et al., 2008). Discrete-time survival analyses was used to determine the onset of drinking and binge drinking during the two year follow-up of the study and to evaluate the predictive effect of executive functioning.

Methods

Participants.

Participants were recruited from several mainstream and special education (SE) schools in the Netherlands, to ascertain variation in drinking behavior of participants. Adolescents in SE schools have been found to drink more heavily (Kepper et al., 2011) compared to adolescents from mainstream education. Adolescents attend these SE schools when they have behavioral problems (e.g. conduct problems, hyperactivity, attention problems), although they may not necessarily be diagnosed with a behavioral disorder. Males were slightly overrepresented (69% boys versus 31% girls) because more boys than girls attend SE schools (Oswald et al, 2003). For both samples, passive parental consent of parents was requested. In the mainstream sample, 37 parents declined participation of their child. For the SE sample, 15 parents and 7 students declined participation in this study. The original mainstream sample included 250 adolescents (78 boys, 172 girls), selected from a national survey study, which was part of the international Health Behavior of School-aged Children-survey (HBSC, Currie et al,. 2012). Adolescents who participated in the Dutch national study were contacted for additional assessments after the completion of the main survey. The SE sample included 374 adolescents (336 boys, 45 girls). For the purpose of this study, adolescents between 12-15 years were selected, resulting in a sample of 534 (371 boys, 163 girls) adolescents.

Data were collected at intervals of 6 to 8 months across four waves. At baseline, 525 adolescents participated in the study (98% of 534, note that some adolescents were absent during the first wave but participated in the following waves). Overall, 415 (78%) adolescents participated in wave 2, 399 (75%) adolescents participated in wave 3, and 425 (80%) adolescents participated in wave 4. Missing cases were imputed using a multiple imputation program (i.e., multiple imputation by chained equations (MICE), which is explained below). The data over four waves were collected either via the Internet (in the case of mainstream education) or via a trained research assistant (in the case of SE education). Adolescents from SE completed the questionnaire with pen and paper followed by a computer session to assess the computer tasks. Five of the SE students completed only the computer tasks at baseline and did not complete the questionnaire. Since we used multiple imputation to handle missing cases, we included these adolescents in the study for further analysis.

Measures.

Alcohol use. To determine the onset of drinking and binge drinking (five or more glasses on one day), we asked participants to indicate, for weekend and weekdays separately, the number of glasses they consumed on any single day. For the purpose of the survival analysis, this continuous measure was recoded as dichotomous variable. The onset of alcohol was defined as drinking at least one glass per day. Binge drinking was defined as consuming five or more glasses on one day. Participants received either a "one" or a "zero" on both variables, which served as an indicator of the occurrence of the event (i.e., onset or binge).

Working memory. Working memory performance was assessed with the Self Ordered Pointing Task (SOPT; Petrides and Milner, 1982). Participants completed a concrete version of the SOPT. Pictures were presented on a screen, starting with a practice trial of 4 pictures followed by four trials with 6, 8, 10, and 12 pictures, respectively. Participants were asked to select each picture once but not to select pictures that were not located at the same place as the previous picture. After they selected a picture, the order and placing of pictures changed. Adolescents were encouraged to complete the task without any errors. Irrespective of the errors made, all participants received the feedback "well done" after each trial. With respect to the second instruction, the task was programmed not to allow selecting the same location twice in a row. For each test trial, a proportional error score was computed by dividing the number of correct responses by the number of total pictures within each trial to account for task difficulty (Cragg and Nation, 2007). The total SOPT score was calculated by taking the mean of the proportion of correct scores of the four trials. Higher scores indicated better working memory functioning.

Cognitive control. Cognitive control was assessed using the Stroop task (Stroop, 1935). The Stroop task, as a measure of cognitive control, has been used successfully in previous studies (Houben and Wiers, 2009; Peeters et al., 2012). Participants were instructed to indicate the color of the word (i.e., red, green, blue, or yellow) that appeared on the screen by pressing the corresponding key on the keyboard while ignoring the meaning of the word. Participants started with a practice block, which consisted of forty trials with symbols (e.g. @@@@ or &&&&). The practice block was followed by a test block with twenty-eight trials. Trials could be congruent (i.e., meaning of the word matches the color), neutral (i.e., colored symbols instead of words), or incongruent (i.e., meaning of the word differs from the color), and they were presented in random order between participants. Each trial was repeated until a correct answer was given. An error message, including a description of the keys used and their corresponding color, followed an incorrect response. A cognitive control score was calculated by subtracting the reaction times (RT's) on neutral trials from the RT's on incongruent trials, with higher RT's indicating more problems with control. For analytical purposes, RT's were divided by 1000.

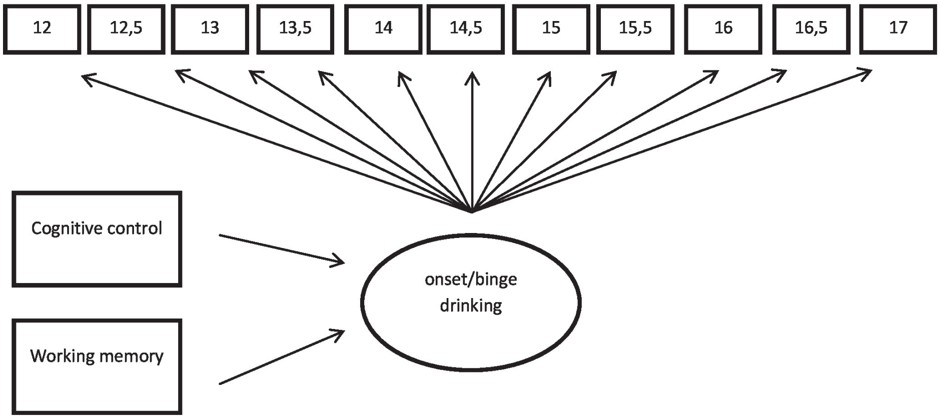
Missing data.

Because we wanted to determine whether a participant initiated drinking and/or binge drinking during study follow-up, it was necessary to have a data set that was as complete as possible. Missing data, especially when it involves a risk factor or event, is particularly problematic in survival analyses (Van Buuren et al., 1999). Multiple imputation (MI) is a commonly used method to handle missing data. Previous results indicated that MI is a reliable and valid method (Sterne et al., 2009). However, to check whether this was also the case for the present sample, a sensitivity analysis was performed (performed on the high-risk sample, which had the largest number of missing data, paper submitted for publication). To determine the best method to handle the missing data, several options were compared, including listwise deletion, manual fill in methods (e.g. looking at previous or subsequent wave/ looking at majority/ filling in zero's at each missing), and MI. The results revealed that multiple imputation was the optimal method to handle the missing data in the current study. We used the program MICE (R-package in R) to create 5 different imputation files, which were transported to Mplus version 7 (Muthen and Muthen, 1998-2012) for survival analyses. MICE replaces the missing information with plausible values by both minimizing the uncertainty and the bias of the model (Van Buuren et al., 1999). Plausible values are imputed based on carefully chosen confounding variables that serve as predictors of the missing values. For the present study, we checked correlation matrices to determine the variables that should be used to predict missing data. Both covariates and the outcome measure were included in the imputation model, as recommended by the developers (van Buuren and Oudshoorn, 2000). For the binary variables, we chose the logistic regression method. For all other continuous covariates, we used the predictive mean matching method. Lifetime alcohol use, daily smoking, drug use (cannabis, ecstasy, cocaine, hallucinogens), gender, age, and personality (impulsivity, sensation seeking, anxiety, and hopelessness) were selected as predictors of missingness.

Analytical procedure.

First, descriptive statistics for executive functioning were presented for the total sample and for the onset group and the binge group separately. Second, the five imputed data files were prepared for discrete-time survival analysis. Since the aim of the study was to examine executive functioning as risk factor of alcohol onset, we excluded all adolescents who already consumed alcohol at baseline (for the onset sample) and all adolescents who already engaged in binge drinking at baseline (for the binge sample)[1]. For each adolescent, the age of the onset and the age of the first binge drinking episode were assessed every half a year (e.g. 12, 12.5, 13…..17), resulting in 11 possible time points at which the event could have occurred (see Figure 1). Using Mplus for the discrete-survival analysis, a latent factor of the probability that an individual would experience the event at a certain time point (i.e. age) was estimated. Next, the hypothesized predictors (i.e., working memory and cognitive control) of the occurrence of the event (i.e., onset/binge) were selected for the analysis. Survival analyses were conducted using Mplus version 7 (Muthen and Muthen, 1998-2012). Maximum likelihood with robust standard errors (MLR) was used as estimator.

Figure 1. Structural survival model with age indicators (12 -17 years) and predictors (i.e. cognitive control and working memory) of onset and binge drinking.



[1]We used t-tests to examine whether possible differences in executive functioning emerged between the group who already engaged in drinking at baseline (excluded from the study) compared to alcohol naïve adolescents at baseline (included in the study). Significant differences on executive functioning at baseline emerged between the two groups with lower scores for working memory and higher scores for response inhibition indicating relatively weaker executive functioning for the drinkers (working memory: t = 3.26, p = .01; cognitive control: t = -2.36, p =.02).

Results

Descriptives

Table 1 includes descriptive statistics of age and executive functioning at baseline for the total sample and the two analytical samples (i.e. onset and binge drinking) separately. There are no notable difference between the descriptive statistics of the three samples.

Prediction of onset and binge drinking

Table 2 shows the results of the survival analysis with working memory and cognitive control as predictors of the onset of drinking and binge drinking[2]. Both executive functions were analyzed in a multivariate model to examine the unique influence of each function on the onset of drinking and binge drinking. Both working memory and cognitive control uniquely predicted the onset of drinking behavior. Weaker working memory (β = - .51, OR = 0.15, p = .01) and poorer cognitive control (β = .80, OR = 3.12, p = .01, higher scores indicate poorer cognitive control) increased the likelihood that adolescents would initiate drinking during study follow-up. Working memory, but not cognitive control predicted the onset of binge drinking. Lower scores on working memory (β = -0.08, OR = 0.33, p = .01) increased the likelihood that adolescents would initiate binge drinking during study follow-up.

Table 1. Descriptive statistics for the total sample, the onset sample and the binge drinking sample.

	Total (N = 534)		Onset (N = 336)		Binge (N = 458)	
	M	SD	M	SD	M	SD
Age baseline	13.75	.76	13.69	.77	13.73	.78
Alcohol use	2.19	6.45	0	0	.35	.83
Cognitive control	.16	.32	.15	.29	.16	.31
Working memory	.75	.11	.75	.15	.76	.11

[2]The factor loading assessing the probability that the event would occur (see figure 1 onset/binge) were fixed at one (see figure 1 age indicators) to assume that the effect of executive functioning on the onset of alcohol use/binge drinking was the same for each age. Residual variances were fixed at zero (Muthen and Muthen, 1998-2012)

Table 2. Odd's ratio's and standardized regression coefficients for cognitive control and working memory predicting onset of drinking and binge drinking.

	Onset (N = 336)			Binge (N = 458)		
	Odds	β	p	Odds	β	p
Cognitive control	3.12	.80	.01	1.22	.37	.53
Working memory	0.15	-.51	.01	0.33	-.08	.01

Discussion

The present study was one of the first to examine the predictive effect of executive functioning on the onset of drinking and binge drinking among young adolescents. The results indicated that relatively weak working memory predicted both the onset of drinking and the onset of binge drinking beyond the effect of cognitive control. In addition, relatively poor cognitive control predicted the onset of drinking beyond the effect of working memory but did not predict the onset of binge drinking.

The findings of this study are in agreement with those of Khurana and colleagues (2012) who found that executive functioning, and more specifically working memory, predicted increase in frequency of drinking among young adolescents. Fernie and colleagues (2012) found similar results, revealing that response inhibition (and two other measures of impulsivity) predicted alcohol use six months later. Nigg and colleagues (2006) found that executive functioning predicted problem drinking behavior in high risk adolescents (adolescents from alcoholic families). Poor response inhibition at age 12-14 predicted the onset of alcohol related problems at age 15-17. However, unlike Nigg et al. (2006), we did not find a predictive effect of cognitive control on binge drinking. A different sample of adolescents, a different task, a different outcome variable and a different analysis technique were used in the current study, which might explain the divergent results. Khurana and colleagues (2012) found that impulsivity fully mediated the effect of working memory on the drinking behavior of adolescents, suggesting that weaknesses in working memory affect behavior through disinhibition and impulsivity. Contrary to what Khurana and colleagues (2012) found, the results of the present study indicated that at least two executive functions uniquely contributed to the prediction of the onset of drinking behavior. In addition, in the present study, working memory was a unique predictor of binge drinking in adolescents while disinhibition was not. The latter finding is in agreement with several studies that have found associations between binge drinking and working memory functioning (Crego et al., 2009; Squeglia et al., 2011; Stephens and Duka., 2008). However, these cross-sectional studies (Crego et al., 2009; Squeglia et al., 2011) do not shed light on the direction of the relation. Although the results of the present study do not rule out a reverse effect of alcohol use on impairments in cognitive functioning (Tapert et al., 2002; Squeglia et al., 2009), the results do reveal that some weaknesses in executive functioning precede the onset of drinking behavior. The continued use of alcohol may aggravate the pre-existing impairments (Khurana et al., 2012; Peeters et al., 2014a), causing delay in development or even decline in the performance on executive functioning tasks.

Besides the strengths of the study, such as the large sample size of young adolescents and the inclusion of a high-risk sample, some limitations should be considered. Although the exact same measures with the same instructions were used in the two different samples (mainstream and SE education), the assessment procedure was slightly different. Adolescents in the high-risk sample completed tasks under the guidance of a research assistant while adolescents in the mainstream sample completed assessment at home (i.e., online assessment). Nevertheless, recent studies have suggested that online assessment is a reliable method (Houben and Wiers, 2008). In addition, multiple imputation has been criticized as method of handling missing data because it could add noise to the data (Rubin, 1996). This critique has lost its value because recent sophisticated imputation methods are able to handle missing data better compared to older methods, such as list wise deletion (Rubin, 1996; Sterne et al., 2009). In addition, the sensitivity analysis in the present study supported this critique. Moreover, in the present study binge drinking was defined as drinking 5 or more glasses on one day. Generally, binge drinking refers to drinking five or more glasses at one occasion (Wechsler and Nelson, 2001). However, it seems unlikely that adolescents of this age (12-16 years) regularly have the opportunity to drink in the afternoon as well as in the evening on weekend days. Moreover, binge drinkers consumed on average almost 9 glasses on one day, which can be interpreted as heavy drinking for such young adolescents. Nevertheless, it is possible that some of the adolescent binge drinkers in this study did not consume all five glasses in a row or at one occasion. Finally, we only found an effect of working memory on binge drinking. It is possible that the Stroop task used in this sample to asses cognitive control was less sensitive in detecting differences compared to the working memory task, perhaps explaining why we did not find an unique effect of cognitive control on the onset of binge drinking.

Despite these limitations, the findings of this study demonstrate that the pre-existing impairments in executive functioning predict the onset of drinking and binge drinking among young adolescents. The results suggest that relatively weak working memory and disinhibition are risk factors for the early onset of drinking. Moreover, weak working memory functioning is a risk factor for binge drinking. A continued heavy drinking pattern might further worsen the executive functions (Squeglia et al., 2009; Tapert et al., 2002), beyond these pre-existing effects. In addition, it has been demonstrated that these executive functions moderate the effect of implicit cognitive motivational processes on alcohol and substance use in adolescence (Grenard et al., 2008; Peeters et al., 2012, 2013; Thush et al., 2008). As these processes get stronger with increased drinking, delay of the onset of drinking appears to be a good general strategy to prevent problematic alcohol use in adolescents (Koning et al., 2009; Koning et al., 2011). As some adolescents appear to be at a greater risk for an early onset of drinking, additional targeted prevention might be warranted as well (cf. Conrad et al., 2008). Recently several promising interventions have been introduced to increase executive control in adolescents and young adults (Houben et al., 2011a; Klingberg et al., 2005). These training methods contribute to an increase in executive control, and they might eventually postpone the age of the onset and prevent further escalation of alcohol use in young adolescents.

Automatic processes in at-risk adolescents: The role of alcohol-approach tendencies and response inhibition in drinking behavior.

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Abstract

This study examined the association between automatic processes and drinking behavior in young adolescents who just started drinking, in relation to individual differences in response inhibition. It was hypothesized that strong automatic behavioral tendencies toward alcohol-related stimuli (alcohol-approach bias) were associated with higher levels of alcohol use, especially among adolescents with relatively weak inhibition skills. To test this hypothesis structural equation analyses (SEM) were performed, using a zero inflated Poisson (ZIP) model. A well-known problem in studying risk behavior, is the low incidence rate resulting in a zero dominated distribution. A ZIP-model accounts for non-normality of the data. Adolescents were selected from secondary Special Education schools (a risk group for the development of substance use problems). Participants were 374 adolescents (mean age of M = 13.6 years). Adolescents completed the alcohol Approach Avoidance Task (a-AAT), the Stroop Color Naming Task (Stroop) and a questionnaire that assessed alcohol use. The ZIP-model established stronger alcohol-approach tendencies for adolescent drinkers ($p < 0.01$) and the interaction revealed a stronger effect of alcohol-approach tendencies on alcohol use in the absence of good inhibition skills ($p < 0.05$). Automatically activated cognitive processes are associated with the drinking behavior of young at-risk adolescents. It appears that alcohol-approach tendencies are formed shortly after initiating of drinking and particularly affect the drinking behavior of adolescents with relatively weak inhibition skills. Implications for prevention of problem-drinking in adolescents are discussed.

Introduction

Dual process models have recently been applied to specific outcome behaviors (e.g. behavioral attitudes (Kahneman, 2003), judgments (Olson and Fazio, 2004), including the development of addictive behaviors (Wiers et al., 2007). According to the general class of dual process models, specific behaviors such as alcohol use are the joint outcome of two qualitatively different information processing streams, namely reflective and impulsive processing (Deutsch & Strack, 2006; Wiers et al., 2010a). Reflective processing is relatively slow, and results in intended behavior. Behavioral options are evaluated and assessed for their effectiveness. Impulsive processing, in contrast, is fast and elicits behavioral response-tendencies (Strack and Deutsch, 2004; Wiers et al., 2007). Depending on the response time and the value attached to the behavioral outcome, either a “reflective” or “impulsive” behavioral response wins (Gladwin et al., 2011). With respect to addictive behavior, it has been argued that an automatically activated motivational orientation toward stimuli associated with the addictive behavior plays an important role (Wiers et al., 2007). Moreover, the impact of this “approach bias” may become stronger as addictive behavior develops in adolescence, as a result of the negative impact of the substance on the developing executive control functions (Casey et al., 2010; Gladwin et al., 2011; Wiers et al., 2007). Associations between alcohol and outcome behavior (e.g. drinking beer and feeling happy) form the basis for automatic processes and automatically guide behavior (Stacy, 1997). Recent studies on alcohol use in adults and adolescents confirm the relationship between alcohol use and alcohol associations (Field et al., 2008a; Grenard et al., 2008; Palfai and Ostafin, 2003; Wiers et al., 2009a). Strong alcohol-associations are related to more alcohol use (Grenard et al., 2008; Palfai and Ostafin, 2003) and it may therefore be of interest to gain insight in the relationship between automatic processes and (problematic) alcohol use in adolescence.

Response inhibition

With respect to reflective processing it is important that behavioral options are kept active and inappropriate automatic responses are inhibited, two important executive functions. It is assumed that executive functions play an important role in addictive behavior and perhaps even more in adolescence as these functions are not yet fully developed (Casey et al., 2010;

Gladwin et al., 2011; Wiers et al., 2007). Deficits in behavior regulation for instance, are associated with substance use and alcohol dependence (Sher et al., 2000; Sher et al., 1994). Individuals with relatively weak inhibition skills tend to have a bias toward automatic information processing (Gladwin et al., 2011).

Recent studies suggest that the influence of automatic processes on alcohol use is moderated by the level of executive functioning (Grenard et al., 2008; Thush et al., 2008). Other studies reported similar results for sexual interest, eating (Hofmann et al., 2008a; Hofmann et al., 2009) and aggressive behavior after alcohol use (Wiers et al., 2009b). The influence of automatic processes on behavior will be less dominant in individuals who are able to regulate behavior and inhibit automatic responses, compared to those who have problems with inhibition (Wiers et al., 2010a). Therefore, it is assumed that automatic processes have more influence on behavior in individuals with weaker inhibition skills.

Automatic approach tendencies

Automatically activated approach and avoidance tendencies are examples of automatic processes that precede behavioral responses (Rinck and Becker, 2007). The impulsive system automatically inclines to either approach or avoidance behavior, in response to environmental stimuli (Strack and Deutsch, 2004). Robinson and Berridge (2008, 1993) differentiate between two neural systems that mediate appetitive behavior: “liking” and “wanting”. While these processes normally work in concert, in addictive behaviors, classically conditioned stimuli signaling the drug of abuse trigger a “wanting” response, which may persist even in the absence of “liking”. At a behavioral level, this reaction has been associated with an attentional bias for the substance and a tendency to approach the substance. For instance, in heavy alcohol-users, attention is automatically guided to alcohol cues (Field et al., 2008a) and these alcohol-cues automatically elicit approach behavior (Cousijn et al., 2011).

Studies using a variety of experimental psychological methods have found that relatively weak avoidance motivation is associated with drinking problems (Palfai and Ostafin, 2003). Alcohol stimuli evoke automatic approach tendencies in heavy but not in light drinkers (Field et al., 2008a). Similar results were found for other substances, for example, heavy cannabis use was associated with an automatic approach bias, and this bias predicted escalation of use in problematic users (Cousijn et al., 2011). These results indicate that substance use is associated with an automatic motivational orientation toward stimuli associated with the substance. These effects appear to be moderated by executive functions. Grenard and colleagues (2008) found that substance-associations predicted alcohol and cigarette use, most strongly among at-risk adolescents with lower working memory capacity. Similarly, in a Dutch at-risk sample, it was found that automatic associations predicted alcohol use in adolescents with relatively weak working memory (Thush et al., 2008).

Unlike other studies on alcohol use and automatic processes in at-risk adolescents (Grenard et al., 2008; Thush et al., 2008) we used the alcohol approach avoidance task (a-AAT) (Wiers et al., 2009a) to measure the strength of the automatic alcohol-approach bias. This task has successfully been used in previous studies (Cousijn et al., 2011; Wiers et al., 2009a). Compared to other tasks which assess automatic approach tendencies (e.g. the so called Stimulus Response Compatability –SRC- (Field et al., 2008a) and the Implicit Association Task –IAT- (Palfai and Ostafin, 2003), the AAT differs in the attention given to the relevant parts of the task (Cousijn et al., 2011). Because participants receive the instruction to respond to the shape of the stimuli, which is an irrelevant feature of the task, instead of the content of the stimuli (alcohol versus soft-drink) it should result in a more pure assessment of the relevant automatic processes than a task with explicit categorization of the relevant stimuli, as is the case in the SRC and IAT (De Houwer, 2003).

The present study

The current study examines the role of dual process models in drinking behavior of young adolescents who are as a group at risk for developing problem drinking. The adolescents in the risk group were characterized by externalizing behavior problems (ADHD/conduct disorders), behavioral problems that have been associated with binge drinking, early use of alcohol (Slutske et al., 1998) and alcohol dependence (Chassin et al., 2002). The adolescents in this study are at risk for early alcohol use (onset age weakly use; M = 13.1, SD = 1.1) (Kepper et al., 2011) which has been associated with later problem drinking and alcohol disorders (De Wit et al., 2000). It could be very meaningful to get a better understanding of the processes that reinforce drinking behavior of young adolescents, particularly in this group of adolescents since they are at risk for problem drinking.

We hypothesized, in line with adults studies (Field et al., 2005; Palfai and Ostafin, 2003), that strong automatic approach tendencies are associated with more alcohol use. We assumed a moderating effect of response inhibition, with particularly strong influences of approach tendencies on alcohol use when adolescents had relative weak inhibition skills, in line with studies in young adults (Houben and Wiers, 2009) and at-risk adolescents when working memory capacity was the moderator (Grenard et al., 2008; Thush et al., 2008).

Methods

Participants

Participants were 374 students (330 boys, 44 girls) from seventeen secondary Special Education schools in the Netherlands with a mean age of M =13.6 years (SD =0.9). Similar to the population of special education (75% boys) (Oswald et al., 2003), males were overrepresented in this sample (88% boys). In accordance with Dutch ethical standards, the voluntary nature of participation was explained, anonymity was ensured and passive parental permission was obtained through an informative letter about the purpose of the study. In total, fifteen parents (3.8%) did not give their permission. During data collection seven adolescents (1.7%) declared that they did not want to participate in the study.

Adolescents were asked to fill out a questionnaire and complete some computer tasks. Due to illness or absence, 21 adolescents (6,1%) participated only in one part of the study. Four participants were excluded from analysis since they had an incomplete Stroop or AAT task. In total 25 participants (6,7%) were excluded from analysis, resulting in a sample of 349 participants with complete data.

Measures

Alcohol use and problem drinking. Participants were asked to indicate on a 14-item rating scale (never, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10-times, and three ratings consisting of aggregate scores; 11-19, 21-39, 40-times or more”) on how many occasions in the last year they had consumed alcohol. Additionally, participants were asked to report the drinking days during the week (Monday till Thursday) and weekend (Friday till Sunday) and the average alcoholic drinks consumed on weekdays and weekends. Responses could range from zero glasses to 20 glasses or more (Koning et al., 2009). A continuous score for alcohol use was computed by multiplying drinking days by alcoholic drinks. Requested glasses were standard glasses of alcohol containing approximately 12.5 ml alcohol. Problem drinking was assessed with the CRAFFT (Knight et al., 1999). The scale includes six items with a "yes" or "no" response option (e.g. "Do you drink alcohol when you are by yourself"?). A cutoff score of two or more "yes" responses has been used in clinical settings to establish alcohol abuse and dependence among adolescents (Cook et al., 2005). In this study we applied this screening instrument for establishing a continuous score for problem drinking. The internal consistency of the scale was acceptable (Cronbach's Alpha = .74). We used a frequency and quantity measure and a measure for problem drinking to assess different dimensions of alcohol use. To test whether there was an underlying latent factor with respect to the alcohol measures we first applied a confirmatory factor analysis (CFA) using Mplus version 6.0 (Muthen and Muthen, 1998-2010). The analysis revealed significant factor loadings for all three indicators (alcohol use last year: .76 (R^2 = .57), alcoholic drinks during the week: .76 (R^2 = .57), problem drinking: .75 (R^2 = .56)), confirming that we could use this factor for further analysis.

Stroop Colour-Word Task. The Stroop Task (Macleod, 1991; Stroop, 1935) was used to assess response inhibition (Houben and Wiers, 2009). Participants started with a practice block consisting of 40 trials with symbols to learn the colour with the corresponding key (e.g. @@@, &&&), followed by a test block with 12 neutral (i.e. colored symbols instead of words) 4 congruent (i.e. meaning of the word matches the color) and 12 incongruent trials (i.e. meaning of the word differs from the color) in random order. An error penalty was estimated by adding the response time for an incorrect response to the RT of the correct response. An inhibition score was computed by subtracting the mean scores of the neutral trials from the mean scores of the incongruent trials, with higher scores indicating more problems with inhibition. The test-retest reliability of the task was acceptable (r = .73).

Approach Avoidance Task (AAT). The alcohol-AAT (Wiers et al., 2009a) was used to assess the alcohol-approach bias. Depending on the condition, participants were instructed to respond with a push or pull response to a certain type of picture, by using the arrows on the keyboard (arrow up for pushing the picture, arrow down for pulling the picture). Contingent upon a pull or push movement the picture zoomed out (became larger on the screen) or zoomed in (became smaller on the screen, (Cousijn et al., 2011; Wiers et al., 2009a). Participants were asked to respond as quickly as possible and press the correct arrow three times so that the picture would disappear. Half of the participants received the instruction to pull the picture when it was left rotated (i.e. 3°); others when it was right rotated (i.e. 3°) (Cousijn et al., 2011). No preference effect of condition was found. The total task included 80 trials in which pictures of alcoholic drinks (i.e. twenty pictures) or soft drinks (i.e. twenty pictures) appeared. Each stimulus was presented twice (in random order), once left and once right rotated. An incorrect response was followed by a red "X" and an instruction for the correct response. Median instead of mean scores were used to minimize the influence of outliers. By doing so, it is unnecessary to define a cutoff point for extreme values. (Rinck and Beckers, 2007; Wiers et al., 2009b; Wiers et al., 2010b). The difference in reaction time between alcohol push minus alcohol pull was measured, with positive scores indicating a faster approach for alcohol stimuli. The test-retest showed acceptable levels of reliability (r = .60). Both the AAT and the Stroop trials were measured in millisecond which resulted in large variances. For analytical purpose, RT's were divided by 1000.

Table 1. Means and standard deviations for the whole sample (N = 349) and means, standard deviations and Pearson correlations for drinkers (N = 188) and self-reported non-drinkers (N = 161).

	Whole sample (N = 349)	Drinkers (N = 188)	Self-reported non-drinkers (N = 161)				
	M (SD)	M (SD)	M (SD)	1	2	3	4
1. Alcohol last year	4.69 (9.15)	8.28 (10.80)	-				
2. Drinks a week	3.28 (7.85)	5.90 (9.86)	-	.50**			
3. Problem drinking	0.83 (1.34)	1.47 (1.47)	-	.41**	.45**		
4. Approach bias	0.03 (0.30)	0.05 (0.30)	0.00 (0.29)	.18*	.15*	.12	
5. Response inhibition	0.21 (0.35)	0.22 (0.35)	0.19 (0.36)	.05	.06	.08	.01

Drinkers have a score of one or more on one of the three alcohol indicators. Self-reported non-drinker have zero scores on all three alcohol indicators.

** p < .05, * * p < .01.*

Strategy for analysis

First, descriptions of the sample and Pearson correlations are provided. Second, the main effects and the interaction effect of automatic approach tendencies and response inhibition are discussed. Given that a considerable part (46%) of our participants has never consumed alcohol, results are dominated by zero values. A Poisson analyses accounts for zero counts, however in the case of overdispersion (variance is larger than the mean), standard errors are underestimated (Böhning et al., 1997). In this study the variances of the indicators exceeded the mean, therefore we applied a Zero Inflated Poisson model (ZIP) (Lui and Powers, 2007). ZIP-regression is an efficient statistical approach to deal with non-normal count data with an excess of zero counts. The model uses two subpopulations (Lambert, 1992; Pardini et al., 2007); one subpopulation, the non-drinkers, who solely produce zero observations (structural zeros), another subpopulation, the drinkers, producing observations in a certain range including zero (sampling zeros). Some drinkers may produce zero counts, since they may not have consumed alcohol last year, while not belonging to the non-drinkers. An analogy may explain the procedure: suppose there a two groups, the first group went fishing, the second group did not. Both groups failed to catch fish, nevertheless, the first group could have caught fish, while the latter group would certainly score zero. The ZIP-regression distinguishes these groups by using two distributions and combining the two components (binary model); (1) a component consisting of "certain zero's" which produces a logistic coefficient (an odds ratio indicating the chance of being non-drinker), and (2) a component consisting of (possible) drinkers producing a regression coefficient. Both drinkers and non-drinkers are included in the analysis, however the use of a binary model controls for the influence of zero score's.

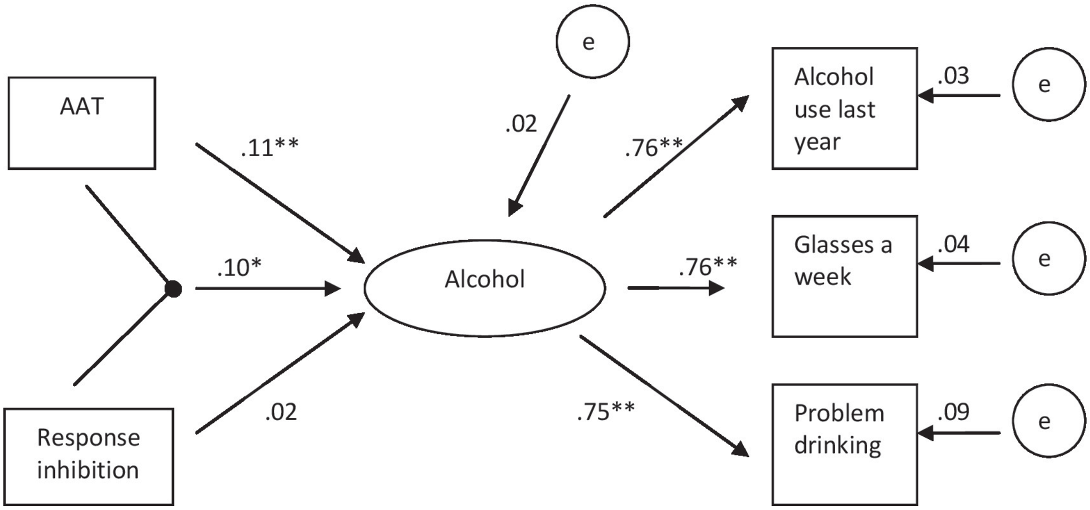
The ZIP-model was estimated with Mplus version 6.0 (Muthen and Muthen, 1998-2010) using the maximum likelihood with robust standard errors as estimation method and full information maximum likelihood (FIML) regarding missing values. Participants were nested within schools, therefore we corrected for clustering effects.

Results

Descriptives for the whole sample, the non-drinkers and descriptives and Pearson correlations for the drinkers are presented in Table 1. Since we used a latent factor with three zero inflated indicators, it was difficult to determine the mean scores for drinkers and non-drinkers on the three indicators separately. For descriptive purpose only, we identified adolescent as non-drinkers (zero on all three measures) and as drinkers (score of one or more on one of the three measures). Notable is the non-significant difference between drinkers and non-drinkers on the approach avoidance task (Cohens' d = 0.17; one-tailed t-test; t = 1.42, df = 335, p = .08). It may be that the non-drinking sample includes adolescents who actually consumed alcohol but reported not having consumed alcohol. The non-significant mean difference might be biased because the non-drinkers sample includes both true non-drinkers and latent drinkers. ZIP-regression compensates for this and the following section summarizes the results of this ZIP-analysis.

Main effects of automatic approach tendencies and response inhibition on alcohol use were analyzed. A SEM analysis (N = 349) revealed a significant main effect of automatic approach tendencies on alcohol use (β = 0.16, p < 0.01). Stronger approach tendencies were associated with more alcohol use. No significant main effect of response inhibition on alcohol use was found (β = 0.07, p = 0.10).

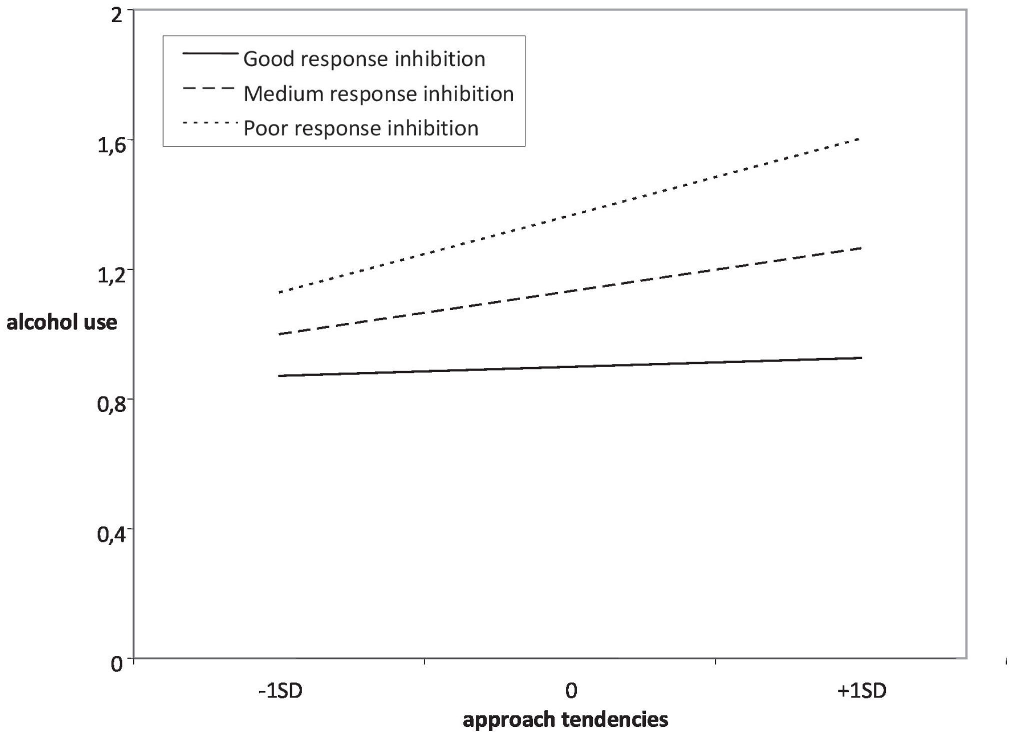
Figure 1. Model with standardized factor loadings for alcohol and standardized path coefficients for automatic approach tendencies (AAT), response inhibition and the interaction between AAT and response inhibition (N= 349).



** p < .05, * * p < .01.*

In the next step, response inhibition was included as moderator. Approach tendencies and response inhibition were both centered. The results of the ZIP-model, including the results of the confirmatory factor analysis of alcohol, and the interaction effect (β = 0.10, $p < 0.05$) are presented in Figure 1. A visual representation of this interaction effect is presented in Figure 2. Figure 2 shows that as response inhibition decreases, the influence of alcohol-approach tendencies on alcohol use becomes stronger, indicated by the rising dashed line for medium skills, and the strongest effect for the dotted line representing adolescents with the weakest inhibition skills.

Figure 2. Interaction of response inhibition on the association between alcohol use and approach tendencies (N = 349).



Discussion

Results of this study indicate that automatic alcohol-approach tendencies are already present among adolescent drinkers who just started drinking (mean difference in age of onset/current age = 5 months) and are at risk for the development of alcohol-related problems at the group-level. Results supported the hypothesis: Automatic approach tendencies were stronger for at-risk adolescents who drink more alcohol, particularly when inhibition skills were relatively weak.

Results of the current study are in line with previous studies on the role of dual-processes in adolescents and young adults, which indicate that relatively poor inhibition skills (Houben and Wiers, 2009), and more generally, relatively weak executive functioning (Grenard et al., 2008) increase the influence of automatic processes on responses such as alcohol use. The ability to overcome automatically triggered response-tendencies is less well-developed in individuals with relatively poor inhibition skills (Wiers et al., 2010a) and relatively weaker executive functioning (Grenard et al., 2008; Hofman et al., 2008a; Hofmann et al., 2008b).

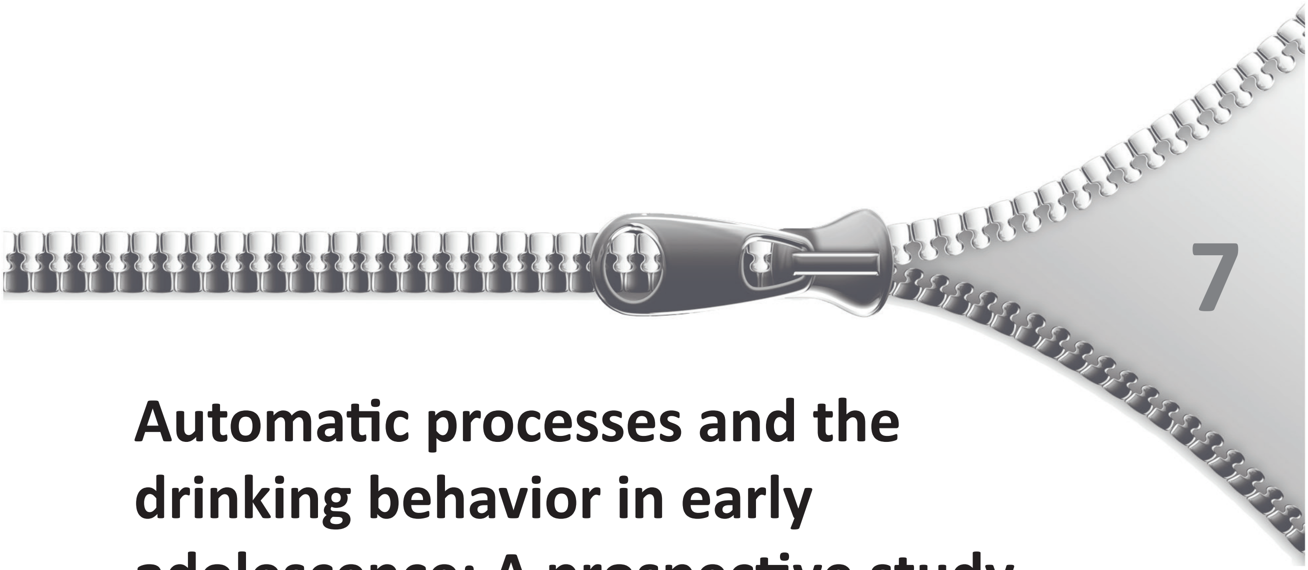
The results of previous research combined with the results of the current study indicate that the drinking behavior of at-risk adolescents with weaker inhibition skills is influenced relatively strongly by automatic processes compared to the drinking behavior of adolescents with relatively well-developed inhibition skills. The higher alcohol use among at-risk adolescents with weaker inhibition skills may therefore be explained by relatively automatic processes triggered by alcohol-cues, combined with a relatively weak reflective system. Particularly among adolescents who already have relatively poor inhibitions skills, early use of alcohol could reinforce drinking behavior later in life by the early development of automatic alcohol-approach tendencies. In line with this suggestion, a recent prospective study found that automatic cannabis-approach tendencies were the best predictor of escalation of cannabis use in at-risk adolescents (Cousijn et al., 2011).

In the current paper we used a different reaction time paradigm for the assessment of automatic processes, i.e. the AAT task. Grenard and colleagues (2008), and Thush and colleagues (2008, 2007) already found that the IAT and the Memory Association Task both predict alcohol use in at-risk adolescents with relatively weak executive functions. The present study demonstrates that the AAT also qualify as measure for automatic processes in the prediction of alcohol use in at-risk adolescents.

Present results differ from those in a recent study by van Hemel-Ruiter and colleagues (van Hemel-Ruiter et al., 2010) who found no significant effect of automatic approach tendencies on alcohol use in young adolescents. A possible explanation, also suggested by the authors, is that adolescents who participated in the study were not heavy drinkers. The three positive studies (Grenard et al., 2008; Thus et al., 2008), present study) were all conducted with adolescents who are at-risk for developing alcohol-problems at a group level, while participants in van Hemel-Ruiter were unselected adolescents. In addition, sample sizes of the positive studies were markedly higher than in the study of Van Hemel-Ruiter (43, cf. 349 here). Finally, a different test of executive functions was used in that study, for which no study has found moderation effects, while the classical Stroop test used here was found to be a successful moderator of the impact of automatic processes on behavior in several studies with young adults (Houben and Wiers, 2009; Wiers et al., 2009b).

The results of this study have to be interpreted with some caution. First, although the results are consistent with previous studies on dual process models and alcohol use, alternative explanations are possible. Recently, some authors have questioned the empirical evidence and have criticized the theoretical framework of dual process models (Keren and Schul, 2009; Kruglanski and Gigerenzer, 2011). It has been suggested that there is a lack of evidence for the existence of a dual systems instead of a uni-system or multiple systems model (Keren and Schul, 2009) but see Gladwin and colleagues (2011) for a discussion about the concerns that have been raised. Findings of our study suggest that two different processes influence drinking behavior; an automatically activated appetitive process and a reflective process, leaving aside if it is an exhaustive enumeration of the processes that influence drinking behavior of adolescents and how exactly the neural implementation of these processes should be described in detail. Second, the adolescents in our study were selected from special education and were expected to be at-risk for alcohol use. Although similar results were found in an at-risk sample in low-level vocational schools (Grenard et al., 2008), our findings may not generalize to other (at-risk) samples. Third, alcohol use was assessed by self-report, a measurement method which has been criticized for its validity and reliability (Leigh et al., 1998). Although we used ZIP-analysis to compensate for the latent drinkers, it is difficult to obtain a true alcohol score. Nevertheless, the reliability of self-reported alcohol use in adolescents has been examined and results indicated that self reports about quantity and frequency of alcohol use are reliable (Koning et al., 2010). Finally, the design of the study does not allow us to draw conclusions about the direction of the association between alcohol use and automatic approach tendencies. It is assumed that strong automatic approach tendencies lead to more alcohol use, which in turn strengthens approach tendencies (Wiers et al., 2007) as was recently found in prospective study for the escalation of cannabis-use (Cousijn et al., 2011). However, more longitudinal research is needed to explore this bidirectional link for alcohol use both in adults and adolescents.

This study contributes to previous studies on automatic alcohol-approach tendencies (Field et al., 2008a; Field et al., 2005; Palfai and Ostafin, 2008; Wiers et al., 2009a; Wiers et al., 2010b, Wiers et al., 2011), by showing that approach tendencies not only influence the drinking behavior of adults, but also the drinking behavior of young at-risk adolescents who just started drinking. By knowing the risk factors and the possible working mechanism responsible for the development of problematic alcohol use, we perhaps are able to intervene in this process at young age and prevent future problems. Previous studies already provide promising results in retraining automatic processes in hazardous drinkers (Wiers et al., 2010b) and alcoholic patients (Wiers et al., 2011). New training methods could change automatic motivational orientation and reduce the influence of strong automatic approach tendencies in adolescents at risk for developing problematic alcohol use. An alternative could be to strengthen inhibition (Houben et al., 2011b) or working memory capacity (Houben et al., 2011a). In conclusion, the present study found that in at-risk adolescents, automatic alcohol-approach tendencies develop rapidly after onset of drinking, and in individuals with relatively weak inhibitory capacities, they predict drinking.



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Automatic processes and the drinking behavior in early adolescence: A prospective study

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Abstract

This study examined the bidirectional prospective link between automatic alcohol-approach tendencies and alcohol use in a group of young adolescents (mean age = 13.6 years). The adolescents in the present study were assumed to be at risk for early alcohol use and later problem drinking. It was hypothesized that alcohol use and automatic approach tendencies would reinforce one another particularly in the absence of well-developed inhibition skills. 347 adolescents (N = 279 at follow-up) from special secondary education, a risk group for the development of substance use problems, participated in the study. Automatic approach tendencies were assesed with the alcohol-approach avoidance task (a-AAT), inhibition skills were assesed with the Stroop task, and alcohol used was measured using a self-report measure. Zero inflated Poisson analysis revealed a significant effect of automatic approach tendencies predicting alcohol use six months later, although only for adolescents with weaker inhibition skills. Automatic approach tendencies predict future drinking behavior of young adolescents with relatively weak inhibition skills. The findings of the present study have important implications for alcohol interventions for adolescents. Results are discussed in terms of risk factors for the development of problematic alcohol use in young adolescents.

Introduction

Recently, studies on substance use by young adolescents have evaluated and examined the relevance of dual processing in risky health behavior (Grenard et al., 2008; Thush et al., 2008). Research suggests that two systems of information processing are responsible for behavioral outcomes (Deutsch and Strack, 2006; Strack and Deutsch, 2004). The reflective system, a slow and controlled system, elicits deliberated responses and a fast and automatic system that evokes impulsive responses (Fazio and Towles-Schwen, 1999). Recently, there is some discussion about the neural implementation and psychological reality of dual process models (cf. Gladwin et al., 2011; Keren and Schul, 2009; Kruglanski and Dechesne, 2006).

Studies have revealed that automatic processes predict future smoking behavior (Chassin et al., 2010) and escalation of cannabis use (Cousijn et al., 2011) in (young) adults. In adolescents, cross-sectional relations have been identified between alcohol use and automatic processes (Rooke et al., 2008). In our previous cross-sectional study for instance (Peeters et al., 2012), it was found that automatic processes were associated with current drinking behavior in young at-risk adolescents. However, to date this relationship has not been studied in a longitudinal design, therefore it is unclear if automatic processes and drinking behavior of young adolescents influence each other over time. It might be that early formed alcohol associations affect future drinking behavior of young adolescents, and that alcohol use strengthens the association, which subsequently enhances the likelihood of automatic processing. Thereby, automatic processes might play an important role in the escalation of alcohol use.

Approach tendencies

It has been suggested that there is an automatic approach orientation toward positively evaluated stimuli. According to Robinson and Berridge (1993; 2008) this automatically activated approach bias is a behavioral response activated by an incentive motivational process. Many learned associations automatically trigger appropriate and relevant behavior (e.g., washing hands after a visit to the toilet). However, learned associations can also trigger inappropriate responses resulting for instance in compulsive behavior, like with addiction. Robinson and Berridge (1993, 2008) argue that besides associative learning, an incentive motivational process underlies compulsive behavioral responses, which the authors define as “wanting”. Two different appetitive processes, “liking” and “wanting”, can operate in parallel; however, with respect to addictive behavior, learned associations can trigger “wanting” responses even in the absence of a “liking” component. This “wanting” component can automatically trigger an attentional bias or approach tendency for the substance (Robinson and Berridge, 2008). For instance, with respect to heavy drinking behavior, there is a strong automatic action tendency to approach an alcohol stimulus rather than avoiding it (Wiers et al., 2010b). Field and colleagues (2008a) examined automatic approach tendencies in heavy and light drinkers. Results indicated that heavy drinkers had stronger approach tendencies for alcohol stimuli. Similar results were found by Palfai and Ostafin (2003), who studied the relation between binge episodes and automatic approach tendencies. It was found that strong automatic approach associations were associated with higher alcohol consumption. Both studies found a cross-sectional relation between automatic approach tendencies and alcohol use. An effect over time between substance use and automatic approach tendencies was found by Cousijn and colleagues (2011). Results indicated that strong automatic approach tendencies predicted changes in cannabis use of heavy users, six months later. These results, in combination with the assumption that learned alcohol associations are strengthened by the repeated use of alcohol (Gladwin et al., 2011; Robinson and Berridge, 1993) seem to indicate a reciprocal relation between automatic processes and early alcohol use which might affect behavior as adolescents mature.

Response inhibition

Deficits in the regulation of behavior have been associated with problematic substance use (Sher et al., 2000) and with an increased risk of alcohol abuse and alcohol dependence (Finn et al., 2000). Impairment or reduced functioning of regulatory skills will interfere with the execution of more reflective and controlled responses. Especially in adolescence, when the (pre)frontal cortex is not yet fully developed (Blakemore and Choudhury, 2006) and perhaps less reinforcement of reflective behavior has been experienced, there tends to be a bias toward fast and automatically generated responses versus slow and deliberated responses (Gladwin et al., 2011). Recent studies indicate that relatively poor executive functioning and more specifically, relatively poor inhibition skills increase the chance of automatic information processing resulting in more automatic behavior (Field et al., 2008b; Houben and Wiers, 2009). Particularly in the absence of good self-regulatory skills, control over drinking behavior seems to be weakened by strong alcohol associations (Ostafin et al., 2008). Response inhibition may therefore be an important factor in the development of problem drinking.

The present study

The aim of the present study was to examine the prospective and reciprocal effects of alcohol use and automatic approach tendencies in a sample of young at-risk adolescents (Kepper et al., 2011) . Since previous studies suggest that strong alcohol associations affect drinking behavior particularly in the absence of good inhibition skills (Field et al., 2008a,b; Houben and Wiers, 2009) it was assumed that automatic approach tendencies at baseline would predict future alcohol use, and that alcohol use at baseline would predict automatic approach tendencies at follow-up, especially among adolescents with relatively poor inhibition skills. We tested our hypotheses in a latent cross-lagged panel model.

Methods

Participants

374 students (330 boys, 44 girls) from seventeen different secondary special education schools (cluster four) in the Netherlands with a mean age of M =13.6 years, SD =0.9) participated in the study. Special education (cluster four) is for adolescents who are not able to participate in mainstream education because of their externalizing behavioral problems (ADHD/conduct disorder). The gender disparity (88% boys) in the present study is similar to that in the overall population of special education students (Valdes, 1990). Due to incomplete data at the first wave, 27 students were excluded from the analysis, resulting in a sample of 347 students. In the follow up study six months later, 279 students participated (response rate = 75%). Twenty-nine adolescents did not participate in both parts of the data collection due to illness or absence or had incomplete data sets, and were therefore excluded from the analysis resulting in a sample of 250 students (223 boys, 27 girls, mean age = 14,1, SD = 0.9), with complete data on both data waves. Adolescents who dropped out of the study did not differ on the study variables, age, or gender from the study sample.

In accordance with Dutch ethical standards, anonymity was ensured and adolescents were informed about the voluntary nature of participation. Because adolescents were underage, passive parental permission was obtained through an informative letter about the purpose of the study. In total, fifteen parents (3.8%) and seven students (1.7%) declined to participate in the study. Adolescents first individually completed some tasks at the computer under supervision of a trained research assistant. After that adolescents completed a questionnaire. Six month later during follow-up, this assessment procedure was repeated and the same tasks and questionnaire were completed by the adolescents.

Measures

Alcohol use and problem drinking. The frequency of alcohol use was measured with a 14-item rating scale (ranging from “never” to “ten times, and three ratings consisting of aggregate scores; 11-19, 21-39, 40 times or more”) (O’Malley et al., 1983). Participants were asked on how many occasions they had consumed alcohol in the last month. The quantity of regular alcohol use was assessed by ratings of drinking days during the week (i.e., Monday to Thursday) and weekend (i.e., Friday to Sunday) (Engels and Knibbe, 2000) and the average number of alcoholic drinks consumed on weekdays and during the weekend (Engels et al., 1999). Responses could range from zero glasses to twenty glasses or more. Next, the quantity of alcohol use was computed by multiplying drinking days by alcoholic drinks (Koning et al., 2009). Problem drinking was measured with the CRAFFT; an alcohol screening instrument which includes six items (e.g., “Do you drink alcohol when you are by yourself”?) with a “yes” or “no” response categories (Knight et al., 1999). The internal consistency of the scale was acceptable (Cronbach’s Alpha = .74).

Approach Avoidance Task (AAT). Wiers and colleagues (2009) adapted the AAT as a measure of alcohol-approach tendencies, and it has recently successfully been applied in a sample of young adolescents (Peeters et al., 2012). In the present study participants were instructed to push or pull a certain picture (i.e., forty alcohol and forty soft drink pictures), by using the arrows on the keyboard (i.e., arrow up for pushing the picture, arrow down for pulling the picture). Note, that in the original AAT a joystick was used as response device. Participants were asked to respond as quickly as possible and to press the correct arrow three times to make the picture disappear. Picture sizes increased and decreased to give participants the impression they were pulling or pushing the target stimuli. In the first condition, participants received the instruction to pull the picture when it was left skewed (i.e., 3° left rotated); in the second condition participants had to pull when pictures were right skewed (i.e., 3° right rotated). Twenty unique alcohol pictures and twenty unique soft drink pictures appeared twice on the screen (in random order): once left rotated and once right rotated. The instructions shifted attention from the content of the picture (i.e., soft drink or alcohol) to the appearance of the picture (i.e., right or left rotated) (Cousijn et al., 2011) which has been assumed to result in better assessment of automatic processes (De Houwer, 2003). For all trials the last key press was assessed and difference scores for the alcohol category were measured (i.e., push minus pull with positive scores indicating a faster approach for alcohol stimuli). The RT's were measured in milliseconds, which resulted in large variances; therefore we divided each trail by 1000.

Response inhibition. The Stroop color naming task (Stroop, 1935) was used to assess level of response inhibition (Miyake et al., 2000). The Stroop task as a measure of response inhibition has successfully been used as moderator in previous studies (Houben and Wiers, 2009; Wiers et al., 2009a). Participants were instructed to indicate the color of the word (i.e., red, green, blue or yellow) that appeared on the screen by pressing the corresponding key on the keyboard, while ignoring the meaning of the word. Participants started with a practice block which consisted of forty trials with symbols (e.g., @@@@ or &&&&). The practice block was followed by a test block with twenty-eight trials. Trials could be either congruent (i.e., meaning of the word matches the color), neutral (i.e., colored symbols instead of words) or incongruent (i.e., meaning of the word differs from the color), and were presented in random order between participants. Each trial was repeated until a correct answer was given. An incorrect response was followed by an error message including a description of the keys used and their corresponding color. The mean score for each block (i.e., congruent, incongruent, and neutral) was calculated, as well as a difference score between incongruent and neutral stimuli, with higher scores indicating greater inhibition problems. The test-retest reliability of the task was acceptable (r = .73).

Data analysis

First, the descriptives of the relevant variables are provided (Table 1). Second, to test whether there was an underlying factor (alcohol use index; hereinafter referred to as alcohol use) with respect to the three alcohol measures (alcohol frequency, drinks per week, and problem drinking) we applied a confirmatory factor analysis. The results of the measurement model are discussed in Figure 1. Likewise, a CFA was applied using the twenty AAT-trials. Three indicators for our latent factor AAT revealed low reliability and were removed from further analysis, the other seventeen trails were used for creating three parcels using the loadings of the items as guide for creating parcels (Little et al., 2002) The three parcels served as indicators for the latent construct of the AAT, (cf. Cunningham et al., 2001; 2004; McCarthy and Thompsen, 2006). Third, results of the cross-lagged panel design are presented. Stability and cross-lagged paths are presented (figure 2a). Based on the mean on the Stroop task (i.e., above and below the mean), two groups were identified. A t-test revealed that the groups significantly differed from each other (t (281) = 21.56). The group with high scores represented the adolescents with weaker inhibition skills while the group with low scores represented adolescents with stronger inhibition skills. A mutigroup analysis was conducted, with low and high Stroop scores as the group indicator (Fig. 2b). A Zero Inflated Poisson regression (ZIP) was applied for the analysis in the present study. First because there was overdispersion (i.e., variances exceed the mean) of the dependent variable (i.e., alcohol) in our study. Second, the three indicators of alcohol were not distributed normally and revealed a typical Zero Inflated Poisson distribution (i.e., left skewed with many zero counts). If the sample includes many zero counts, the mean of the sample will reflect the zeros and provide a less accurate representation of the sample statistics for the non-zero counts (Liu and Powers, 2007). Using a mixture distribution method such as a Zero Inflated Poisson model solves the problem of inflation and prevents the zero counts from dominating the distribution (for a more detailed description of ZIP-regression see Peeters and colleagues, 2012). In ZIP-models standard correlations (as with continuous-normal variables) between the study variables are not available, therefore only means and standard deviations are provided in Table 1. The ZIP model was estimated with Mplus Version 6.0 (Muthén and Muthén, 1998-2010) using the maximum likelihood estimation method with robust standard errors. Full information likelihood (FIML) was used to deal with missing data which allowed us to include all participants in the cross-lagged analysis. FIML uses all available information instead of deleting cases with missing variables. That is, in case of missing values, parameter

Table 1.

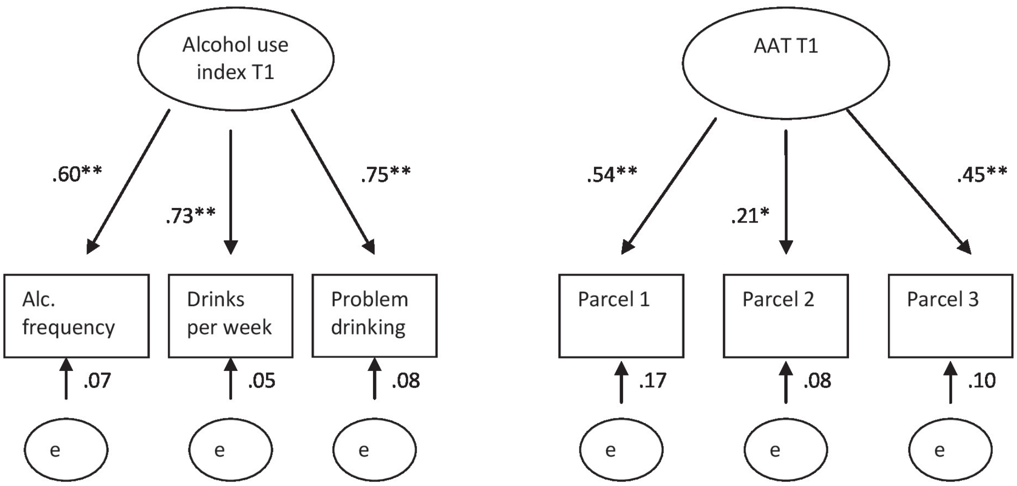
Descriptive statistics of the alcohol use index indicators and alcohol-AAT at baseline and follow-up.

	T1 (N = 347)	T2 (N = 250)
Percentage drinkers	51,2%	47,0%
Total sample		
1. Alcohol use last month	1.45 (2.97)	1.57 (3.06)
2. Drinks per week	3.35 (8.00)	3.68 (8.79)
3. Problem drinking	0.83 (1.32)	0.82 (1.28)
4. Approach bias parcel 1	0.03 (0.57)	0.01 (0.42)
5. Approach bias parcel 2	-0.01 (0.42)	-0.04 (0.45)
6. Approach bias parcel 3	-0.02 (0.60)	0.02 (0.49)
Good inhibition skills	M (SD) (N = 187)	M (SD) (N = 137)
1. Alcohol use last month	1.20 (2.59)	1.43 (2.65)
2. Drinks per week	2.98 (7.11)	3.23 (6.78)
3. Problem drinking	0.74 (1.23)	0.73 (1.20)
4. Approach bias parcel 1	0.02 (0.61)	-0.01 (0.35)
5. Approach bias parcel 2	-0.01 (0.41)	-0.04 (0.39)
6. Approach bias parcel 3	-0.04 (0.56)	0.03 (0.36)
Poor inhibition skills	M (SD) (N = 160)	M (SD) (N = 113)
1. Alcohol use last month	1.74 (3.33)	1.68 (3.46)
2. Drinks per week	3.80 (8.99)	4.21 (10.75)
3. Problem drinking	0.93 (1.42)	0.93 (1.37)
4. Approach bias parcel 1	0.05 (0.52)	0.03 (0.50)
5. Approach bias parcel 2	-0.02 (0.44)	-0.04 (0.51)
6. Approach bias parcel 3	0.00 (0.64)	0.01 (0.61)

estimation is based on "borrowed" information of other correlated observed values. In this way, all missing cases can be included in the analysis with actually imputing the missing values. Compared to traditional approaches (e.g. listwise/pairwise deleting), FIML has been found to be the most reliable and efficient approach and equally reliable as multiple imputation (Enders and Bandalos, 2001; Neworking memoryan, 2003).

The multigroup option in Mplus required no missingness on the grouping variable response inhibition, resulting in a sample of 347 adolescents for the cross-lagged analysis. Participants in our study were nested within schools. To account for clustering effects Mplus provides the option to adjust the chi-square test of model fit and standard errors in nested samples. We corrected for clustering effects in all our analyses.

Figure 1. Measurement model with factor loadings for alcohol use index and approach avoidance task (AAT) at baseline. Because measurement invariance was ensured, only confirmatory factor analysis (CFA) results for baseline are presented.



*p < 0.05, **p < 0.01

Results

Descriptives

Table 1 presents the mean scores and standard deviations for the three indicators for alcohol and for the AAT task for both groups (i.e., stronger and weaker response inhibition) and both measurements (i.e., baseline and follow-up) separately. Important to note is the fact that the descriptives in Table 1 represent both the drinkers and non-drinkers in our sample, thus the actual alcohol consumption among the drinkers, and more important, the increase in alcohol consumption between the two waves, will be higher. Using a ZIP-model allows one to analyze the non-zero counts (drinkers) separately from the zero-counts (non-drinkers) and thereby controlling for the influence of non-drinkers. However, this analytical strategy is not processed in the descriptive table and we therefore added the percentage of drinkers (i.e. scoring one or more on of the three alcohol indicators) in Table 1.

Measurement model

Analyses revealed significant factor loadings for all three indicators of the alcohol use index (i.e. frequency, drinks per week and problem drinking) that were stable over time. Factor loadings for the three AAT parcels were also significant (see Figure 1).

Since we assessed alcohol use and approach tendencies over time, it was necessary to ensure that both factors measured the same underlying construct at baseline as well as at follow-up. Therefore we assumed measurement invariance over time. To test this assumption we constrained both the factor loadings and the intercepts to be equal over time. For both alcohol and AAT there was a decrease in Bayesian information criterion (BIC) after adding constraints (alcohol; BIC unconstrained: 4713 (19) versus BIC constrained 4630 (14), AAT; BIC unconstrained: 1948 (19) versus BIC constrained: 1923 (14), suggesting better model fit for the more restricted model and thus indicating that both factors are time invariant.

Cross-lagged panel design

Figure 2a presents the stability paths and cross-lagged paths without accounting for group differences in inhibition skills. All estimated parameters were constrained to be equal among adolescents with stronger inhibition skills and adolescents with weaker inhibition skills. Stability paths for both latent factors were significant (alcohol; β = .90, p < .01; approach tendencies; β = .66, p < .01). No cross-lagged relation was found between alcohol use at baseline and alcohol-approach tendencies six month later and vice-versa[1].

In the second model (Fig. 2b) we went a step further and unconstrained the cross-lagged path, which allowed the relation between alcohol use at baseline and approach tendencies at follow-up, as well as that between approach tendencies at baseline and alcohol use at follow up to vary for adolescents with stronger inhibition skills and for adolescents with weaker inhibition skills. The second model, which accounted for group differences, showed significantly better model fit (BIC : 7500 (39) versus 8883 (37), R^2 = .73 for alcohol, R^2 = .45 for alcohol-AAT). In this multigroup model, stability paths for alcohol (β = .85, p < .01) and approach tendencies (β = .66, p < .05) were significant. The correlations at baseline and at follow up between alcohol use and approach tendencies were both non-significant. The cross-lagged relation between alcohol use at baseline and approach tendencies six months later were not significant for adolescents with either relatively weak as relatively good inhibitions skills (β = -.06, p > .05 and β = -.11 p > .05). We did find a significant cross-lagged relation between alcohol-approach tendencies at baseline and alcohol use at follow-up (β = .25, p < .05) for adolescents with relatively weak inhibition skills, but not for adolescents with relatively good inhibition skills (β = .06, p > .05).

[1] The non-significant baseline relation between alcohol and approach bias does not correspond with previous work (see for instance Peeters et al., 2012). One explanation is that the effect over time is stronger than the cross-sectional effect. This assumption was supported by an additional analysis. We repeated the multigroup analysis cross-sectionally and results revealed a significant correlation between AAT and alcohol for those with relatively poor inhibition skills, a finding previously found in this sample without using a latent construct for the AAT (Peeters et al., 2012).

Figure 2a. Zero inflated Poisson model without multiple groups (BIC = 8883 (37)

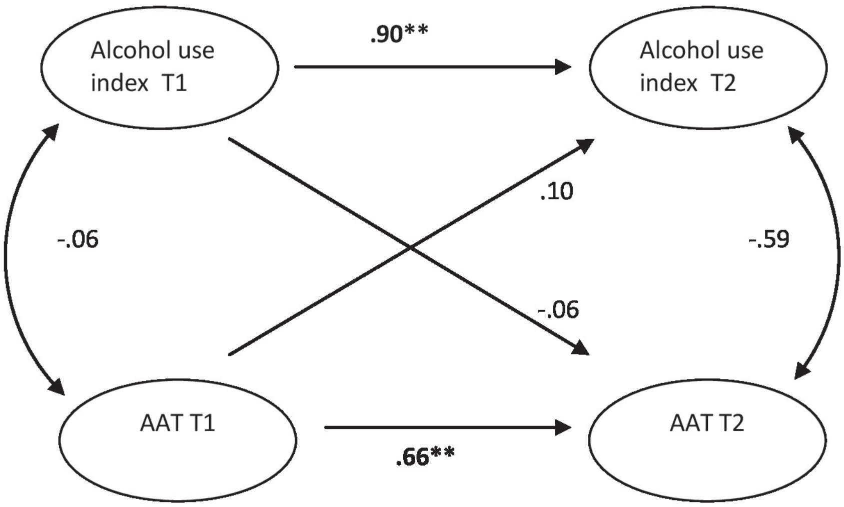
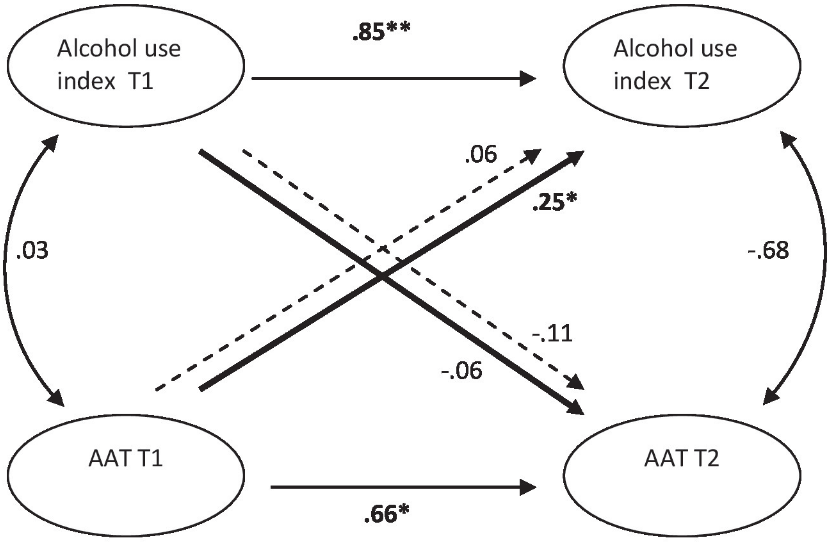


Figure 2b. Zero inflated Poisson model with multiple groups (i.e., high versus low Stroop score). Straight bold lines represent results for adolescents with weaker inhibition skills (BIC = 7500 (39).



*$p < 0.05$, **$p < 0.01$

Discussion

The present study examined the bidirectional prospective relationship of automatic approach tendencies and alcohol use in a group of young adolescents who are at risk of developing problematic alcohol use. We hypothesized that stronger approach tendencies and alcohol use would predict heavier alcohol use six months later and vice versa. It was anticipated that the cross-lagged relation would be particularly strong for adolescents with relatively poor inhibition skills. The analysis revealed that stronger automatic approach tendencies did indeed predict future alcohol use, but only in adolescents with weaker inhibition skills. No predictive effects were found for adolescents with relatively good inhibition skills. We did not find any significant effect of alcohol use in predicting future approach tendencies.

The findings of the present study are in line with previous research examining the influence of automatic processes on alcohol use in young adolescents (Grenard et al., 2008; Thush and Wiers, 2007). The results add to previous studies by establishing not only a cross-sectional relationship (Field et al., 2008a; Palfai and Ostafin, 2003; Peeters et al., 2012), but also a prospective effect of automatic approach tendencies on the drinking behavior of young at-risk adolescents. Furthermore, while Thush et al. (2008) demonstrated short term effects of alcohol associations predicting alcohol use, i.e., over one month, the present study showed that these effects are maintained over a period of 6 months. Thush and colleagues (2008) and Grenard and colleagues (2008) found that working memory moderated the relationship between alcohol use and alcohol associations in young (at-risk) adolescents. In the present study we demonstrated the moderating effect of another type of executive functioning, i.e., response inhibition. The results suggest that particularly the drinking behavior of at-risk adolescents who have weaker self-regulatory skills is susceptible to the influence of automatic processes. This would imply that reflective processing is an important element in controlling drinking behavior. Once drinking has been initiated, adolescents with relatively poor inhibition skills might be less able to avert strong automatic responses and therefore consume more alcohol than their peers with relatively good inhibition skills who are able to inhibit these strong alcohol-associated responses. In a sample of adolescents assumed to have relatively good self-regulatory skills and not specifically at-risk for alcohol use, Pieters and colleagues (2012) indeed found no support for working memory as moderator in the relation between alcohol use and alcohol approach tendencies. It appeared that rule setting by parents regarding alcohol use was a more important moderator for adolescents with relatively good self-regulatory skills. Taken together, these results (cf. Grenard et al, 2008; Pieters et al., 2012; Thush et al, 2008 and the present study) suggest that in the presence of strong alcohol-associated responses, the ability to regulate behavior significantly affects drinking behavior in young adolescents.

We did not find any effect of alcohol use predicting automatic approach tendencies six months later. Perhaps, a possible explanation is that automatic approach tendencies are strengthened by drinking behavior at the onset of alcohol use, but become stable as a regular drinking pattern has developed. In the present sample, most adolescents were already drinking regularly at baseline and only a small proportion of adolescents iniated alcohol use during follow-up. It would be interesting to test this effect in a sample of largely non-drinking adolescents who initiate alcohol use during the study follow-up.

The findings of this study have important implications for interventions aiming to reduce alcohol use among young adolescents. The present study emphasizes two issues. First, it seems that approach behavior is an important factor in predicting alcohol use by young adolescents. Therefore, weakening strong automatic approach responses might be a means to reduce alcohol use. Previous findings indicate that automatic approach responses can be re-trained (Wiers et al., 2010b; 2011). Second, intervention seems to be especially important for adolescents with weaker inhibition skills (cf. Salemink and Wiers, 2011). Reflective processing could be impaired through depleted regulatory skills. A combination of increasing self-regulatory behavior in adolescents (see Houben et al., 2011a and 2011b for training working memory and response inhibition) and intensified external control, for instance rule setting by parents (Pieters et al., 2012), might be the most effective approach to reduce alcohol use in young adolescents. This is also supported by the results of a recent effectiveness study, showing that a combined intervention, aimed at both parents and adolescents, was effective in delaying the age of onset of alcohol, while the parent and adolescent intervention separately were not (Koning et al., 2011).

The findings of the present study should be interpreted with some caution. First, we examined the relationship between alcohol use and automatic approach tendencies in a sample of adolescents at risk for early alcohol use, thus our findings may not generalize to other groups. Second, a two-wave cross-lagged model was used to test the reciprocal relationship between alcohol use and automatic approach tendencies. This model allows inferences on directionality, nevertheless it is necessary to include more waves to examine change over time or development. The results support a unidirectional relation between approach tendencies and alcohol use; however, additional time points could provide a better understanding of the development of the relationship between alcohol approach tendencies and alcohol use which might have a bidirectional instead of a unidirectional character earlier or later in the adolescent development. Third, one of the factor loadings of the parcels of the alcohol-AAT was small (i.e. .19). However, the overall model fit of the confirmatory factor analysis of the AAT was satisfactory (CFI = .98, RMSEA = .02), and the factor loading was significant. Therefore we decided to proceed with this parcel and include it in the final model. Furthermore, a well known phenomenon in measuring automatic processes is the error variance associated with the implicit reaction time tasks (Egloff and Schmukle, 2002). We attempted to reduce the measurement error by using a latent construct for the AAT. In comparison with self-report measures the reliability of the AAT is modest, however implicit measures, particularly irrelevant feature measures assess different processes than explicit measures. Reliability reduces when participants are asked to respond to different features than the one of interest (Krieglmeyer and Deutsch, 2010). A trade-off between reliability and better assessment of automatic processes by using an irrelevant feature task was made in the present study. Previous reliability studies of implicit reaction measures present similar stability estimates. For instance, Cunningham and colleagues (2001) found a stability of .46 for the implicit association test (IAT) and Egglof and Schmunkle (2002) reported a stability estimate of .57 for the IAT. Cousijn and colleagues (2011) found an internal consistency of Cronbach's α = .68 for the AAT task. Therefore, the stability coefficient of .66 in the present study should be regarded as acceptable.

Despite these limitations, the present study is the first to demonstrate that alcohol approach tendencies predict future drinking behavior of young at-risk adolescents with relatively weak inhibition skills. The earlier the use of alcohol, the earlier the development of automatic approach tendencies which may continue to reinforce alcohol use as adolescents mature. In combination with relatively poor inhibition skills, alcohol-approach tendencies may cover the underlying working mechanism responsible for the escalation of drinking behavior and thereby highly relevant in the etiology of alcohol addiction.

8

Context effects of alcohol availability at home: Implicit alcohol associations and the prediction of adolescents' drinking behavior.

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In revision.

Abstract

Recent studies suggest that the predictive effect of implicit alcohol associations is context dependent. Findings indicate that implicit associations are more easily retrieved in an alcohol associated setting or context (e.g. bar) compared to a neutral setting. In line with this reasoning we hypothesized that alcohol availability at home might be a moderating factor in the relationship between implicit alcohol associations and future drinking behavior of adolescents. Participants were 279 at-risk adolescents (236 boys, 27 girls) with a mean age of 14.13 (SD = 0.86) years at baseline. Adolescents completed a questionnaire and a modified version of the Implicit Association Test (i.e. Single Category Implicit Association Test; SC-IAT). Stronger implicit alcohol associations predicted future frequency of alcohol use (controlled for baseline drinking), however this was only the case in adolescents who indicated that alcohol was available at home. No moderating effects were found for future quantity of alcohol use and problematic alcohol use. The findings of the present study suggest that alcohol availability at home is a contextual factor which influences the predictive effect of implicit alcohol associations on future drinking behavior of adolescents. Only frequency of alcohol use revealed an effect suggesting that particularly the decision whether or not to drink in adolescents, is influenced by implicit alcohol associations.

Introduction

Recent research has demonstrated the relevance of automatically activated or implicit processes in the understanding of adolescents' drinking behavior (reviews: Wiers et al., 2007; Stacy and Wiers, 2010). That is, adolescents are more likely to drink heavily when action tendencies are predicted by implicitly triggered neurocognitive processes (Grenard et al., 2008; Peeters et al., 2012, 2013; Thush et al., 2008). Dual process theories of addiction suggest that strong automatic processes in combination with relatively poor reflective processing (e.g. cognitive control), increases drinking among adults and adolescents (Rooke et al., 2008; Wiers et al., 2007). In the presence of alcohol stimuli, like the sight of a glass of beer, implicit associations can trigger behavioral responses towards alcohol and increase drinking behavior (Grenard et al., 2008; Thush and Wiers, 2007). Implicit associations reflect learned memory associations between a behavioral response and a outcome which can be primed by a specific stimulus (e.g. a glass of beer, Stacy et al., 1994; Wiers and Stacy, 2006). Both individual and social interacting factors are relevant when considering the relationship between alcohol associations and alcohol use. Individual factors such as working memory (Grenard et al., 2008; Thush et al., 2008), response inhibition (Peeters et al., 2012, 2013) and personality (Zack et al., 2002) for instance influence the predictive value of alcohol associations on alcohol use in adults and adolescents. Social factors, such as the context in which behavioral decisions are made, determine the extent to which implicit associations are accessible from memory (Krank and Goldstein, 2006). Alcohol associations for example, are more easily activated in an alcohol setting (e.g. bar) than in a neutral context (Havermans et al., 2004; Lau-Barraco et al., 2009). It could be hypothesized that availability at home enhances accessibility of implicit alcohol associations in a similar way. The enhanced accessibility of these associations is likely to subsequently influence drinking behavior of adolescents (Krank et al., 2005). The home setting has not yet been examined as interacting factor. In the present study we therefore examined to what extent alcohol availability at home influenced the relationship between implicit alcohol associations and adolescent drinking behavior.

Alcohol associations and context

Several experimental studies established that drinking behavior is affected by the context and situation in which behavioral decisions are made. Wall and colleagues (2000; 2001) for instance, examined whether alcohol expectancies were retrieved more easily in a "bar setting" compared to a "neutral setting". Results revealed that in a bar setting, reaction times for alcohol associations were faster than in a neutral setting, suggesting that retrieval of alcohol-related information depends on the environmental context. In addition, Lau-Barocco and Dunn (2009) found that participants primed with an alcohol related context (e.g. simulated bar setting) demonstrated stronger implicit alcohol-associations and consumed more alcohol than controls. Similarly, Dunn and Yniguez (1999) found that children (between 9 and 10 years) exposed to alcohol commercials more likely activated positive alcohol memories compared to children who were exposed to soft-drink commercials. Moreover, Krank and colleagues (Krank et al., 2005; Krank and Wall, 2006) demonstrated that the predictive effect of implicit associations on alcohol use increases when they are retrieved in an alcohol related setting. These findings together indicate that not only drinking behavior is context dependent but also the accessibility and the predictive validity of implicit alcohol associations is influenced by the environmental context in which they are primed. Drinking behavior might more strongly increase because of the enhanced accessibility of alcohol associations in settings where more alcohol is available. In line with experimental research (Krank et al., 2005; Lau-Barraco and Dunn, 2009; Wall et al., 2000; Wall et al., 2001) showing that in an alcohol context, the influence of implicit alcohol associations on alcohol use is stronger, it is hypothesized that this may also be the case in the home context. When alcohol is visible for adolescents, the home context might serve as an alcohol associated environment. That is, alcohol availability at home could serve as a prime and could activate implicit alcohol associations in adolescents. As a consequence, behavioral decisions related to drinking behavior are more likely guided by implicit alcohol associations, when alcohol is easily available at home. This study is the first to examine the role of alcohol availability at home as a potential moderating factor in the relation between implicit associations and adolescents' alcohol use. We hypothesized a stronger predictive effect of implicit alcohol associations on future drinking behavior for adolescents who were exposed to alcohol at home, compared to adolescents who were not exposed to alcohol at home.

Methods

Participants

Participants in the current study took part in a longitudinal study consisting of four waves over a period of two years (6-8 months between the waves). For the current study we used data from the second (T1) and third wave (T2). At T0, adolescents were recruited from 17 different secondary Dutch Special Education (SE) schools for students with externalizing behavioral disorders (e.g. attention-deficit-hyperactivity-disorder, ADHD, conduct disorder). Boys were overrepresented in this sample (i.e. 88%), which is a reflection of the population in SE schools for students with behavioral disorders (Valdes, 1990). This group of adolescents revealed an increased risk for early onset of drinking and heavy alcohol use (Kepper et al., 2011). Participants were 279 adolescents (236 boys, 27 girls) with a mean age of 14.13 (SD = 0.86) years at T1. At T2, approximately six months later, 230 adolescents (response rate = 82%) participated in the study.

Parental permission was obtained through passive consent. Adolescents were informed about the voluntary nature of the study and confidentiality. Fifteen parents (3.8%) and seven students (1.7%) declined participation before the first data collection started. At each wave, participants completed a questionnaire and a task on the computer under the guidance of a trained research assistant. If possible, some adolescents completed the questionnaire under the guidance of a teacher when adolescents were not present at the time of assessment. Some adolescents had incomplete data on the computer task (N = 29) or questionnaire (N = 17). We used Full Information Maximum Likelihood (FIML) to handle missing data, however adolescents with missing data on our grouping variable (i.e. alcohol availability) were excluded from further analysis. This resulted in a sample of 262 adolescents eligible for analyses at T1.

Measures

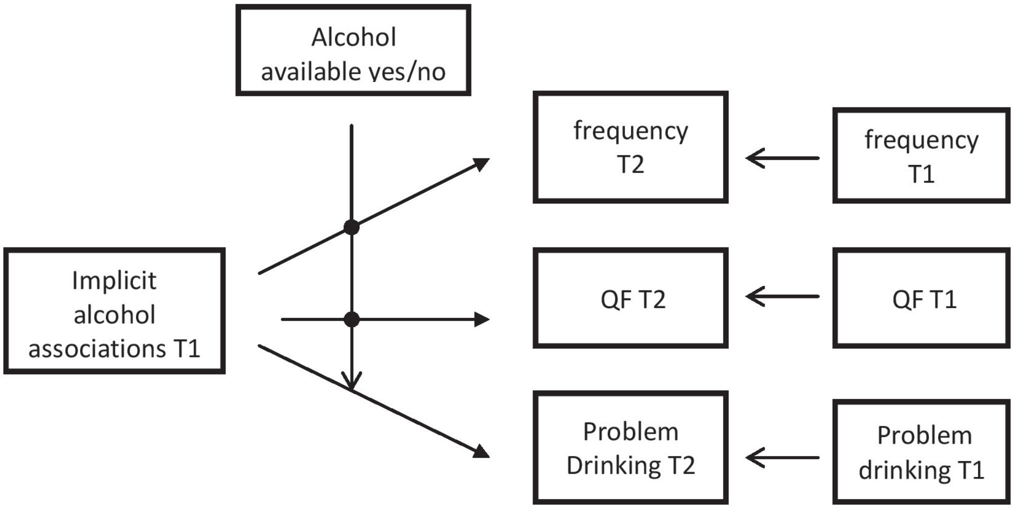
Alcohol use and problems. Three different outcome measures were used to assess alcohol use and related problems. First, participants rated the number of occasions on which alcohol in the last month was consumed. Possible answer categories ranged from zero to forty times or more (“0 to 10”, 11-19,20-39,40 or more, O’Malley et al., 1983). The quantity of regular alcohol use was assessed by counting the drinking days during the week (Monday to Thursday) and during the weekend (Friday to Sunday, Engels and Knibbe, 2000) and the average number of alcoholic drinks consumed on weekdays and during the weekend (Engels et al., 1999) . Responses could range from "zero" to "20 glasses or more". A quantity measure of alcohol was established by multiplying drinking days by glasses (with a maximum of 20 glasses). Problem drinking was assessed with an adapted version of the CRAFFT scale (Knight et al., 1999; Ko et al., 2008) which is a screening instrument used in clinical settings to identify adolescent problem drinkers (and substance users). The scale consist of six items (e.g. "Do you drink alcohol when you are by yourself"?) with "yes" or "no" responses (2 or more "yes" answers indicate problematic alcohol use).

Alcohol availability. Alcohol availability at home was assessed with a seven-item scale (Van Zundert et al., 2006). The seven items in this scale assessed the degree to which alcohol beverages (i.e. wine, beer, mixed-drinks and liquor) were available at home (e.g. "Do you parents have wine or beer at home?"). Response categories ranged from "never" to "always" with higher scores indicating greater availability of alcohol at home. Internal consistency of the scale was good (i.e. Cronbach's Alpha = .88). We created two groups, one group who indicated that there was no alcohol-available at home (zero scores on all seven items), another group scored one or more items with a non-zero value (alcohol-available at home). Hereafter referred to as the "alcohol-available group" and the "alcohol non-available group".

Implicit associations. Implicit associations were assessed with the Single Category Implicit Association test (SC-IAT, Karpinski and Steinman, 2006; Thush and Wiers, 2007) which is a modified version of the original Implicit Association Test (IAT, Greenwald et al., 1998) and includes only a single attribute category. The SC-IAT is an easier and shorter version of the IAT, and therefore ideal for this group of young adolescents. This task was successfully used before in such a sample (Thush & Wiers, 2007). The SC-IAT consisted of one practice block and two testing blocks, presenting one attribute category (i.e. alcohol) and two valence categories (i.e. pleasant versus unpleasant). Participants were asked to categorize the words that appear in the middle of the screen. These words could either be pleasant (e.g. funny, nice), unpleasant (e.g. mad, annoying) or alcoholic (e.g. beer, wine). In the first test block (i.e. 20 trials), the categories "pleasant" and "unpleasant" were presented on the screen. The attribute category "alcohol" was presented together with "pleasant". Participants were asked to categorize the words as fast as possible by pressing the key representing the right category. In the second test-block (i.e. 20 trials), the attribute category "alcohol" was presented together with "unpleasant".

Participants with positive associations towards alcohol were assumed to respond faster in categorizing words in the “alcohol- pleasant” situation compared to the “alcohol-unpleasant” situation. Reaction times scores were calculated for each test block based on the D-algorithm (Greenwald et al., 2003) which incorporates a penalty scores for incorrect trials and divides each block with its own standard deviation instead of the standard deviation across the two test blocks together. Higher scores indicated more positive implicit alcohol associations. The SC-IAT was completed before adolescents answered questions about alcohol use to avoid priming effects.

Figure 1. Structural model of implicit alcohol associations predicting alcohol use, moderated by alcohol availability at home.



Strategy for analysis

First, descriptive statistics of the three alcohol measures (at T1 and T2) and the implicit associations (T1) are provided for the total sample, and for the alcohol-available and non-available group separately (Table 1). Second, a confirmatory factor analysis (CFA) was carried out to test whether there was a single underlying factor for the three alcohol indicators. Results revealed that this was the case (factor loadings: frequency: .64 QF: .81 problem drinking: .78, Comparative Fit Index, CFI: .96, Root Mean Square Error of Approximation, RMSEA: .05) and measurement invariance between waves was ensured. Third, a multigroup analyses was carried out with implicit alcohol association as predictor (T1) and alcohol use as outcome variable (T2), while controlling for alcohol use at T1, for the alcohol-available group and non-available group. Unfortunately, the multigroup model did not converge and further analysis revealed that the non-available group was too small (N = 41) to run this complex model (e.g. estimated parameters increased with adding latent factor for two groups). Therefore, we decided to run a model for each alcohol indicator (i.e. frequency, QF and problem drinking) separately. Similar problems with the complexity of the model were experienced while adding covariates. Because the two groups (alcohol-available versus alcohol non-available) significantly differed in ethnic composition (phi = 0.31, p = 0.01) we examined whether ethnicity was a significant covariate. It is likely that alcohol use is affected by the ethnic background of parents and adolescents (Amundsen et al., 2005). We examined whether or not originating from an Islamic country (e.g. one or both parents, or adolescents themselves being born in Turkey or Morocco) would predict differences in alcohol use or implicit alcohol associations. No such effects were found, suggesting that ethnicity was not likely to be a confounding variable and was therefore not included in our final model.

Figure 1 presents the final model. The findings of the main effect of implicit alcohol associations on alcohol use are described briefly before the results of the multigroup analysis are discussed. Table 2 represents the results of the multigroup analysis. All analyses were completed with Mplus version 7 (Muthén and Muthén, 1998). Maximum likelihood with robust standard errors (MLR) was chosen as estimation method to control for non-normality of the data. We used FIML to deal with missing data. Participants were nested within schools, therefore we corrected for clustering effects.

Table 1. Descriptive statistics for the study variables for the whole sample and for the two groups (i.e. alcohol available versus alcohol non-available) seperately.

	Whole sample	Alcohol available	Alcohol non-available
	M (SD) (N = 262)	M (SD) (N = 221)	M (SD) (N = 41)
Boy	254	197	37
Ethnicity (non-Islam)	208	177	20
Implicit Associations1	-0.19 (0.47)	-0.16 (0.48)	-0.28 (0.45)
Alcohol frequency1	1.58 (3.14)	**1.77** (3.33)	**0.58** (1.41)
QF1	3.79 (8.80)	3.75 (8.32)	2.49 (11.20)
Problem drinking1	0.85 (1.30)	**0.95** (1.32)	**0.30** (1.05)
Alcohol frequency2	2.80 (6.27)	**3.61** (6.69)	**1.24** (3.19)
QF2	4.29 (9.21)	5.19 (9.28)	2.58 (8.83)
Problem drinking2	0.88 (1.37)	0.95 (1.40)	0.53 (1.21)

QF = Quantity by frequency measure of alcohol use

Bold mean scores for the alcohol measures represent significant differences between the two groups (available vs non-available).

Results

Descriptives

Descriptive statistics for the total sample, and for the two groups (i.e. alcohol non-available and available) separately are presented in Table 1. In the alcohol non-available group relatively more adolescents had a Islamic origin ((phi = 0.31, p = 0.01). Adolescents in the alcohol-available group scored significantly higher on three out of six alcohol use measures at T1 and T2 when compared to the alcohol non-available group: **frequency T1**: t = -3.78, p = .01; **QF T1**: t = .69, p = .25; **problem drinking T1**: t = 3.49, p = .01; **frequency T2**: t = 3.53, p = .01; **QF T2**: t = 1.72, p = .09; **problem drinking T2**: t = -1.99, p = .05. An increase in alcohol use between T1 and T2 was observed in both groups (with the exception of problem drinking for the alcohol-available group which remained stable).

Table 2. Regression analyses of implicit associations predicting future alcohol use for the two groups (i.e. alcohol availability versus non-available) separately

	Alcohol Frequency T2		QF T2		Problem drinking T2	
	available	non-available	available	non-available	available	non-available
	β (SE)	β (SE)	β (SE)	β (SE)	β (SE)	β (SE)
Alcohol Frequency T1	0.54 (0.11) ***	0.51 (0.15) ***				
Implicit associationsT1	0.17(0.07)*	-0.22 (0.14)				
QF T1			0.74 (0.11)***	0.92(0.05)***		
Implicit associations T1			0.07 (0.05)	0.08 (0.05)		
Problem drinking T1					0.67 (0.09)***	0.67 (0.07)***
Implicit associations T1					0.09 (0.07)	0.23 (0.16)

QF = Quantity by frequency measure of alcohol use.
** $p < .05$, ** $p < .01$, *** $p < .001$*

Multigroup model

A main effect of implicit alcohol associations at T1 on alcohol use at T2, while controlling for alcohol use at T1, was only found for alcohol frequency (**alcohol frequency**; $\beta = 0.15$, $p = 0.02$, $\chi2(1) = 0.43$, $p = .51$, **QF**; $\beta = .08$, $p = 0.12$, $\chi2(1) = 0.20$, $p = .66$, **problem drinking**; $\beta = 0.11$, $p = 0.14$, $\chi2(1) = 0.08$, $p = .77$). This finding indicates that more positive implicit alcohol associations at T1 predict a higher frequency of alcohol use at T2.

The results of the influence of implicit alcohol associations on alcohol use as moderated by alcohol-availability (frequency, QF and problem drinking) are presented in Table 2. Model fit for all models was good: **alcohol frequency**: χ 2 (3) = 2.19, $p = 0.53$; **QF**: χ 2 (3) = 2.27, $p = 0.52$; **problem drinking**: χ 2 (3) = 2.24, $p = 0.52$[1]. Only for the frequency of drinking, differential effects across the two groups were found (Wald $\chi2$ (1) = 8.82, $p = 0.01$). For the alcohol-available group, more positive implicit alcohol associations predicted an increase in frequency of alcohol use six months later: $\beta = 0.17$, $p = 0.02$. No such effect was found for the alcohol non-available group: $\beta = -.22$, $p= 0.12$. For both QF and problem drinking, no moderating effect was found: **QF**: Wald $\chi2$ (1) = 0.01, $p = 0.93$; **problem drinking**: Wald $\chi2$ (1) = 0.58, $p = 0.45$.

Discussion

The present study examined the moderating effect of alcohol availability in the home context on the relationship between implicit alcohol associations and alcohol use in adolescents. Results revealed that implicit alcohol association predicted frequency of alcohol use six months later only in adolescents who indicated availability of alcohol at home. No (differential) effects of implicit alcohol associations on alcohol quantity- or problem drinking were found. The influence of implicit associations on frequency of drinking is in line with two previous studies (Grenard et al., 2008; Thush et al., 2008). Grenard et al., (2008) found an effect of implicit alcohol associations on frequency of use.

[1] Confirmatory Fit Index (CFI) and the Root Mean Square Error of Approximation (RMSEA) were not reported because of the low amount of free parameters. RMSEA is set to zero when the $\chi2$ test is smaller than the degrees of freedom (Kenny, 2000).

In addition, Thush et al. (2007) found that implicit alcohol associations differed between abstainers and drinkers and predicted the frequency of binge episodes one year later. Differently from these studies, the design of the current study provides the potential to draw conclusions about the varying influence that implicit alcohol associations have on different aspects of adolescents' drinking behavior; frequency, but not quantity was found to be influenced by implicit alcohol associations. A possible explanation for this finding might be that a craving process is activated through the enhanced accessibility of implicit alcohol associations (Field et al., 2007; Robinson and Berridge, 1993). The present findings may indicate that implicit associations primarily affect the decision whether or not to drink (i.e. drinking occasion) and not so much the amount of alcohol when one is already involved in drinking (for instance on a night out). The urge to drink may be more pronounced in a situation wherein someone decides to drink and is not drinking yet. This might specifically be true for adolescents, because other social processes, such as peer imitation, could affect drinking quantity and overrule the effect of more subtle processes such as implicit alcohol associations (Crone and Dahl, 2012; Larsen et al., 2012).

The effect of implicit associations on the frequency of drinking was only found for adolescents who reported that there was alcohol-available at home. This finding can be understood in two, non-exclusive, ways. First, alcohol availability at home can activate memory associations about alcohol use which guide behavior towards drinking occasions, which is supported by experimental research on the influence of alcohol primes (Krank et al., 2005). For example, alcohol in the refrigerator might activate a positive association about drinking beer which increases the likelihood that alcohol will be consumed when the possibility to drink occurs. Similarly, Krank et al. (2005) found that when adolescents were primed with alcohol related words (e.g. alcohol related setting), implicit alcohol associations were stronger and these associations better predicted current and future alcohol use in adolescents. Thus, the alcoholic context itself may enhance the retrieval of positive associations about alcohol that subsequently predict more frequent drinking.

Second, alcohol availability at home could reflect drinking behavior of parents. Adolescents of whom parents' have alcohol-available at home might consume more alcohol and serve as role model for their off-spring. The impact of adolescents' implicit alcohol associations on drinking frequency might be strengthened through a process of social learning (Krank and Goldstein, 2006; Van Der Vorst et al., 2013). This suggests that parents can influence the development of implicit alcohol associations in their offspring unintentionally, for example through their parenting behaviors and own drinking. Van der Vorst et al., (2013) demonstrated that parental alcohol use predicted the onset of drinking in adolescents, and this relationship was mediated by implicit alcohol associations. Similarly, Pieters and colleagues (2012) found a positive association between automatic processes and adolescent alcohol use in families with a permissive alcohol-specific parenting style, but no such association was found for strict alcohol-specific parenting. The findings of the present study, however, provide no simple answer in favor of one of these processes and more research is needed to reveal the underlying process. In any case, the findings are one of the first to demonstrate that the home context is relevant in relation to implicit alcohol associations. Furthermore, we found that availability of alcohol at home is a decisive factor in the prediction of adolescent' alcohol use by implicit alcohol associations.

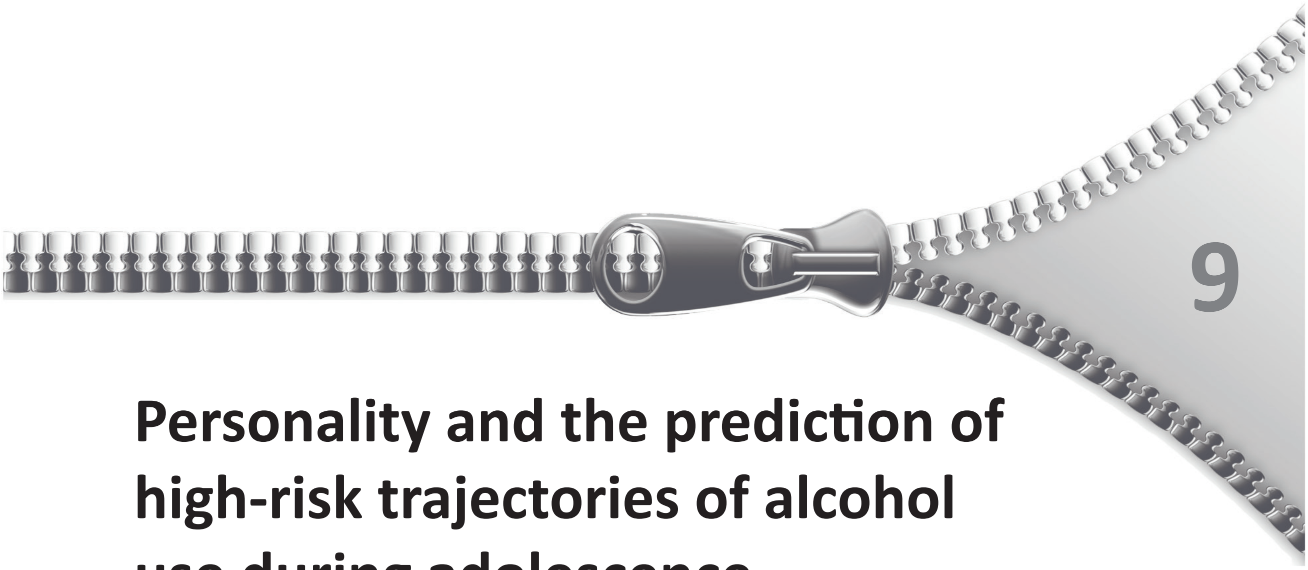
Strengths and limitations

Besides the strengths of this study, such as the longitudinal design, some limitations should be mentioned. First, due to the non-experimental character of the study, we were unable to control for group size. As a consequence, our alcohol non-available group was relatively small compared to the alcohol-available group (41 vs. 221) which may have contributed to a situation in which relatively large regression coefficients not reached significance level. Unfortunately, this is inherent is choosing a natural setting. Future research could attempt to replicate these findings in a more controlled setting, by selecting adolescents based on the alcohol availability at home. Second, we used a fixed order in the SC-IAT, which is good for studying individual differences in prediction (focus here), but not for determining whether adolescents' positive or negative alcohol-associations are stronger. Third, we selected a high risk sample for the current study to ensure enough variation in drinking behavior. This limits the generalizability of the results to other adolescent drinking samples. Fourth, we used self-report measures to assess alcohol use and alcohol availability at home. The reliability and validity of self-report measures has been questioned (Leigh et al., 1998). Nevertheless, a recent study by Koning et al. (2010) demonstrated that self-report of quantity and frequency of alcohol use was a reliable method among adolescents.

Implications

The current findings have important implications for future research on alcohol prevention. This study points at the importance of taking the availability of alcohol in the home context into account. Next to the fact that alcohol availability is strongly associated with adolescent alcohol use (Van Zundert et al., 2006; Eijnden et al., 2011), we have also shown that is strengthens the impact of implicit associations on the frequency of adolescents' drinking. Krank and Goldstein (2006) argue to minimize the effects of positive associations with alcohol to reduce drinking behavior. Prevention programs could benefit from making parents aware of the risk associated with the availability of alcohol at home. This aspect could be integrated in existing evidence-based interventions targeting parenting, such as the program Prevention of Alcohol use Among Students (PAS; Koning et al., 2009; Koning et al., 2011). In the PAS-program, parents are encouraged to set strict rules about alcohol. This message to parents could be complemented by advising parents to reduce the visibility of alcohol at home in order to diminish the accessibility of implicit alcohol associations to memory, particularly during a period when adolescents start with drinking (in the Netherlands often in early adolescence). Randomized clinical trials are needed to investigate whether informing parents about the importance of alcohol at home has a causal effect in less frequent drinking among their offspring.

Overall, these results indicate that the predictive effect of implicit alcohol associations on adolescent alcohol use is stronger in an alcohol related setting; an assumption previously confirmed by Krank et al., (2005). The current study adds to this knowledge by demonstrating that not only priming with alcohol related words enhances the accessibility of implicit alcohol associations, but the home setting also appears to play a significant role in the prediction of future alcohol use by implicit alcohol associations among adolescents.



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Personality and the prediction of high-risk trajectories of alcohol use during adolescence.

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Abstract

Early onset of alcohol use and persistent use of alcohol during adolescence have been associated with later problem behavior, such as heavy drinking and the use of other substances. Several personality characteristics have been related to the onset and persistent use of alcohol during adolescence. In the present study we examine the relation between personality and different high-risk trajectories of alcohol use in adolescents. Participants were 374 (330 boys, mean age = 13.6) 8th graders from 17 different secondary Special Education Schools (e.g. for adolescents with externalizing behavioral problems) in the Netherlands. Adolescents were followed for two years (i.e. four waves) and alcohol use and personality characteristics (SURPS) were assessed. Using latent transition analysis (LTA), three trajectories of alcohol use were identified, a non-drinking group (reference group), an onset group (after wave 1), and an early onset (before wave 1) persistent drinking group. Baseline high sensation seeking predicted group membership of the onset (OR = 2.55) and early onset persistent group (OR = 3.57). Baseline low anxiety sensitivity predicted group membership of the early onset persistent drinking group (OR = 0.42). Particularly in this latter group, high prevalence rates of illegal substance use (i.e. cannabis, ecstasy and cocaine) were found two years later. High sensation seeking and low anxiety sensitivity appear to be important predictors of the early onset of adolescent's alcohol use. Moreover, a combination of early onset and persistent alcohol use demonstrates a heightened risk for the use of other illegal substances in adolescence. Implications for interventions are discussed.

Introduction

Many adolescents start experimenting with the use of alcohol. For instance, the mean age of alcohol onset is around 14 to15 years of age in North- America, (Kosterman et al., 2000; Vega et al., 2002) and around 13 to 14 years in Europe (Hibell et al., 2012). Once initiated, it is easy to transition to more intense use (Monshouwer et al., 2003). The combination of early onset and persistent drinking at an early age has been linked to later problem behavior (De Wit et al., 2000; Maggs and Schulenberg, 2005). For decades, personality is already a factor of interest in the prediction of alcohol use (Arnett, 1996; Eysenck, 1957; Zuckerman et al., 1972) and more recent studies support the relevance of personality in predicting drinking behavior (Castellanos-Ryan et al., 2013; Chassin et al., 2002; Chassin et al., 2004; Krank et al., 2011). However, these studies have not yet examined the influence of personality on the early onset in combination with the subsequent course of alcohol use during adolescence. In the present paper, we therefore focus on personality as a predictor of high-risk alcohol trajectories (i.e. the transition from early onset to persistent drinking) in adolescents at risk for problematic alcohol use with special focus to the prediction of the actual onset during study follow-up.

Variable-centered approaches are particularly relevant for identifying predictors of adolescent alcohol use in homogenous groups. Person-centered approaches can add value when one wishes look at how influences of predictors are reflected in different subpopulations (Muthén and Muthén, 2000; Schulenberg and Maggs, 2002). Many studies on adolescent alcohol use have analyzed alcohol trajectories to consider individual differences in the development of patterns of alcohol use (Flory et al., 2004; Maggs and Schulenberg, 2005). Trajectories of alcohol use can be identified by two different person centered approaches (Muthen and Muthen 2000); (1) growth mixture modeling (i.e. latent subgroups of development over time, as applied in Chassin et al., 2002, 2004) and (2) latent transitions analysis (i.e. latent subgroups of transition patterns over time, as applied in Lanza et al., 2010). LTA is particularly suitable for examining trajectories of drinking onset as this method allows individuals to switch from one latent class to another during study follow-up.

Multiple alcohol trajectories and patterns of use in adolescence have been identified, with four trajectories of alcohol use being the most common outcome; a non-using, infrequent/ low using, moderately using, and persistently (heavy) using group (Chassin et al., 2002; Chassin et al., 2004; Hill et al., 2000; Maggs and Schulenberg, 2004). Particularly the persistent using trajectory, characterized by an early onset of alcohol use, has hereby been linked to the most adverse outcomes, such as fast escalation of alcohol use and a heightened risk of the use of other illegal substances such as cannabis or other hard drugs (Chassin et al., 2004; Flory et al., 2004).

Research on personality has identified several personality characteristics associated with the time of onset and continuation of alcohol use (Castellanos-Ryan et al., 2013; Earleywine and Finn, 1991; Elkins et al., 2006; Krank et al., 2011; Woicik et al., 2009). In particular, overcontrolled/inhibited and undercontrolled/disinhibited personality characteristics (Caspi et al., 1996) are linked to adolescents' alcohol use (Chassin et al., 2002; Chassin et al., 2004). Undercontrolled personality characteristics, such as impulsivity and sensation seeking, are associated with both early onset (Elkins et al., 2006; Wong et al., 2006) and heavy alcohol use in adolescents (Chassin et al., 2004; MacPherson et al., 2010; Nigg et al., 2006). Persons high on sensation seeking tend to search for new experiences (Zuckerman and Kuhlman, 2000) and might therefore be more inclined to experiment with alcohol (Arnett, 1996; Sher et al., 2000). Individuals who have problems with behavioral inhibition appear to act without careful planning and are sensitive to rewards (Zuckerman and Kuhlman, 2000). This might explain the relation between impulsivity and sensation seeking with early onset and heavy use of alcohol that has been found in several studies. Yet, to the best of our knowledge, only one study (Chassin et al., 2004) examined the effect of personality on alcohol trajectories in young adolescents, and only for impulsivity. Thus little is known about the influence of undercontrolled personality characteristics on the course of alcohol use, and in particular on the high risk trajectory of early onset and persistent use.

Overcontrolled or inhibited personality characteristics such as fearfulness and social withdrawal have also been linked to alcohol use. Behavioral disorders closely related to these personality characteristics, such as anxiety and depression, reveal high comorbidity with alcohol use (Rohde et al., 1996; Saraceno et al., 2009). Depressive symptoms appear to be associated with an increased risk for early initiation (Kaplow et al., 2001) and heavy use of alcohol (Rohde et al., 1996). Directly associated, relations between hopelessness and alcohol use and misuse have been found for young adolescents (Krank et al., 2011). Anxiety symptoms of adolescent females (14-18 years) are associated with heavy alcohol use (Rohde et al., 1996). In contrast, a negative association has been found between the initiation of alcohol use and anxiety in early adolescence (12-16 years, Castellanos-Ryan et al., 2013; Krank et al., 2011), suggesting that anxiety might influence alcohol use differently in early or late adolescence. It is important to note that the latter studies examined anxiety sensitivity, a concept closely related to neuroticism and defined as a belief that the experiences of anxiety/fear will have adverse consequences, such as embarrassment or nervousness (Reiss et al., 1986; Reiss, 1991).

In the present study we investigated the predictive effect of personality characteristics on trajectories of alcohol use in young at-risk adolescents. Based on previous literature, we hypothesized that undercontrolled personality styles (impulsivity and sensation seeking) and hopelessness would predict an early onset and persistent use of alcohol (Chassin et al., 2004; Kaplow et al., 2001; Wong et al., 2006). In addition, and in line with Castellanos-Ryan and colleagues (2013) and Krank and colleagues (2011) who also examined anxiety sensitivity in adolescents, we hypothesized that anxiety sensitivity would negatively be associated with engagement in drinking behavior. The high-risk group was selected because of their increased risk for early onset of alcohol use and the use of other substances (Kepper et al., 2011). Because we were interested in the transition of non-use to use of alcohol, latent transition analysis (LTA) was the most suitable method to evaluate different patterns of alcohol use over two years. LTA analysis can identify different latent groups and trajectories, and is particularly suitable for examining transitions of substance use in heterogeneous groups (Lanza et al., 2010; Muthén and Muthén, 2000).

Methods

Participants

Participants were 374 (330 boys, 44 girls) 8th graders from 17 different secondary Special Education Schools in the Netherlands. In the Netherlands, adolescents are referred to these schools when it is no longer possible for them to attend mainstream education because of behavioral and attention problems such as seen in adolescents with Attention-Deficit-Hyperactivity-Disorder (ADHD) or conduct disorder. Participants were followed over a period of two years with 6-8 months between the waves. At baseline, 374 adolescents (mean age = 13.55, SD = 0.86) participated in the study. In the second wave, 279 adolescents (mean age = 14.10, SD = 0.86) were included in the study (75 % response). In the third and fourth waves, 230 adolescents (mean age; 14.60, SD = 0.79, 62 % response) and 196 adolescents (mean age; M = 14.95, SD = 0.76, 53 % response) participated respectively. In total, 381 adolescents completed at least one wave (note that the total number of participants is higher compared to the starting sample, i.e. 374, as adolescents could participate in the study even if they missed the first wave. In addition, some participants missed the second or third wave and again participated during the fourth wave). Three adolescents had missing data on all three alcohol measures; therefore, they were excluded from the LTA analysis. This resulted in a sample of 378 adolescents. Several possible predictors of dropout were examined (e.g., gender, age, alcohol use, smoking, externalizing behavioral problems, and divorce). First, each predictor was analyzed separately. Second, all significant predictors (i.e. smoking, alcohol use and age) were analyzed in a multivariate model, and the results revealed that only age remained a significant predictor of dropout, indicating that older participants were more likely to dropout. To deal with missing data, we used Full Information Maximum Likelihood (FIML), which is an appropriate and frequently used method to deal with missing data (Neworking memoryan, 2003).

Parental permission was obtained through passive consent. Parents and adolescents were notified that the study included questions about alcohol and drugs use. Adolescents were informed about the voluntary nature and confidentiality of the study. Participants could decline participation in the entire study, but could also decline participation in a single wave. Fifteen parents (3.8%) and seven students (1.7%) declined participation before the onset of the study. At each wave, participants completed a questionnaire under the guidance of a trained research assistant. If possible, some adolescents completed the questionnaire under the guidance of a teacher when they were not present at initial time of assessment.

Measures

Alcohol use and problems. Three different alcohol measures were used to assess alcohol use and related problems (Peeters et al., 2012). First, participants rated the number of occasions on which alcohol in the last month was consumed. Possible answer categories ranged from zero to forty times or more (“0 to 10”, 11-19,20-39,40 or more, O’Malley et al., 1983). Additionally, participants were asked to report the drinking days during the week (Monday–Thursday) and weekend (Friday–Sunday), and the average number of alcoholic drinks consumed on weekdays and weekends. Responses could range from 0 glasses to 20 glasses or more (Engels et al., 1999; Engels and Knibbe, 2000). A quantity by frequency score for alcohol use was computed by multiplying drinking days by alcoholic drinks (Koning et al., 2009; Peeters et al., 2012). Problem drinking was assessed with the CRAFFT scale (Knight et al., 1999) which is a screening instrument used in clinical settings to identify adolescent problem drinkers. A modified version of this scale, including only questions referring to alcohol, was used (Ko et al., 2008). In the original scale the questions referred to alcohol or drugs. The scale consist of six items (e.g. “Do you drink alcohol when you are by yourself”?) with “yes” or “no” responses. In the present study, we used this scale as a continuous measure instead of using a cut-off score which is more common (2 or more “yes” answers indicate problematic alcohol use). Cronbach’s alpha for the scale was acceptable (Kline, 2005), ranging between 0.70 and 0.75, respectively for wave one to four.

Table 1. Descriptive statistics for the three alcohol indicators for each wave (N = 378). Means and SD’s are reported for observed cases.

	Wave 1 M (SD)	Wave 2 M (SD)	Wave 3 M (SD)	Wave 4 M (SD)
Alcohol frequency	1.45 (2.95)	1.59 (3.13)	2.57 (5.92)	2.85 (6.45)
Alcohol quantity by frequency	3.36 (7.99)	3.71 (8.64)	4.12 (9.01)	5.59 (10.97)
Problem drinking	0.81 (1.35)	0.85 (1.31)	0.86 (1.39)	0.95 (1.38)
Impulsivity	2.36 (0.73)	2.24 (0.68)	2.19 (0.70)	2.18 (0.79)
Sensation seeking	2.66 (0.74)	2.67 (0.78)	2.71 (0.75)	2.76 (0.76)
Anxiety sensitivity	1.94 (0.51)	1.62 (0.65)	1.66 (0.73)	1.64 (0.74)
Hopelessness	1.71 (0.65)	1.60 (0.58)	1.61 (0.59)	1.55 (0.57)

Personality characteristics. The Substance Use Risk Profile Scale (SURPS, Woicik et al., 2009) was used to assess four different personality characteristics associated with increased risk of substance use, anxiety sensitivity, hopelessness, impulsivity and sensation seeking. The SURPS includes 23 items with four response categories ranging from “strongly disagree” to “strongly agree”. The different subscales reflect patterns of traits that have been related to increased risk for substance misuse in adolescents (Castellanos-Ryan et al., 2013; Krank et al., 2011). The sample anxiety sensitivity item is “I get scared when I experience unusual body sensations”, the sample hopelessness item is “I feel that I’m a failure”, the sample sensation seeking profile is “I enjoy new and exciting experiences even if they are unconventional”, and the sample impulsivity item is “I usually act without stopping to think”. A Dutch version of the original SURPS scale was used (Malmberg et al., 2010). This translated version has been successfully applied in a Dutch adolescent sample. The internal reliability, validity, and test-retest reliability of the original scale are acceptable (Krank et al., 2011; Woicik et al., 2009). Internal reliability of the four subscales in the present sample was acceptable and comparable with Woicik et al. (2009). Sensation seeking: .68, Impulsivity: .74, Hopelessness: .81, Anxiety sensitivity: .70.

Substance use. Cannabis use was assessed by asking adolescents to indicate whether they had used cannabis in the past six months. Adolescents could respond with “ yes” or “no”. Lifetime prevalence of ecstasy and cocaine use was established by asking adolescents to rate the number of occasion on which they used cocaine and/or ecstasy. Response categories ranged from zero to forty times or more (“0 to 10”, 11-19, 20-39, 40 or more). Responses were recoded to either “use” or “non-use” to analyze all three measures on comparable scales.

Strategy for analysis

First, descriptive statistics for the three alcohol indicators and the four personality characteristics are presented (Table 1). Second, to determine different alcohol trajectories, we applied a latent transition analysis (LTA). LTA is an analytic approach that combines longitudinal analyses with a clustering strategy. For each wave, the participant receives a probable class membership (i.e.,latent class), which may or may not be the same group at each wave (e.g. non-drinking for each wave vs. moving from non-drinking to drinking, Lanza et al., 2010; Muthén and Muthén, 2000). As a first step of this analysis, we determined the optimal number of latent classes. One way to do this is running separate latent class analyses (LCA) and subsequently run a LTA to

Table 2. Fit measures for the LTA models tested.

	Entropy	BIC
2 class solution	.85	7178
3 class solution	.88	6765
4 class solution	.87	6493
5 class solution	.87	6311

establish developmental patterns. Another option is to combine these two steps in one analysis, the LTA. Since the focus of the study were trajectories of alcohol use, we adopted the latter approach. Class membership was determined by three indicators; (1) alcohol frequency, (2) alcohol quantity by frequency, and (3) problem drinking. We constrained one of the classes to include only adolescents with zero counts on all three alcohol measures, thus the non-drinking group. This allowed us to define a onset trajectory including adolescents who transitioned from non-use to use. Then we added a second, third and fourth class-solution. Three criteria were used to determine the number of latent classes; (1) entropy, (2) Bayesian Information Criteria (BIC), (3) content of classes. The entropy is a fit measure of the quality of the classification of latent classes. Values close to one indicate good classification. For the BIC, a drop in value indicates a better model fit (Geiser, 2013). The content of the classes was another important criteria. For instance, the amount of class members for each class and the theoretical meaning of the class were evaluated. The BIC and entropy of each model are summarized in Table 2.

Next, measurement invariance over time of the latent classes was examined. Then, observed patterns were transported to IBM SPSS 20 and transitions between classes were evaluated to determine different trajectories of adolescents' involvement with alcohol. Trajectories of alcohol use were determined based on most likely group membership at each measurement and transition between groups over time. Descriptive statistics of the three alcohol trajectories separately are presented in Table 3. The LTA analysis was performed using Mplus version 7 (Muthen and Muthen, 1998-2010) and FIML was used as method to deal with missing data. Because the data were non-normal, maximum likelihood with robust standard errors was used to run the LTA. LTA patterns were transported to IBM SPSS 20 since it is not possible to create trajectories of the patterns in Mplus. If the entropy is high enough (i.e. > 0.80), transporting patterns to other statically programs is allowed (Clark and Muthen, 2009).

Third, the results of a multinominal logistic regression with the four baseline personalities characteristics as predictors and the trajectories as outcome measures are presented in Table 4. Finally, to examine substance use in relation to alcohol trajectories we observed group mean differences between alcohol trajectories in the use of cannabis, ecstasy, and cocaine at baseline and at two-year follow-up (Table 5). A one-way ANOVA and post hoc analysis were applied to determine which trajectories significantly differed in the use of substances.

Table 3. Descriptive statistics for alcohol use for the three trajectories separately (N = 330; a fourth trajectory (N = 48) has been left out, see result section)

	Non-drinking (N = 132)	Onset (N = 54)	Persistent (N = 144)
Alcohol frequency 1	0	0	3.07 (3.64)
Alcohol quantity by frequency 1	0	0	8.11 (11.10)
Problem drinking 1	0	0	1.84 (1.44)
Alcohol frequency 2	0	0.45 (0.81)	3.55 (4.10)
Alcohol quantity by frequency 2	0	1.02 (2.88)	8.54 (11.83)
Problem drinking 2	0	0	1.87 (1.46)
Alcohol frequency 3	0	1.05 (1.68)	6.76 (8.36)
Alcohol quantity by frequency 3	0	2.30 (6.48)	11.14 (12.32)
Problem drinking 3	0	0.66 (1.32)	2.19 (1.44)
Alcohol frequency 4	0	2.87 (6.81)	5.63 (6.98)
Alcohol quantity by frequency 4	0	4.76 (10.76)	14.12 (14.24)
Problem drinking 4	0	0.74 (0.86)	2.42 (1.49)

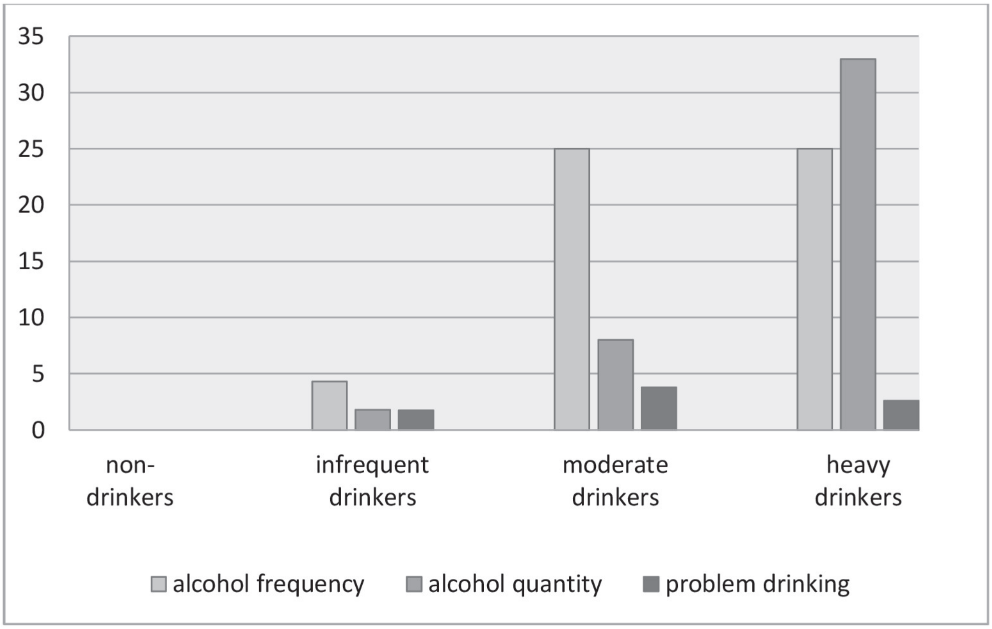
Results

Latent classes

LTA analysis for multiple classes were compared with respect to entropy, BIC and content of the classes (see Table 2). Based on the entropy, a three-class solution turned out to be the best classification index for the four waves. However, the Bayesian Information Criteria (BIC) favored the four-class and five-class solution. Compared to a four-class solution, adding a fifth class yielded no new information since a relatively small group was further reduced in a smaller group, both representing similar drinking groups. Based on the content of the classes and based on previous literature that frequently identified four groups of alcohol users (i.e. non-users, infrequent-, moderate- and heavy-users; Chassin et al., 2004; Hill et al., 2000), a four-class solution was chosen. The means and variances of the latent indicators were restricted to be equal over time (i.e. measurement invariance). In this way we ensured that each latent class represented the same class for each wave. The entropy for the unconstrained model was lower (.85) than for the constrained model (.87) suggesting better classification when constraints are imposed. However, the model fit based on the BIC favored the unconstrained model (BIC constrained = 6492, BIC unconstrained = 6130). Since we exported class membership to SPSS to determine trajectories, a high entropy was preferred and we therefore selected the model with the highest entropy.

Figure 1 presents the scores on alcohol use for each class. The first class included only non-drinking adolescents (i.e. constrained class). The second class included the low infrequent alcohol users. Both frequency and quantity of alcohol use were relatively low in this group. The third group, the moderate drinking group, consumed alcohol several times last month. The last group, the heavy drinkers, consumed more frequent as well as more in quantity during the week. Although this latter group was small (N = 2 to 10; sample sizes within classes differ among the four waves) this group emerged in a 3-class solution as well as in a 4-class solution, suggesting that this group is evident.

Figure 1. Latent classes and mean scores on the three indicators



Note. Class means for each group were the same four all four waves because measurement invariance was assumed

Alcohol trajectories

The LTA identified class membership patterns for each participant. In total, 256 drinking patterns emerged; however, many of these possible patterns included very few or no cases. In a first step, group membership patterns were exported to SPSS version 20 and matching trajectories were identified (e.g., stable, increasing, decreasing). The patterns included either (1) non-drinking adolescents (N =132) or (2) adolescents who had a relatively stable drinking pattern (N = 116). The third pattern included adolescents who increased their alcohol use over time (onset; N = 54 or increasing alcohol use; N = 28). The fourth pattern included adolescents (N = 48) who consumed alcohol at baseline, but stopped or decreased drinking over time. This latter pattern was excluded from further analysis since this trajectory was a combination of drinkers and non-drinkers after wave 2. Based on these results, three trajectories were selected for further analysis (N = 330). One group, the non-drinking group (N = 132), did not initiate alcohol use at follow-up. One group, the onset group (N = 54), initiated alcohol use after baseline (onset during study follow-up). The third group, the so called early onset persistent drinking group (hereafter referred to as persistent group, N = 144), comprised adolescents who consumed alcohol at baseline and continued using alcohol at each follow-up measurement (onset before the start of the study).

Table 4. Multinominal logistic regression for the four risk-personality (reference category is non-drinking group) correcting for all other predictors in the model.

Alcohol trajectories	Baseline predictors	Odds Ratio	95% Confidence interval
Onset group	Sensation seeking	2.55 **	1.57 - 4.33
	Impulsivity	1.05	0.63 - 1.74
	Anxiety sensitivity	0.83	0.48 - 1.42
	Hopelessness	0.92	0.46 - 1.85
Persistent group	Sensation seeking	3.57 ***	2.04 - 4.39
	Impulsivity	1.27	0.76 - 1.58
	Anxiety sensitivity	0.42 ***	0.35 - 0.77
	Hopelessness	1.34	0.71 - 1.85

** p < .05, ** p < .01, *** p < .001*

Personality

Table 4 presents odd's ratios (OR) and confidence intervals (CI) of the multinominal logistic regression analysis with baseline risk personality profiles as predictors and alcohol trajectories as outcome variable. The non-drinking group was the reference category. All four risk personalities were analyzed in a multivariate model (X2 = 60.28, df = 8, p < .01) to examine the unique influence of each profile. Higher scores on baseline sensation seeking predicted the onset (OR = 2.55, CI = 1.51 - 4.33) and persistent drinking group membership (OR = 3.57, CI = 2.33 – 5.49). Lower scores on baseline anxiety sensitivity predicted persistent drinking group membership (OR = 0.42, CI = 0.27 – 0.66). No predictive effects of impulsivity and hopelessness were found. Additional analyses with the onset group as reference category revealed that lower scores on anxiety sensitivity predicted persistent dinking group membership (odds ratio = 0.51, CI = 0.30 - 0.87). Other personality characteristics were not significant predictors of this relationship.

Table 5. Descriptive statistics of cannabis and illicit drug use for each alcohol trajectory separately.

	T1			T4		
	(N = 303)	(N = 303)	(N = 303)	(N = 159)	(N =159)	(N = 159)
	Cannabis	Ecstasy	Cocaine	Cannabis	Ecstasy	Cocaine
Non-drinking (N = 122*)	2 (2%)[a]	0 (0%)[a]	0 (0%)[a]	1 (2%)[a]	0 (0%)[a]	0 (0%)[a]
Onset (N = 48*)	1 (4%)[a]	0 (0%)[a]	0 (0%)[a]	4 (10%)[a]	1 (2%)[a]	2 (5%)[ab]
Persistent drinking (N = 133*)	47 (35%)[b]	9 (7%)[b]	10 (8%)[b]	26 (46%)[b]	8 (14%)[b]	7 (13%)[b]

Counts within columns that do not share a subscript were significantly different between groups. Percentages are between parentheses.

*Samples sizes differ from previous results, because data on substance use was not available for every participant. Results are based on observed information.

Chapter 9

Substance use

Table 5 presents the number of cannabis, ecstasy, and cocaine users at baseline and fourth wave by each alcohol trajectory. Cannabis users at baseline were overrepresented in the persistent group. There were no cocaine or ecstasy users in the onset or non-drinking group at baseline. At wave 4, the number of substance users in the non-drinking group remained virtually stable (i.e. non-existent). The number of cannabis, ecstasy, and cocaine users in the onset group increased slightly over two years. Substance use in the persistent group also increased; however, ecstasy and cocaine users almost doubled. A one-way ANOVA was applied to examine whether groups differed from each other on drug use at wave 1 (ANOVA **cannabis** $F = 37.15$, $p < .01$, **ecstasy** $F = 5.99$, $p < .01$, **cocaine** $F = 6.71$, $p < .01$) and wave 4 (ANOVA **cannabis** $F = 25.91$, $p < .01$, **ecstasy** $F = 6.34$, $p < .01$, **cocaine** $F = 4.44$, $p < .05$). Post-hoc analysis were performed to determine how groups differed. At baseline, the persistent group significantly differed from the onset and non-drinking group on all three drug measures. Two years later, the persistent group differed significantly from the onset and non-drinking group on cannabis and ecstasy use but only from the non-drinking group on cocaine use.

Discussion

The aim of the present study was to evaluate the predictive effect of undercontrolled and overcontrolled personality characteristics with different (high-risk) trajectories of alcohol use in adolescence. Three trajectories were identified, a non-drinking group who did not initiate alcohol use during follow-up, an onset group who initiated alcohol use after baseline and a persistent group who had an early alcohol onset and continued drinking during follow-up. Similar to previous studies (Chassin et al., 2004; Maggs and Schulenberg, 2004), the latter trajectory was identified as a risk trajectory for adverse behavior (e.g., escalation of alcohol use and the use of other substances). With respect to personality, both the onset and the persistent drinking group scored higher on sensation seeking at baseline compared to non-drinkers. These results suggest that sensation seeking might be important for the onset and persistent use of alcohol among at-risk adolescents. Contrary to previous research (Castellanos-Ryan et al., 2013; Krank et al., 2011), impulsivity was not a differentiating personality characteristic in relation to alcohol use trajectories in this study. It is possible that in this at-risk group, impulsivity scores are already relatively high on a group level, and therefore impulsivity may not be a distinctive dimension for onset and persistent drinking. This assumption was supported by data from a community sample of adolescents (paper submitted), who significantly scored lower on this impulsivity measure than the at-riks adolescents in the current study ($t = 2.841$, $p < .01$). The externalizing behavior problems that characterize this group have often been associated with impulsivity and problems with inhibition (Barkley, 1997; Eisenberg et al., 2001).

With respect to the overcontrolled personality characteristic no significant prospective effects on onset or persistent alcohol use were found for hopelessness. Compared to the onset and non-drinking group, adolescents in the persistent group had lower scores on anxiety sensitivity. These results are in agreement with Krank and colleagues (2011) and Castellanos-Ryan and colleagues (2013) who found that anxiety sensitivity was not a risk personality but rather a promotive factor (Sameroff and Fiese, 2000) for the early onset and persistent use of alcohol in young adolescents. That is, lower scores on anxiety sensitivity increase the likelihood of engagement in alcohol use. It has been suggested that anxiety sensitivity relates to avoidance behavior (as opposite to approach behavior, Reiss, 1991), which might explain a negative association between alcohol use and early onset in adolescence (Castellanos-Ryan et al., 2013; Krank et al., 2011). Early heavy drinking indeed has been linked to approach behavior in this at-risk sample (see Peeters et al., 2012, 2013). Fear from adverse outcomes might prevent adolescents who are high on anxiety sensitivity from experimenting with alcohol and from entering social situations in which alcohol is consumed. This might change for anxious individuals when drinking is initiated later in adolescence. Alcohol might then diminish the stress responses experienced in social stressful situations, such as parties and in pubs (Finn and Pihl, 1988; Morris et al., 2005). This finding supports the importance of understanding the influence of personality characteristics on alcohol use in a broader context (Sher et al., 2000), in which risk personalities in relation to alcohol use might underlie motivational and appetitive processes such as reward seeking and increasing of positive- and decreasing negative affect (Cooper et al., 1995).

Regarding the use of illicit substances, the results are in agreement with previous studies linking (early) persistent alcohol use to an increased risk for (later) substance use (Gruber et al., 1996; Kosterman et al., 2000; Wagner and Anthony, 2002). Among the persistent drinkers the percentage of drug users at baseline as well as two years later, is much higher compared to the onset and non-drinking group. Among the non-drinkers almost none of the adolescents had experimented with drugs. The onset group reveals a slight increase in the number of substance users after two years, but included relatively few substance using adolescents after two years compared to the persistent group. When alcohol use is no longer alluring, experimenting with other drugs might be the next step (a phenomenon also described by the Gateway Hypothesis (Kandel, 2002). There appears to be a strong relation of early onset with persistent alcohol use and the use of other illegal substances.

A possible limitation of this study is that we included adolescents in the onset drinking group when they started drinking after baseline, irrespective of the time of the onset. Due to the small amount of adolescents in this trajectory, it was not possible to evaluate the onset for each wave separately. Nevertheless, 43% of the adolescents in the onset group started using alcohol at wave 2. Considering the fact that we followed our sample for two years (i.e. until the age of 16), onset after baseline is still indicative for early onset in this group. In addition, the generalizability of these results is restricted due to the specific characteristics of the sample (e.g. behavioral disorders, few girls, 12%). Unfortunately, we could not control for behavioral disorders in our analysis because information about DSM IV behavioral disorders was not collected due to feasibility and ethical reasons. Behavioral disorders might explain susceptibility to some of these personality characteristics (Barkley, 1997) and perhaps explain why some adolescents are more vulnerable for heavy alcohol use than others (Sher et al., 2000). With respect to gender, we repeated the analysis for boys only, finding similar outcomes. Nevertheless, anxiety sensitivity may still be a relevant risk factor in a more balanced gender sample as previous studies reveal particularly for high anxious females, an increased risk on alcohol use (Stewart et al., 1995). Several studies (Chassin et al., 2002; Groenman et al., 2013; Nigg et al., 2006) indicate that this group of adolescents is at-risk for the development of problematic patterns of substance use. This study not only confirms this increased risk, but also provides information to identify this subgroup based on specific personality characteristics (Conrod et al., 2008) even before the onset of drinking. In addition, for the analysis where FIML was not available (Table 4), the drop-out rate for wave four was relatively high. Therefore, the results related to the sub-question examining drugs use among the different trajectories, should be interpreted with some caution. Nevertheless, an ANOVA takes sample size differences into account while identifying significant differences between groups. A last limitation is associated with the sequence of substance use. Although there is a strong relation between early and persistent alcohol use and the use of other illegal substances, we do not know whether alcohol is the first or subsequent drug of use because adolescents in the persistent trajectory already initiated alcohol use before the study started.

The results indicated that contrary to previous findings based on mainstream samples, impulsivity is not a differentiating risk personality factor for the onset or heavy alcohol use in this at-risk sample. High sensation seeking appears to be a risk factor for persistent (heavy) drinking in this group. Low anxiety sensitivity is associated with persistent use of alcohol. Regarding adverse outcome behavior, the high risk alcohol trajectory of persistent alcohol use is clearly linked to (later) substance use and increased drinking behavior during two year follow-up. Personality-targeted interventions (Conrod et al., 2008) may help prevent the escalation of use. However, interventions should start early, as adolescents who initiate drinking at a young age (i.e. mean age is 13.1) are most susceptible to the escalation of substance use.

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How to handle missing data in at-risk populations: A comparison of different approaches.

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Abstract

Many researchers have to face the problem of missing data in longitudinal research. Particularly high risk samples are characterized by missing data which can complicate analyses and the interpretation of results. The high risk sample in the current study includes adolescents at risk for problematic alcohol use. An early onset of drinking is associated with later problem drinking, and onset of drinking was therefore examined. This study evaluates different techniques to handle missing data, and advocates a solution to efficiently handle substantial amounts of missing data. Five frequently used methods to deal with missing data are discussed and evaluated. A simulation study was conducted to determine the most optimal method to deal with the missing data. Participants were 374 adolescents (mean age is 13.6 years) at baseline. Adolescents completed a questionnaire, including questions about alcohol use, personality and background information. Onset of drinking during study follow up was the outcome variable. Results revealed that multiple imputation (MI) using predictive mean matching was the most optimal method with respect to lowest bias and the smallest confidence interval (CI) while maintaining power. Listwise deletion and last observation carried backward also scored acceptable with respect to bias, however CI's were much larger and sample size almost halved using these methods. In high risk samples, where enrollment of participants is difficult and missingness is inevitable, it is important to retain sample size. In the present study only MI could accomplish this while keeping the bias low. Longitudinal research in high risk samples could benefit from using MI in future research to handle missing data.

Introduction

Longitudinal studies are essential for addiction research, as they can be used to track individual change across the lifespan and predict individual differences in such changes (Biederman et al., 1997; Jackson et al., 2002; Maggs et al., 2008). However, following the same people for a particular period of time does not always result in valid conclusions, due to missing data. The issue of missing data occurs when longitudinal surveys fail to observe the complete set of measurements of respondents. Respondents may have (consciously or unconsciously) skipped some items or they may have missed entire waves of the study. Missing data are increasingly problematic when researchers are interested in event occurrence, or levels of change over time (Van Buuren et al., 1999).

There are already many textbooks and tutorial papers on how to deal with missingness (Enders, 2010; Hallgren and Witkiewitz, 2013; Jeličić et al., 2009; Schafer and Graham, 2002). Most researchers know that not dealing with missing data may lead to invalid results. Despite all this, many researchers still ignore the issue of missing data. For instance, out of the 85 prospective studies (190 papers in total) published in Addiction in 2012, only 55 (65%) reported on how the researchers had handled missing data. Among these papers, two reported to have no missing data, four reported to used ad hoc imputation methods (e.g. replace missing values with non-use or continued use), 33 papers used listwise or casewise deletion to deal with missings (23 of these studies carried out an attrition analysis), four reported to have used the default settings of a software package, six reported to have used full information maximum likelihood (FIML, explained in more details later). Lastly, six papers reported to have used multiple imputation (MI) techniques to deal with missing data. The other 35% of the studies ignored the topic of missing data altogether. In the current paper we will evaluate the above mentioned methods (i.e. with the exception of FIML) to handle missing data and highlight the pitfalls associated with each of these methods using an empirical illustration of a high relevance to addiction research: The relation between drinking onset and undercontrolled personality styles in adolescence.

Specifically when studying high risk populations, missing data is more common than in community samples and loss of participants during the study is almost unavoidable (Windle, 1990; Wolke et al., 2009). Background variables associated with missingness, often are also of interest in studying risk behavior, and many times these variables are correlated with each other (missing at random, MAR). Socioeconomic status for instance has been linked to substance use (Fergusson et al., 1996; McGee et al., 2000), as well as to missingness (Van Beijsterveldt et al., 2002). In addition, factors such as single-parent households and disruptive behavior in children have been associated both with attrition (Kazdin et al., 1993; Wolke et al., 2009) and substance use in adolescents (Barrett and Turner, 2006; Kepper et al., 2011; Wong et al., 2006). The difficulties of having missing data that characterize these high risk populations, strikingly often reflect the reasons why particularly these groups are at risk and should receive attention from researchers. This observation is supported by several studies who highlight the importance of studying risk groups (Moffitt and Caspi, 2001) and risk factors (Hawkins et al., 1992) in relation to substance use in adolescents, but at the same time struggle with missing data (Bonomo et al., 2004; Carroll et al., 2012; Fergusson et al., 2007; Grant et al., 2001; Peeters et al., 2014b). Van Buuren mentioned in his book "the occurrence of missing data has long been considered as a sign of sloppy science." (p 5, 24). Directly related, studies with significant amounts of missingness have more often been criticized by reviewers and are more difficult to publish than papers with few missing data (Van Buuren, 2012). This preoccupation will definitely be justified in certain cases, but should not lead to undervaluation of important results when missing data are handled with appropriate imputation techniques.

In what follows we first introduce an empirical example about drinking behavior in at-risk adolescents and highlight why it is important to study such a risk group even when we know beforehand missing data is unavoidable. We will use the example to describe what the drawbacks are if methods like listwise deletion, or ad hoc methods (e.g. replace missing values with non-use) are used to handle missing data. Secondly, we will discuss different types of imputation methods to deal with missing data. A simulation study is conducted and to accommodate replication of our results, the full syntax is provided in the online appendices. Results of the simulation study evaluating different imputation techniques are discussed and concluding remarks, based on this analysis, are provided.

Empirical Example: Drinking behavior in at-risk adolescents

The methodological issue of missing data is demonstrated, using an exemplary longitudinal study carried out in The Netherlands. The sample included adolescents at-risk for heavy alcohol use and problem drinking. Adolescents were selected from seventeen secondary special education (SE) schools in the Netherlands. Previous findings have revealed that particularly adolescents from SE schools are at risk for alcohol related problems (Kepper, et al., 2011). Adolescents are referred to these schools when it is no longer possible for them to attend mainstream education because of behavioral and attention problems such as seen in adolescents with Attention-Deficit-Hyperactivity- Disorder (ADHD) or conduct disorder. At baseline 374 adolescent participated in the study, of whom 330 (88%) boys and 44 (12%) girls (see table 1). Adolescents were between 12 and 14 years of age at the beginning of the study (mean age = 13.6). Assessments were completed at schools under the guidance of a trained research assistant. Respondents were asked to fill out a questionnaire about demographic factors (gender, age) alcohol use, smoking behavior, drug use (cannabis, ecstasy and cocaine), and personality (Substance Use Risk Profile Scale, SURPS, Woicik et al., 2009; Wolke et al., 2009) and completed a set of cognitive tasks on the computer. Assessment took place at school, every six to eight months over a period of two years (i.e. four waves).

Table 1. Description original sample (N = 374)

	Wave 1	Wave 2	Wave 3	Wave 4
N	374	279	230	196
Missing	2%	25%	39%	48%

The variable of interest was the onset of drinking during study follow-up (paper submitted for publication; prediction of age of onset by behavioral undercontrol using survival analyzing techniques). Previous studies indicate that in Europe, the average age of drinking onset is 13 to 14 years (Hibell et al., 2012). In America, the age of onset is around 14 to 15 years (Kosterman et al., 2000). In Europe and America, approximately 50% of the adolescents start drinking before the age of 15. An early onset of drinking is associated with rapid escalation of alcohol use and later problem drinking (Monshouwer et al., 2003). The adolescents in the current high risk sample reveal an increased risk for later problem drinking because of the early and heavy use of alcohol (Kepper et al., 2011).

The alcohol questionnaire in the current study included several measures of alcohol use (e.g. frequency, problem drinking, quantity). For the onset of drinking we used a quantity-frequency measure that assesses amount of glasses consumed during the week and weekend. Participants were asked to indicate on how many days during the week and during the weekend they regularly consumed alcohol. In addition, the amount of glasses on such regular day was reported. Drinking onset was based on drinking one or more glasses on either a weekend or weekday resulting in a dichotomous variable. Adolescents who already consumed alcohol at baseline were not of interest for the analysis because onset could not be determined. This resulted in a sample of 213 adolescents.

Missing data and model

The current study included four waves with data collected every six to eight months. Missigness in this longitudinal study was induced by absence during a particular assessment of the study. Some participants (N =7; 2%) missed the first wave, however they were allowed to participate in the following waves. Participants who at least completed one wave were included in the analysis (see Table 1). Attrition analyses revealed that smoking, age and alcohol use were significant predictors of missigness. Additional analysis revealed that only age remained a significant unique predictor of missingness; particularly older participants had missing data (attrition analysis explained in Peeters et al., 2014b). Although all participants were eight graders at baseline, age differences occur more commonly in SE compared to mainstream education. Students in SE are assigned to a class based on their cognitive level and less frequently based on their age, resulting in larger variation of age within classes. The Dutch compulsory education law mandates youth up to 16 years to attend school. This law can explain the missing data of older adolescents in our sample. It is possible that older adolescents more likely come in contact with the justice system (court visit, serve a sentence), skip school more often and therefore are more likely absent during assessment. Not surprisingly, was the higher substance use among these older participants, resulting in sample with missingness at random (MAR).

We analyzed two models; first, we were interested in how well the missing data handling techniques could replicate the amount of onsetters that we would detect during the study follow-up. Second, to predict onset we evaluated the effect of two undercontrolled personality styles, commonly associated with alcohol use, namely sensation seeking and impulsivity assessed with the SURPS (Woicik et al., 2009). The rationale for this last model lies in the complexity of real life models. As researchers we do not simply want to know the amount/percent of drinkers in a sample, but many times want to predict this outcome by other variables.

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Methods of dealing with missing data

Five methods frequently used in addiction research (methods that were observed during our literature review evaluating paper published in Addiction in 2012), to handle missing data will be discussed[1]. The methods that will be discussed and evaluated are: Listwise deletion (strategy 1), last observation carried backward (strategy 2), conservative imputation (with missing values replaced by non-drinking, strategy 3), multiple imputation using logistic regression (strategy 4), and multiple imputation using predictive mean matching (strategy 5), The first method, listwise deletion, is the easiest way to deal with missing data: an entire record is excluded if any single value is missing on one of the variables that are of interest in the analysis. Since such a procedure limits the amount of usable data, it puts a restriction on the sample size and reduces power. Moreover, it can waste a great deal of multivariate information, resulting in inefficient parameter estimates (Muthén et al., 1987; Wothke, 2000). When the assumption of missing completely at random is not met, this method can result in serious bias (McPherson et al., 2012).

The second method, last observation carried backward is a manual imputation method. A missing value is replaced with the last observed value. If data of wave 3 was missing for participant X, but wave 4 was observed then the value of this wave was used to replace the missing value. Missing values at wave 4 were not replaced. Difficulties occur when there are no observed values after the missing data, and when more than one wave is missing. Therefore we restricted this method to impute values for cases with only one missing. Similar to listwise deletion this method results in loss of information and decrease of power (Graham, 2009; MacCallum et al., 1996).

[1] Full information Maximum Likelihood (FIML) was another method frequently observed in our literature review. This method uses al information available without imputing exact values. Parameter estimation for missing values is based on "borrowed information" of other observed values. Observed values contribute more to the log-likelihood than missing values (Enders & Bandalos, 2001). In case of missingness on the dependent variable, in this case on onset of drinking, FIML is not an available method to handle the missing data and therefore was not examined in the current study. Besides MI, FIML has proven to be successful in handling missing data, as demonstrated by a recent simulation study (Hallgren and Witkiewitz, 2013).

The third method is conservative imputation, a common method used in drop-out after treatment (Croucher et al., 2012; McPherson et al., 2012; Walker et al., 2012). Missing values are replaced with use or non-use depending on the research question. This method assumes to avoid overestimation by replacing missing values in a conservative way. For instance, for studies examining success of smoking treatment, drop-out before follow-up analyses is often rated as treatment failure (i.e. participant is still smoking). However, this method results in biased treatment effects (McPherson et al., 2012).

The last two methods are multiple imputation techniques and have been identified as adequate methods to handle missing data (Rubin, 1996; Sterne et al., 2009). Each missing value is imputed several times to reflect uncertainty, creating several imputed data sets (Schafer and Graham, 2002; Sterne et al., 2009). An important factor associated with reliability and accuracy of multiple imputation is selecting the appropriate MI method (e.g., logistic, linear, Bayesian linear, Royston and White, 2011; Rubin, 1996; Van Buuren and Oudshoorn, 1999). Fortunately, many statistical packages allow researchers to select suitable MI methods to handle the missing data. One such method is logistic regression, which is particularly suitable for incomplete binary variables (Van Buuren and Oudshoorn, 1999).

A slightly different approach is MI using predictive mean matching. Missing values are imputed based on the assumption that closely similar cases provide the best information for incomplete data (Royston and White, 2011). Missing data values are replaced by values of that variable coming from cases that are most similar. These cases can be similar other cases but of course also values of previous waves of the same case. An advantage of this method is that missings are replaced by values that actually appear in the data for that specific variable (e.g. a binary variable is replaced by either one of the two values, Little, 1988).

In the present study we used the R-package (R Development Core Team, 2013) MICE (Multivariate Imputation by Chained Equations; Van Buuren and Oudshoorn, 1999), but other statistical packages are available. We chose MICE for its flexibility and customizability in, amongst others, specifying the imputation model and evaluating the imputations.

Simulation study

A short summary of the simulation is provided in the next paragraph and a comprehensive description can be found in the appendix A (see next page). The syntax needed for the simulation can be found in the online appendix B and C. The simulation study consisted of four steps:

1. Based on the original sample (e.g. using sample statistics such as means and standard deviations, see appendix A for detailed description), 500 new data sets, without missing data, were generated (i.e."true data set").
2. Based on missing data patterns (e.g. proportion of missingness for each wave, distribution of missingness) and information from the original sample, missingness was generated in new data sets (N = 500).
3. The missing data handling methods were applied on all of the datasets (either imputation or deletion).
4. As a last step the models of interest were analyzed (percentage of onsetters, and the regression of sensation seeking or impulsivity on onset of drinking).

We evaluated the model using criteria derived from general suggestions by Van Buuren (2012), namely;

- Remaining missing data expressed in sample size (e.g. power of study, see Table 2)
- Percentage of onsetters (see Table 2).
- Confidence interval (CI) width: 95% confidence intervals lengths for each dataset were calculated (mean over 500 datasets is reported), with respect to the amount of onsetters. Small length confidence intervals indicate more certainty (see Table 2).
- Coverage percentage: As a measure of success, we calculated what proportion (average over 500 datasets expressed in percentage) of these confidence intervals indeed contained the true amount of onsetters that we would have found if there was no missing data (see Table 2).
- Bias indicated in mean, median, minimum and maximum bias over 500 data sets (see Figure 1).
- Predictors sensation seeking and impulsivity: Bias in terms of mean, median, minimum and maximum (see Figure 2), percentage of coverage and confidence intervals width that contain the true regression coefficients of the two predictors (see Table 3).

Appendix A

Simulation study

A simulation study was conducted to evaluate the performance of different missing data handling techniques. The onset variable (i.e. onset of drinking) itself was not generated, because it had to be based on scores from different waves where missing data could appear at different moments in time. The population values for the variables were inspired by the values observed in the sample dataset. Yes/no alcohol scores for the second (onset2), third (onset3), and fourth (onset4) wave, and gender were specified as dichotomous variables. The alcohol quantity-frequency variable (QF) and smoking were generated as zero-inflated count variables (e.g. variables were skewed Poisson distribution with many zero values). All other variables (i.e. age, problem drinking, cannabis use, drug use, lifetime alcohol use) were specified as having a normal distribution. The relations between the variables as found in the original data set were reconstructed by covariances and regressions. The data was generated by means of a Monte Carlo simulation (see Appendix B) in Mplus 7.0 (Muthen and Muthen, 1998-2011). After generating 500 complete data sets, values were made missing on onset2, onset3, and onset4 in R (see Appendix C, Van Buuren and Oudshoorn, 1999; R Package Plyr: Wickham, 2011; R Package Zoo: Zeileis and Grothendieck, 2005). About 13% of the participants had only one missing score over the three waves where missing data was possible. Another 13% missed two onset wave scores and again another 13% missed all three onset wave scores. As a result of this, 39 percent of the final scores on onset over 500 replicated files composed of missing data. All mentioned probabilities and proportions were based on the sample data set (N = 213). No missing data was generated on the independent variables sensation seeking and impulsivity (subscales SURPS), because these were first wave variables on which the proportion of missing data in the sample dataset was negligible (i.e. 2%, see Table 1).

Results

Results dependent variable: Onset

Results for the outcome variable, drinking onset, are discussed first, starting with remaining missing data, followed by percentage of onsetters, 95% CI width and coverage with respect to amount of onsetters (with smaller width and higher coverage indicating more accuracy and better precision) and bias (mean, median, maximum and minimum) in onset of drinking over 500 data sets (with lower bias indicating better approximation of the "true data set").

Table 2. Percentage onsetters (mean over 500 generated datasets) and sample size of the five methods.

	Percentage onsetters	Sample size	CI width	Coverage percentage
"True" data set[1]	43.36%	213		
1. Listwise deletion	41.31%	130	16.88	99.0%
2. Last observation carried backward	41.40%	145	15.99	99.8%
3. Conservative	33.65%	213	12.66	4.6%
4. MI logistic regression	45.33%	213	13.35	98.8%
5. MI predictive mean matching	44.79%	213	13.31	98.4%

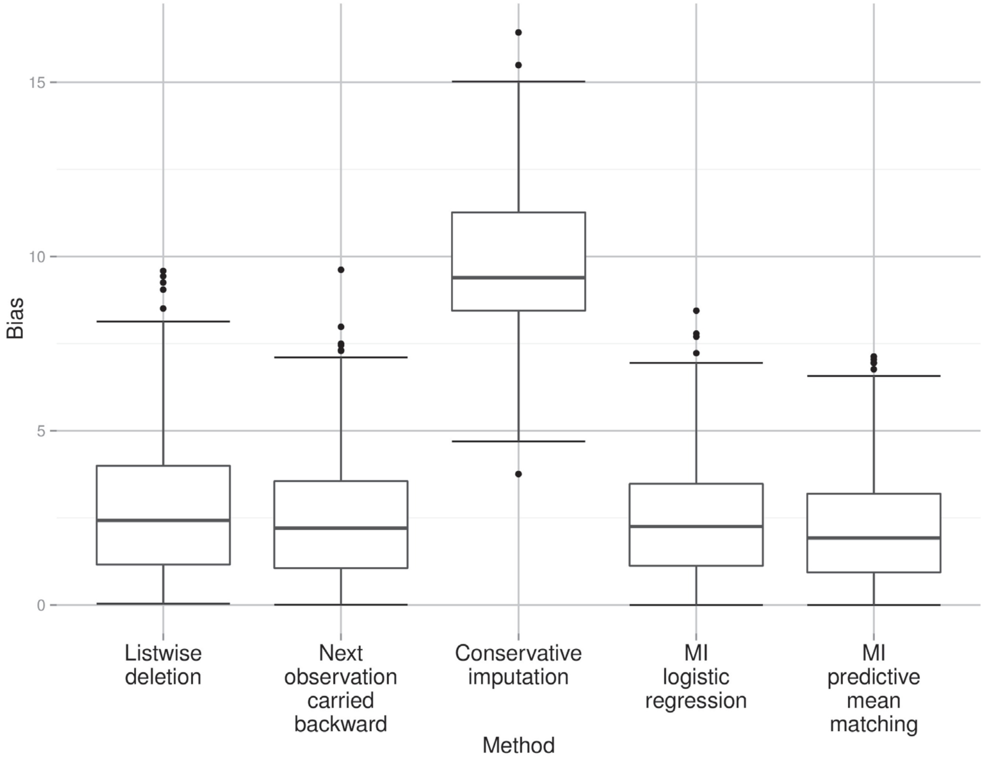
[1] new generated complete data set based on the original sample statistics.

For listwise deletion (strategy 1) the full 39.0 percent of missing data remained, leaving only 130 cases in the analysis. Last observation carried backward (strategy 2) resulted in 31.9 percent of missing data (N = 149). The application of both multiple imputation methods and conservative imputation left no missing data (see Table 2).

Regarding the percentage of onsetters, the following methods hardly differed in outcome with respect to identified percentage of onsetters, namely, listwise deletion (2,03% deviation), last observation carried backward (1.96% deviation) and MI (logistic regression; 1.97%, predictive mean matching; 1.42% deviation).

The 95% CI width for the amount of onsetters and the coverage proportion with respect to the "true" amount of onsetters were calculated. When balancing both the width

Figure 1. Graphical presentation of the mean, median, maximum and minimum bias for onset of drinking (over 500 datasets) for each of the five methods.



and the percentage of coverage, both MI methods (strategy 4 and 5) appeared to be the best methods (see Table 2). The conservative method revealed the smallest CI width (12.66), however this method had the lowest coverage percentage (5%), resulting in only 5 percent of the confidence interval containing the "true" percentage of onsetters. This indicates that conservative imputation does not properly account for the uncertainty associated with missing data and, in fact, considers its results more `certain' about the true value than it actually is. The highest coverage was obtained with last observation carried backward (strategy 2, 99.8%), however, the width of the CI interval for this method was relatively large (15.99), indicating more uncertainty about the estimate than is actually needed.

With respect to bias, the distribution of bias over all 500 sets was evaluated. The absolute lowest bias (0.0), lowest mean (2.32), lowest median (1.89) and the lowest maximum bias (8.10) on onset were obtained with MI using predictive mean matching (strategy 5, for more details, see Figure 1).

Table 3. Regression coefficient coverage and CI width of the five methods.

	CI width		% Coverage	
	β1	β2	β1	β2
1. Listwise deletion	0.66	0.74	100.0	99.6
2. Last observation carried backward	0.62	0.69	100.0	99.8
3. Conservative	0.53	0.59	97.8	99.0
4. MI logistic regression	0.71	0.79	100.0	100.0
5. MI predictive mean matching	0.60	0.66	100.0	100.0

β1 = sensation seeking, β2 = impulsivity.

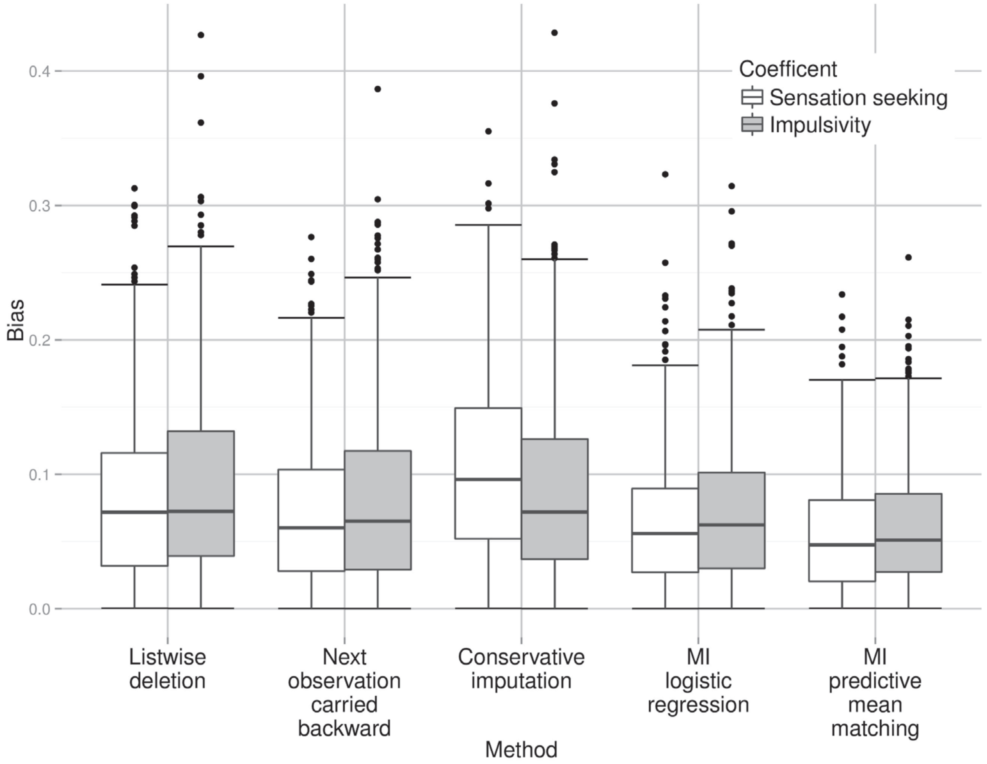
Results predictors: Sensation seeking and impulsivity

The lowest minimum and mean bias for the first regression coefficient (i.e. sensation seeking) were obtained with multiple imputation using predictive mean matching (strategy 5). Conservative imputation (strategy 3) scored worst on all distributional aspects as clearly can be seen in Figure 2. For the second regression coefficient (i.e. impulsivity), differences between methods were smaller. The best overall scores were obtained by predictive mean matching (strategy 5). Multiple imputation using logistic regression (strategy 4) had scores close to that of predictive mean matching. A graphical presentation of the bias for each method and for both regression coefficients can be found in Figure 2. With respect to coverage and confidence interval width, both the length and the width combined were most optimal for multiple imputation using predictive mean matching (see Table 3).

Conclusion

In the present study we evaluated five different methods used in addiction research, to handle missing data. The methods were tested on several criteria, including sample size, percentage of onsetters (i.e., percentage of adolescents who started drinking during study follow-up), CI width and coverage with respect to amount of onsetters and bias across 500 datasets. The results indicate that multiple imputation is the most efficient approach to deal with missing data, yielding accurate, consistent and plausible results with excellent coverage. Performance of

Figure 2. Graphical presentation of the mean, median, maximum and minimum bias for the regression coefficients (sensation seeking and impulsivity) over 500 datasets, for each of the five methods.



listwise deletion, the most used strategy in Addiction (33 studies of the 85 longitudinal studies published in 2012), and last observation carried backward is worse than the performance of multiple imputation. Moreover, listwise deletion and last observation carried backward reduce sample size, which results in loss of power and the use of such methods is therefore strongly discouraged.

The current results also indicate that with a binary outcome, last observation carried backward and other single imputation methods are particularly risky because these methods impute a value that is either 'yes' or 'no' without reflecting any uncertainty. Multiple imputation methods properly account for this uncertainty and take into consideration that the true value remains unknown. In the present example, MI identifies the most optimal amount of onsetters, produces the best CI width and coverage, reveals the least bias and remains the original sample size, even when a substantial amount of data is missing (under conditions of MAR). It should be mentioned that we focused on ignorable missing data in the current study, however in some circumstances the missing data might be non-ignorable (missing not at random, NMAR). There are several methods and statistical package available to handle NMAR missing data (see Schafer and Graham, 2002 for an overview), however it goes beyond the scope of this paper to discuss them all. With respect to the MI method used in the current study, it has been argued that when enough predictors for missingness are included (e.g. auxiliary variables) in the imputation model, the assumption of MAR becomes more likely and the need for specific models under MNAR conditions is less prominent (Van Buuren et al., 1999). According to Graham (2009), "an auxiliary variable is a variable that is not part of the model of substantive interest, but is highly correlated with the variables in the substantive model regardless of whether it is also associated with the probability of nonresponse." (p. 560).

For future research we strongly advise researchers, reviewers and editors to pay special attention to missing data; studies should at least:

- Report the amount of missing data;
- Report on the missing data mechanism (e.g. missing completely at random (MCAR), missing at random (MAR), missing not at random (MNAR);
- Report the way missing data is handled
- Use better methods than list wise deletion or last observation carried backward to deal with missing data; multiple imputation methods are preferred. When multiple imputation methods are applied, auxiliary variables can be selected to improve the handling of missing data.

The results of this simulation study show that none of the methods tested are flawless. As Orchard and Woodburry (1972, p. 697, 43) remarked: "the best way to treat missing data, is having no missing data". But as we have argued in the introduction, this is often not feasible in longitudinal studies, particularly not when it involves a high risk group. In such cases, using MI results in the least bias and maintains the most optimal sample size.

11

Discussion

Goals

This thesis addressed ambiguities in the recent literature on alcohol use and cognitive functioning in young adolescents. The main questions in this study focused on the hypothesized (bi)directional relationships between alcohol use and cognitive processes. First, we examined the bidirectional and prospective relationships between cognitive functioning and alcohol use in young adolescents (both in at-risk and in a community sample of adolescents). Second, we examined the bidirectional relationship between automatic processes and alcohol use in at-risk adolescents, as well as the moderating role of executive functioning within this relationship. Third, we evaluated the moderating effect of the social context on the relationship between alcohol use and automatic processes in at-risk adolescents. The availability of alcohol at home was hypothesized to be a factor, which could moderate the association between automatic processes and adolescent drinking.

Main findings

The bidirectional relationship between alcohol use and cognitive functioning

The literature search on cognitive impairments and adolescent alcohol use (chapter 2) revealed that both impairments in cognitive functioning were found before, as well as after heavy alcohol use in drinking adolescents (Hanson et al., 2011; Khurana et al., 2012; Nigg et al., 2006; Squeglia et al., 2009; Tapert et al., 2002; Wong et al., 2006). This suggests a reciprocal relationship, in such way, that alcohol use can have neurotoxic effects on the adolescents brain, as well as that cognitive impairments predict the increase in alcohol use in adolescents. A logical question following from these findings, but not examined in the above mentioned studies, is whether impairments in cognitive functioning precede the onset of drinking and provoke further delay in development through continued use of alcohol, or whether there is a neurotoxic effect of alcohol use on the adolescent brain without existing impairments prior to the onset of drinking. The studies discussed in this thesis (chapters 3, 4 and 5) were designed to find an answer on this question. In the following we will discuss the main findings of these studies by focusing on two notable differences between the two lines of research (cognitive impairments as risk factor or as a consequence of alcohol use), namely (1) the severity of alcohol use and (2) the cognitive processes that were central in the study. In evaluating the cognitive impairments we will focus on both impairments in executive functioning (e.g. working memory, response inhibition, also referred to as cognitive control), as well as on cognitions associated with processes other than cognitive control.

First, the adolescent samples in the previous studies differed considerably in the amount of alcohol they consumed (as discussed in chapter 2). Impairments in cognitive functioning after prolonged alcohol use were mainly found in clinical (e.g. diagnosed with a DSM IV alcohol use disorder) and heavy drinking samples (Hanson et al., 2011; Tapert et al., 2002). In contrast, in a community sample of adolescents, only a predictive effect of cognitive impairment (weakness in working memory) on adolescent alcohol use was found. In this sample, increase in alcohol use over time was not associated with cognitive impairment (Khurana et al., 2012).Whether or not neurotoxic effects of alcohol on the adolescent brain are found may therefore depend on the amount of, and the frequency by which alcohol is consumed. Support for this conclusion is provided in chapter 3 and 4. In both longitudinal studies we used a cross-lagged model which provides the possibility to draw conclusions about the direction of the examined relationship. In chapter 3, working memory in relation to alcohol use in at-risk adolescents was examined. In this at-risk sample, including adolescents from SE education who consume more alcohol compared to their peers in mainstream education (Kepper et al., 2011), we found support for heavy alcohol use predicting suboptimal development of working memory six months later. However, we also found support for the reverse relationship; relatively weak working memory at the first measurement predicted an increase in alcohol use six months later. The latter relationship was found in two successive waves, while the former relationship was found only in the first wave. These results indicate that in at-risk adolescents, heavy alcohol use might cause a delay in the development of working memory, and this relative weakening of working memory might further predict escalation of alcohol use later in adolescence. Although cross-lagged models are eminently suitable for examining the direction of reciprocal associations (Geiser, 2013), the results of this study were inconclusive with respect to the direction of the effects, making it difficult to draw firm conclusions. The results of chapter 4 were more unambiguous with respect to the direction of the effect. In chapter 4, the predictive effect on alcohol use of three cognitive processes involved in impulsive behavior (inhibition, risk-taking and delay discounting), was examined in an English adolescent community sample. In line with our hypothesis, we only found effects of high impulsivity predicting an increase in alcohol use six months later. No effects were found for the other direction. Together these two studies (chapter 3 and 4) indicate that impairments might arise particularly in heavy drinking adolescents while they are less likely to emerge in adolescents with relatively normal drinking patterns. Nevertheless, since both drinkers and non-drinkers were included at baseline, a conclusive answer on the “chicken and egg” question cannot be given based on the results of these two studies. To evaluate whether impairments are present before alcohol use is initiated, alcohol naive adolescents schould be followed and included in the study (a conclusion drawn in chapter 2), focusing on the age that most adolescents start with drinking (13-15 years, Hibell et al., 2012). Exactly this was done in chapter 5, where we examined the predictive effect of weaknesses in executive functioning (working memory and cognitive control) on the onset of drinking in both at-risk adolescents and a community sample of adolescents. All drinking adolescents at baseline were excluded from the analysis to examine the onset of drinking during study follow-up. Survival analyses revealed that weaknesses in working memory and response cognitive control both predicted the onset of drinking, indicating that at least for executive functioning, impairments appear to be present before drinking is initiated. In addition, weaknesses in working memory also predicted the initiation of binge drinking during study follow-up.

Support for the finding that particularly severe drinking behavior has neurotoxic effects comes from addiction research conducted with young adults and animal (Crews et al., 2000; Duka et al., 2003). Recent studies have suggested that heavy drinking, accompanied by hangovers and binge episodes, might have severe negative consequences for the development of the brain. Particularly a combination of intoxication and withdrawal might cause impairments in brain functioning (for an overview, see Stephens and Duka, 2008). Luckily, not all young adolescents demonstrate such severe drinking pattern, but binge drinking episodes, followed by periods of non-drinking behavior (which might reinforce craving and withdrawal symptoms), as often seen in adolescents, might cause similar, but less severe effects in adolescents. Indeed, Crews and colleagues (2000) found that binge drinking caused more frontal brain damage in adolescent rats compared to adult rats. It is assumed that this brain region undergoes change during adolescence and might therefore be more susceptible to the neurotoxic effects of alcohol.

The second difference between the two lines of research as disucssed in chapter 2, included the cognitive processes that were examined. Cognitive impairments due to heavy alcohol use were found mainly for attention and visuospatial functioning (Hanson et al., 2011; Squeglia et al., 2012; Tapert et al., 2002), while weaknesses in executive functioning (e.g. weak inhibition and working memory) were found to precede increase in drinking behavior (Khurana et al., 2012; Nigg et al., 2006). This suggests that impairments in some cognitive processes (e.g. attention, visuospatial functioning) result from the neurotoxic effects of alcohol while other cognitive impairments might not arise in the 0irst instance from heavy drinking, although they might be affected by alcohol use. Particularly the impairments in executive functioning appear to precede the onset of drinking in adolescents and are not merely a result of heavy alcohol use. The findings of the current thesis support this hypothesis. In chapter 4, we found that weaknesses in executive functioning (i.e. inhibition, delay discounting risk-taking), predicted subsequent increases in alcohol use. Although we found that heavy alcohol use also weakened working memory functioning (chapter 3), it is likely that this observed impairment was already present before alcohol use was initiated, as confirmed by the results of chapter 5, which reported on the predictive effect of relatively weak working memory on the onset of drinking in the same adolescent sample. Moreover, at a behavioral level, chapter 9 provides support for the role of undercontrolled personality styles predicting the onset of drinking and heavy alcohol use among at-risk adolescents. Latent transition analysis revealed that high sensation seeking predicted the onset and continued heavy drinking trajectory. Adolescents scoring high on sensation seeking were more likely to start drinking or continue to drink heavily during study follow-up. Contrary to what was expected, no predictive effect of an impulsive personality style was found for the onset and continued heavy use of alcohol. This might be explained by the risk sample, which at a group level, may score already relatively high on impulsivity (results revealed indeed that this at-risk group significantly score higher on impulsivity compared to a mainstream sample of adolescents).

It should be noted that, many behavioral decisions with respect to risk behavior are made in arousing and emotional circumstances (e.g. drinking with peers, drinking in a bar) wherein intentional and deliberated processes (e.g. executive processes) do not predominate when it comes to deciding whether to engage in risky behaviors (Gladwin et al., 2011; Steinberg, 2005). Differences in the capacity to control and differences in goal-directed behavior might explain a part of the variance in adolescents' drinking behavior, but so called "hot cognitions" (e.g. reward sensitivity, risk-taking) might be equally important in explaining differences in adolescent alcohol use. Chapter 4 already revealed the importance of weaknesses of some of these cognitive processes (i.e. delay discounting and risk-taking) in predicting increase in alcohol use; however, more automatic and motivational processes (e.g. craving, appetitive processes) also appear to be involved (Field et al., 2007; Hofmann et al., 2009; Robinson and Berridge, 2008; Wiers et al., 2007) in drinking behavior. In the next paragraph, these automatic and motivational processes are discussed in more detail.

The bidirectional relationship between alcohol use and automatic processes

Appetitive and cognitive motivational processes (e.g. wanting, craving and expectancies) are assumed to play an important role in the engagement in risky behaviors in adults (Hofmann et al., 2009; Robinson and Berridige, 2008) and adolescents (Field et al., 2007). The extent to which someone (implicitly) expects that, for instance drinking a glass of beer, will lead to having fun or will decrease the feeling of craving, influences behavioral decisions with respect to drinking (Rooke et al., 2008). These alcohol-related cognitions will be automatically activated in the presence of an alcohol stimulus (e.g. peers who drink or the sight of a glass of beer) and the stronger these cognitions are present, the more likely they will influence behavioral decisions with respect to drinking behavior (Stacy and Wiers, 2010). One of these automatic cognitive processes reflects the extent to which someone has an motivational orientation towards alcohol, which can be assessed through automatically activated alcohol approach tendencies. The influence of these alcohol approach tendencies on the drinking behavior of adolescents was examined in chapter 6 and 7.

In chapter 6 it was found that stronger alcohol approach tendencies predicted alcohol use in at-risk adolescents. In chapter 7 we extended this knowledge by examining the association between alcohol use and approach tendencies in a longitudinal design, looking both at the prospective and bidirectional effects. The results of this latter study revealed that automatic alcohol approach tendencies predicted increase in adolescents' alcohol use six months later. This finding was in line with Thush and Wiers (2007) who found that implicit alcohol associations predicted alcohol use one year later in at-risk adolescents. Not only implicit alcohol associations appear to predict future drinking behavior, it was further found that a strong motivational orientation towards alcohol is predictive of future drinking behavior in adolescents. These stronger alcohol approach tendencies were already identified in heavy and social adult drinkers (Field et al., 2008a; Palfai and Ostafin, 2003), and they predicted future cannabis use in young adults (Cousijn et al., 2011). However this thesis provides the first results indicating that alcohol approach tendencies prospectively predict adolescents' alcohol use.

Automatic approach tendencies appear to play an essential role in addictive behavior (Robinson and Berridge, 2008), and experimental studies altering these approach tendencies have proven to be succesfull in reducing relapse in heavy drinkers and adults addicted to alcohol (Wiers et al., 2010b, 2011). In young adolescents, these automatic approach tendencies might underlie the escalation from experimental use of alcohol to more severe and problematic drinking patterns later in life. It might be more difficult for adolescents with a stronger orientation towards alcohol to control their drinking behavior as these automatic processes are more likely to influence behavioral responses, particularly in situations in which information processing time is limited (Gladwin et al., 2011). Therefore, stronger alcohol approach tendencies might increase drinking behavior. It has been suggested that continued drinking might further strenghten automatic approach tendencies (Gladwin et al., 2011), making it even more difficult to retain control over drinking behavior. Unfortenately, we did not find support for this latter hypothesis. Several explanations are possible. First, it might be that the time between the two waves (i.e. 6 months) was too short to reveal any strengthening of automatic approach tendencies which subsequently predict an increase in alcohol use. Second, it is conceivable that at a group level, the amount of alcohol that these young adolescents consume, is too low and too infrequent to identify change in approach tendencies.

Besides the main effect of alcohol approach tendencies on adolescent alcohol use we also examined the interacting effect of response inhibition on this relation. Relative weaknesses in the capacity to inhibit responses appeared to increase the influence of alcohol approach tendencies on adolescent current (chapter 6) and prospective (6 months later, chapter 7) drinking behavior. This finding is in line with dual process theories of addiction, which assume that both strong automatic processes and relatively weak reflective processes increase the likelihood of heavy drinking (Field et al., 2008b; Ostafin et al., 2008; Wiers et al., 2007). Recently, this hypothesis was already confirmed for response inhibition and automatic processing in young adults (Houben and Wiers, 2009), but the findings of this thesis are the first to demonstrate that response inhibition is also an important moderator in the relation between automatic approach tendencies and alcohol use among young adolescents. It is likely that the combination of relatively weak executive functioning and strong automatic and motivational processes, leads to heavier drinking behavior. Adolescents who are more orientated towards alcohol, and have more difficulties to inhibit these automatic responses are more likely to drink heavily and increase their drinking behavior (Wiers et al., 2007).

In sum, the results of chapter 6 and chapter 7 reveal that alcohol approach tendencies are already present in young adolescents and predict both current (chapter 6) and future drinking (chapter 7) behavior. Adolescents who consume alcohol are more likely to have a strong motivational orientation towards alcohol, and this approach orientation predicts increase in drinking behavior over time, particularly in adolescents with relatively weak inhibition skills. Although we have examined these effects within a limited time frame (i.e. 6 months), it is likely, and in line with adult studies (Field et al., 2008a; Palfai and Olson, 2003), that strong alcohol approach tendencies combined with relatively weak inhibitions skills are relevant in the escalation of adolescent alcohol use.

Social context as moderator

Besides individual differences in the capacity to control behavior, social influences also appear to play a significant role in the relationship between automatic processes and alcohol use. In chapter 8, we examined the moderating effect of alcohol availability at home, on the prospective relationship between implicit associations and adolescent alcohol use. Previous studies revealed that implicit alcohol associations became more accessible (important for retrieval and storage in memory) in an alcohol related context (e.g. bar setting versus lab setting, Dunn and Yniguez, 1999; Goldstein and Krank, 2006). Moreover, the predictive effect of implicit alcohol associations on adolescent alcohol use increased in an alcohol related setting (Krank et al., 2005). The findings of the current study (chapter 8) add to this knowledge by showing that the home context, and particularly the availability of alcohol at home, moderated the effect of implicit alcohol associations on adolescents' future drinking behavior. That is, implicit alcohol associations predicted increase in the frequency of alcohol use in adolescents exposed to alcohol at home, but not in adolescents who indicated that there was no alcohol available at home. These results suggest that alcohol availability at home increases the accessibility of implicit alcohol associations (Krank and Goldstein, 2006), which subsequently increase the frequency of drinking in adolescents. According to Krank and Wall (2006), context is important in determining which memory associations are accessible from memory and subsequently influence behavioral decisions. Several context effects such as, (1) media effects (Dunn and Yniguez, 2009), (2) experimental priming (Roehrich and Goldman, 1993), and (3) social settings such as a bar (Havermans et al., 2004; Lau-Barraco et al., 2008) have already been identified as playing a significant role in the retrieval of implicit alcohol associations and the prediction of alcohol use. The present study is the first to demonstrate that the availability of alcohol at home can influence the predictive effect of implicit alcohol associations. The availability of alcohol at home might activate implicit associations in adolescents, which are not or hardly activated in adolescents in home settings were alcohol is not available.

Methodological issues

The findings of the current thesis indicate that particularly high-risk groups should receive attention from researchers. As argued in chapter 10, particularly these at-risk groups are difficult to include in longitudinal studies. The typical characteristic of high risk groups that makes these groups interesting to examine, are often variables associated with missingness. For instance, disruptive behavior and low socioeconomic status are both associated with attrition and substance use (Ferguson et al., 1996; Kazdin et al., 1993; Van Beijsterveldt et al., 2002; Wolke et al., 2009). This problem also occurred in the at-risk sample included in the current thesis. After two years (four waves), almost 50% of our sample was missing due to school dropout or skipping school or other reasons for absence. Particularly for our analysis, where full information maximum likelihood (FIML) as method to deal with missing data was not available, this drop-out resulted in serious analytical problems (as reported in chapter 5). We therefore conducted a simulation study to evaluate the most appropriate method to handle the missing data. The results revealed that multiple imputation (MI) was the most efficient method for reducing bias to a minimum while maintaining sample size. These results support the inclusion of high-risk samples even if this is accompanied by high amounts of missingness. If handled with the appropriate method, the bias resulting from missingness is minimized and the results are reliable. When MI is used, arguments against reliability of findings can be refuted, and reviewers and editors can consider even studies with high numbers of missingness.

Limitations

In addition to the high amount of dropout (typical for high-risk samples), some other limitations of this study should be mentioned. The at-risk population that was studied in this thesis, that is, adolescents who attend SE, could be characterized by specific characteristics that have not been measured properly and possibly covary with the results that have been found. It is known for instance, that these adolescents attend these schools because of their externalizing behavioral disorders such as ADHD and conduct disorder. These disorders coincide with impulsivity and problems with behavioral regulation (Tarter et al., 2003; Whelan et al., 2012; White et al., 2011). Although we included a self-report measure (Strenght and Difficulties Questionnaire, SDQ, Goodman, 1997) designed to assess behavioral problems (e.g. hyperactivity, attention problems, emotional problems, peer problems), we had no official diagnostic information (DSM-IV) for these adolescents due to ethical and privacy regulations. Since the SDQ assesses specific behavioral problems but not clinical disorders, it is difficult to rule out covarying effects of specific disorders such as ADHD or conduct disorder. In addition, although this study was originally designed to study primarily the onset of drinking, it turned out that many adolescents, particularly in the high-risk sample, started drinking before the first wave was completed. This resulted in the exclusion of adolescents from some analyses (see for instance chapter 5), which might have led to the exclusion of a specific group of adolescents. Future research, studying similar populations and focusing on the onset of alcohol use, should include even younger adolescents compared to those in the current study.

Implications for intervention

The results of this thesis revealed that particularly adolescents with weaknesses in executive functioning and relatively strong automatic processes, are at risk for heavy and severe drinking. Several interventions are available, however, the implementation in adolescent samples has not been examined for all of these interventions. Roughly two lines of intervention research can be distinguished (Wiers et al., 2013). First, a number of intervention studies focus on increasing behavior control. Houben et al (2011a) for instance, found that training working memory in drinkers decreased alcohol use. In another study, Houben and colleagues (2011b) found that training heavy drinkers to inhibit responses in the presence of alcohol stimuli (i.e go/no-go manipulation) resulted in decrease of alcohol use. Training methods designed specifically to increase working memory in adolescents with ADHD have also proven to be successful (Klingberg et al., 2005). Particularly for the high-risk group, this intervention method might be useful, however as mentioned previously, increasing cognitive control alone might not be sufficiently to resist engagement in drinking behavior under arousing and tempting circumstances. A recent meta-analysis by Sonuga-Barke and colleagues (2013) questioned the effectiveness of working memory training implemented in its original format (cf. Klingberg et al., 2005). Recently developed training methods that might be more appealing to, and less boring for adolescents, are game-based training methods. An advantage of these training methods is that they both increases motivation to complete the task and better reflect the rewarding and tempting environment in which decisions tot engage in risk behaviors in real life are made (Dovis et al., 2012; Prins et al., 2011).

Second, several interventions aimed at changing automatic action tendencies have been developed. Wiers and colleagues (2011) and Eberl and colleagues (2013) found that training addicts to avoid instead of approach alcohol stimuli decreased relapse. It is Important to note that these interventions have been proven to be succesfull in adult heavy drinkers and addicts. It is unclear whether these interventions are also effective in adolescents, who might have different reasons and motivations for their drinking behavior and be more or less influenced by other factors such as peers.

Besides these specific interventions, more general approaches to reduce alcohol use among adolescents are available. With respect to the findings presented in chapter 8, easy to implement adjustments in the home environment might change drinking behavior of adolescents. That is, minimizing the availability of alcohol at home might decrease the frequency of alcohol use among adolescents. This adjustment could possibly be integrated into existing effective intervention programs such as the PAS-program (Koning et al., 2009, 2011). PAS is an intervention that targets both parents and adolescents, and it has been proven successful in delaying the onset of drinking in young adolescents and reducing more heavy use later in adolescentce; two elements in adolescents' drinking behavior assumed to be strongly associated with problematic alcohol use. Another promising approach concerns targeted interventions for high-risk personally-types, that focus on risk personality factors such as sensation seeking and impulsivity, which were found to be effective in decreasing (binge) drinking among adolescents (Conrod et al., 2008, 2013). As the results of chapter 9 reveal, particularly adolescents high on sensation seeking are at risk for heavy alcohol and other drug use. Targeting these adolescents with specifically designed interventions might be a successful approach to reduce drinking and binge drinking in adolescents.

In sum, several interventions are available and a combination of these training and intervention methods might be particularly effective for targeting adolescents at-risk for heavy use. Nevertheless, for future research it is very important to identify the functional components of each intervention, detailed for specific groups (e.g. early vs late onsetters, community vs. risk sample), to ensure their effectiveness. Previous studies have revealed that not every combination of intervention approaches, is equally effective and not every group of adolescents (Conrad et al., 2013; Danielsson et al., 2011; Thush et al., 2007) obtains similar results. With respect to the findings of this thesis, it would be useful to find a proper alignment between targeting adolescents who are at-risk and intervening at the correct moment (i.e. before alcohol use initiated for the first time). The practical implementation of this intervention will require further examination.

Future directions

The results of this thesis improve our understanding of the relationship between adolescents alcohol use and cognitive functioning, however more research is needed to formulate a comprehensive theory about who is at risk for heavy drinking and why, as well as about related impairments in cognitive functioning. With respect to the neurotoxic effects of alcohol use, further studies are required to identify which cognitive processes are affected by heavy alcohol use, and to explain why some of these processes are more susceptible to the neurotoxic effects of alcohol compared to others. The results of this thesis (chapter 3, 4 and 5) suggest that weaknesses in executive functioning precede the onset of drinking in adolescents. The literature review (chapter 2) indicates that heavy alcohol alcohol use affects mainly attention and visuospatial functioning in adolescents. With respect to the latter finding, the recent literature provides no clear theory about how alcohol affects the brain, and more specifically, how alcohol use affects the *adolescent brain*. With respect to executive functioning predicting alcohol use, existing theories about faster developing reward-related brain areas relative to slower developing cognitive control systems in adolescence (Galvan et al., 2006; Verdejo-Garcia et al., 2008), explain individual differences in adolescents' drinking behavior insufficiently. These theories merely illustrate why adolescents are more likely to engage in risk behavior compared to adults, since this imbalance in maturation is a process assumed to occur in all adolescents. Moreover, differences between drinking and non-drinking adolescents were found both at a brain level (i.e. fMRI, grey/white matter) and at a cognitive level (i.e. cognitive functions such as attention and working memory, DeBellis et al., 2000; Medina et al., 2008; Tapert et al., 2002), however, little is known about how impairments in specific brain areas relate to impairments in cognitive functioning and eventually influence behavioral decisions (e.g. starting with drinking). This applies both to impairments in alcohol naïve adolescents, as well as to impairments after prolonged and heavy use of alcohol. For instance, the question is how precisely impairments in working memory, contribute to the onset of drinking. Furthermore, is it a matter of delay in development in cognitive functioning or a matter of decrease in functioning which has been detected in heavy drinking adolescents. Particularly in adolescence, the flexibility and adaption of brain functioning might also be an important topic of future research (Crone and Dahl, 2012). When it becomes clear how and what kind of cognitions predict alcohol onset and what kind of impairments arise after heavy use, it is important to determine what kind of drinking pattern harms the adolescent brain. What is heavy alcohol use? Does binge drinking or intoxication alter brain functioning (Crews et al., 2000; Stephens and Duka, 2008)? These questions need to be examined in future research to increase our understanding, beyond the insights provided by the results in this thesis, of the relationship between alcohol use and cognitive functioning in adolescents.

With respect to automatic processes, there appears to be a more clear theory in explaining how these automatic processes increase drinking behavior (for an overview see Wiers et al., 2007). Nevertheless, several loose ends still exist about the development of implicit alcohol cognitions and their influence on some adolescents' drinking behavior but not on others. Implicit alcohol cognitions have already been found in alcohol naïve adolescents (Van der Vorst et al., 2012), so the development of these associations does not depend on real behavior experience. Observational learning has been proposed to play a significant role in the development of implicit associations (Goldstein and Krank, 2006). Some progress has been made to identify interacting factors (including the results in this thesis), yet it is unclear how peers for instance, fit into this story. Peers are assumed to play a vital role in drinking behavior of adolescents. Recent studies have suggested that subtle automatic processes may exert less influence on drinking behavior in the presence of peers, since other processes, such as peer imitation, are more likely to explain the engagement in drinking behavior (Larsen et al., 2012).

The results of the current thesis provide a first foundation for a more comprehensive theory that would explain the association of cognition in adolescents with alcohol use. Although several issues have to be examined in more detail, the results provide a starting point for disentangling the cause and effect in the relationship between cognitive impairments and adolescent alcohol use. Various adolescent samples and the longitudinal nature of the discussed studies contribute to a better understanding of the direction of the relationship between adolescent alcohol use and cognition. This thesis demonstrated that the neurotoxic effects of alcohol are not the same for all adolescents and it revealed that severity of drinking is an important factor that differentiates the effects. Weaknesses in executive functioning (e.g. working memory, cognitive control) appear to be an important factor in predicting the onset of drinking in adolescents. Combined with strong automatic appetitive processes, this relatively weak executive functioning increases the likelihood of heavy drinking and might underlie the escalation from alcohol onset and “normal” drinking to more severe drinking patterns in later adolescence.

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Summary

Summary.

As a part of the normative development of adolescents, it is not surprising to observe a peak in risk behavior during this particular period. Regarding drinking behavior for instance, almost 50% of the adolescents have experimented with the use of alcohol before the age of 15. In this same period, the influence of parents decreases and adolescents learn to make independent choices. They continuously adapt to different social roles in an environment that is rapidly changing. Opinions and appreciation of peers are highly valued and are many times a drive force for the engagement in risky behaviors. Sometimes this leads to behavioral choices that seem to be irresponsible and illogical in the eyes of adults, although they are obvious and extremely rewarding for adolescents. The drawbacks of engaging in risky behaviors such as alcohol and drug use, is that it requires behavioral control to override the tempting and desirous feelings which emerge as soon as substance use is initiated. Recent theories suggest that behavioral control is a very important aspect in the drinking behavior of adolescents, and differences in the capacity to control one's own responses are assumed to underlie the escalation from relatively normal drinking patterns to more severe drinking in adults and adolescents. The development of behavioral control coincides with the maturation of the prefrontal cortex and these brain areas are not fully grown until late adolescence. This ongoing maturation process during adolescence has been identified as a vulnerable marker for the neurotoxic effects of alcohol. Alcohol use during adolescence could contribute to delayed development and impairment in cognitive functions as well as differences in brain functioning. At the same time, impairments in cognitive functioning have been found to predict increase in drinking behavior in adolescents. This raises the question of directionality of the relationship and suggests a bidirectional relation between cognitive functioning and adolescents' drinking behavior. Some cognitive impairments might result from heavy alcohol use, while other cognitive impairments found in heavy drinking adolescents, might be present before adolescents started drinking. Therefore, the first aim of this thesis was to establish the direction of the relation between alcohol use and cognitive functioning in adolescents and find an answer to the "chicken and egg" question. To achieve this goal we reviewed the recent literature with respect to this topic and considered the empirical results, supporting either direction of the relationship between alcohol use and cognitive functioning (e.g. cognitive impairments predicting alcohol use and cognitive impairments after (heavy) alcohol use). In addition, we prospectively examined

whether cognitive impairments predicted increase in alcohol use or resulted from heavy alcohol use, both in a high-risk sample selected based on their heavy drinking (chapter 3) and in a English community sample of adolescents (chapter 4). The results with respect to the heavy drinking sample were somewhat inconclusive about the direction of the effect. That is, we found support for heavy drinking predicting relative weakening of working memory, and we found support for relatively weak working memory predicting increase in drinking behavior six months later, suggesting a bidirectional relationship between alcohol use and working memory functioning. The community sample of adolescents revealed a more consistent pattern with respect to the direction of the effect. Weaknesses in three measures of impulsivity predicted the increase in drinking behavior six months later. The studies presented in chapter 3 and 4, and the vast majority of previous studies on cognitive processes in adolescent alcohol use, fall short in including alcohol naïve adolescents to draw a firm conclusion about the "chicken and egg" question. We therefore examined whether impairments in executive functioning predicted the onset of drinking in young adolescents by observing alcohol onset during study follow-up (chapter 5). The results revealed that cognitive impairments (e.g. weaknesses in response inhibition and working memory) at baseline predicted the onset of alcohol use at subsequent waves. Moreover, weaknesses in working memory functioning predicted the onset of binge drinking. Together, these studies suggest that, at least for impairments in executive functioning (e.g. cognitive control), these impairments precede the onset of drinking. Prolonged (heavy) use of alcohol might further weaken these functions, causing delay in the development of cognitive functioning during adolescence or even leading to decreased performance at different levels of functioning (e.g. brain, behavior).

Our second aim was to examine the (prospective and) bidirectional relationship between automatic processes and adolescent alcohol use. Moreover, we evaluated the moderating role of response inhibition in this relationship. It has been suggested that both automatic and impulsive processes, as well as more reflective and deliberated processes are involved in drinking behavior. In heavy drinkers it appears that automatic processes are more likely to drive the behavioral choices of drinking, resulting in fast and 'habit-like' behavior. In heavy drinkers, alcohol stimuli more often capture the attention (i.e. attentional bias) or trigger automatic action tendencies (i.e. alcohol approach tendencies). The reflective system is able to inhibit fast and impulsive automatic processes when time, capacity, and motivation to do so are present. Reflective processing involves cognitive control functions such as response inhibition and working memory which inhibit responses and focus on long-term goals.

In chapter 6 and 7 we examined whether these relatively strong automatic processes were also present in young adolescent drinkers and whether they predict (increase in) alcohol use. We assumed that particularly adolescents with relatively weak response inhibition skills and strong alcohol approach tendencies would drink more and increase their drinking behavior. The results indeed supported this assumption. We found a cross-sectional relation between alcohol use and alcohol approach tendencies, which was moderated by inhibition skills (chapter 6). In chapter 7 we found that alcohol approach tendencies predicted increase in alcohol use six months later, however only in adolescents with relatively weak inhibition skills. In addition, it was assumed that repeated use of alcohol would strengthen these alcohol approach tendencies over time, however, no support for this latter assumption was found in this sample.

Our third aim was to examine the role of the social context in the prediction of adolescent alcohol use by automatic processes. It has been suggested that social context in which alcohol-related cognitions are triggered influences the accessibility and predictive effect of these cognitions on alcohol use. Implicit alcohol associations are more easily accessible in a "alcohol related setting" (e.g. bar, nightclub), compared to a neutral setting. Moreover, the predictive effect of implicit alcohol associations appears to increase when implicit alcohol associations are triggered in an alcohol related setting. Alcohol availability at home has been found to be an important predictor of adolescent alcohol use. Possibly, the availability of alcohol at home might activate implicit alcohol associations in adolescents and subsequently influence their drinking behavior. We hypothesized that the presence or absence of alcohol at home (e.g. in the refrigerator) could influence the predictive effect of implicit alcohol associations on alcohol use. In chapter 8 we tested whether implicit alcohol associations would predict future alcohol use differently when alcohol was available versus when alcohol was not available at home. The results indicated that implicit alcohol associations predicted increase in adolescent alcohol use six months later only when alcohol was available at home.

Together, the findings of this thesis suggest that both controlled as well as automatic processes play a significant role in the drinking behavior of adolescents. Weaknesses in executive functioning appear to precede the onset of drinking and heavy drinking in adolescents. Prolonged use of alcohol might further impair these functions, resulting in a vicious circle in which behavioral control problems, either by themselves or in combination with automatic processes, increase alcohol use. Heavy drinking further impairs these cognitive functions. This process creates a double risk for adolescents with behavioral control problems. Because of an early onset of drinking they are not only at an increased risk for escalating in their drinking behavior, but they are also more likely to encounter problems in their cognitive development. The combination of strong automatic processes and relatively weak cognitive control might therefore play a vital role in the escalation of adolescent alcohol use and explain the progress from "normal" drinking behavior to more severe drinking patterns in adolescents, which may have serious consequences for the normal development of adolescents.

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Samenvatting

Samenvatting.

Als onderdeel van de normale ontwikkeling van adolescenten, is het normaal om een piek in risicogedrag te zien gedurende deze periode. Kijken we bijvoorbeeld naar het drinkgedrag van adolescenten dan zien we dat bijna 50% van de jongeren wel eens geëxperimenteerd heeft met het gebruik van alcohol voor de leeftijd van 15 jaar. In deze zelfde periode neemt de invloed van ouders af en leren adolescenten zelfstandig beslissingen te maken. Ze leren zich aan te passen aan de verschillende sociale rollen die de omgeving van hun eist. Meningen en opvattingen van peers worden steeds belangrijker en zijn vaak een drijvende kracht achter risicogedragingen. Dit leidt soms tot gedrag, dat in de ogen van volwassenen onverantwoordelijk lijkt, maar voor jongeren volkomen normaal en belonend is. Het nadeel van risicogedragingen zoals alcohol- en drugsgebruik is dat ze vaak gepaard gaan met gevoelens van “craving”, en het vergt impulscontrole om deze gevoelens de baas te blijven. Recente theorieën suggereren dat de mate van impulscontrole bepalend is voor het al dan niet escaleren van alcoholgebruik. De prefrontale cortex, en daarmee de vaardigheid om impulsen te controleren, is bij adolescenten nog niet volledig ontwikkeld. Er wordt gesteld dat juist in deze periode het brein extra gevoelig is voor de negatieve effecten van alcohol. Het gebruik van alcohol zou bij kunnen dragen aan een vertraagde en verminderde ontwikkeling van impulscontrole. Tegelijkertijd wordt deze suboptimale ontwikkelde vaardigheid in verband gebracht met het toegenomen risicogedrag gedurende de adolescentiefase. Deze bevindingen roepen de vraag van oorzaak en gevolg op en suggereren een mogelijk bidirectionele relatie tussen alcoholgebruik en cognitief functioneren. Sommige cognitieve tekortkomingen kunnen een gevolg zijn van alcoholgebruik terwijl andere afwijkingen mogelijk een verklaring bieden voor de start van het gebruik van alcohol. Het eerste doel van deze studie was om een antwoord te vinden op de vraag wat nu wat veroorzaakt, de zogenaamde “kip en ei” vraag. Als eerste hebben we recente bevindingen vergeleken die beiden richtingen van deze relatie (cognitieve tekortkomingen die alcohol gebruik voorspellen en verminderd cognitief functioneren door alcohol gebruik) hebben onderzocht. Daarna hebben we longitudinaal bekeken of cognitieve beperkingen alcohol gebruik voorspellen of juist een resultaat zijn van alcoholgebruik, zowel in een risico sample (geselecteerd op hun verhoogde alcohol gebruik, hoofdstuk 3) als in een doorsnee sample van jonge adolescenten (hoofdstuk 4). Voor de risico groep waren de resultaten niet eenduidig; zowel effecten door alcohol gebruik als effecten van cognitieve beperkingen op alcohol gebruik werden gevonden.

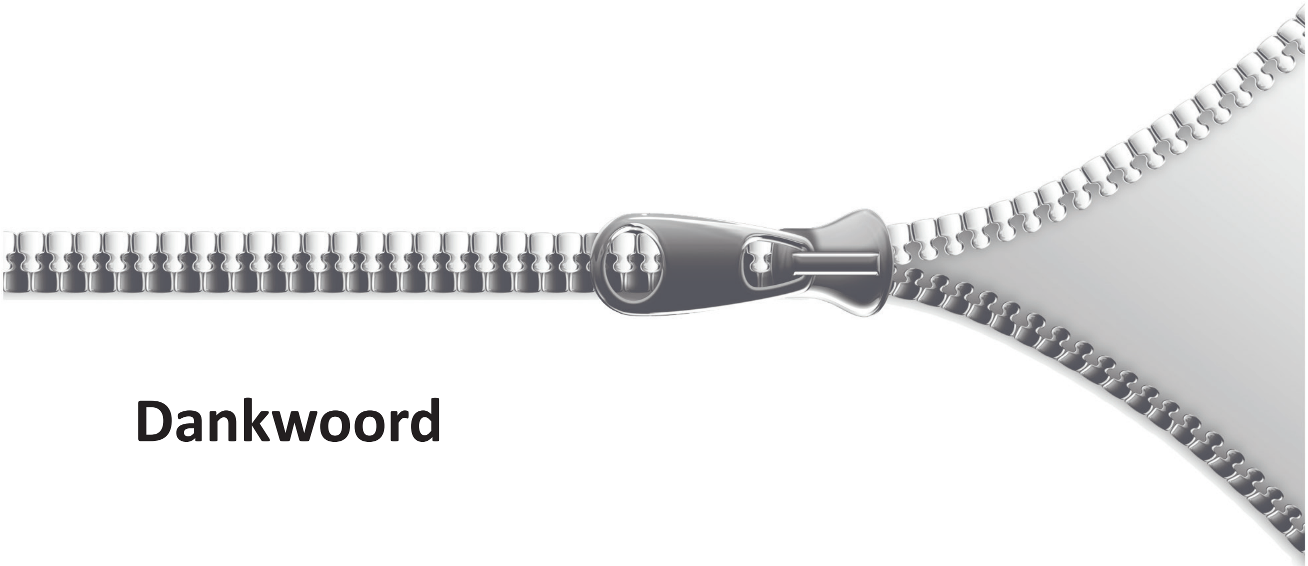
Verminderd werkgeheugen, een maat gerelateerd aan impulscontrole, werd geconstateerd na alcohol gebruik, maar verminderd werkgeheugen bleek ook een voorspeller van toename in alcoholgebruik 6 maanden later te zijn. In de algemene adolescenten groep vonden we duidelijke voorspellende effecten van cognitie op alcoholgebruik. Dat wil zeggen, jongeren met relatief lage impulscontrole lieten een toename zien in alcoholgebruik na 6 maanden. Zowel de studie in hoofdstuk 3 als in hoofdstuk 4, en het merendeel van andere recente studies over dit onderwerp, schieten tekort door de afwezigheid van niet-drinkende jongeren ten tijde van de start van de studie. Hierdoor wordt het bemoeilijkt om een volledig en eenduidig antwoord te geven op de richting van de relatie. In hoofdstuk 5 hebben we getracht dit probleem te voorkomen door alleen niet-drinkende adolescenten te includeren in onze studie, en deze adolescenten te volgen gedurende twee jaar. Op deze wijze zijn we in staat om tekortkomingen in impulscontrole, voorafgaand aan het gebruik van alcohol, mogelijk te linken aan de start van drinken en binge drinken. De resultaten van deze studie laten zien dat verminderd werkgeheugen en cognitieve controle (response inhibitie) inderdaad van belang zijn in het voorspellen van de start van gebruik van alcohol en in de escalatie van alcoholgebruik. Relatief verminderd executief functioneren voorspelt een vroegere start van alcohol en escalatie van gebruik. Het is mogelijk dat het veelvuldig en langdurig gebruik van alcohol deze verminderde cognitieve functies verder aantast.

Het tweede doel van deze studie was het onderzoeken van de longitudinale en mogelijk bidirectionele relatie tussen automatische processen en alcohol gebruik van adolescenten. Ook hier hebben we gekeken naar de modererende rol van impulscontrole (response inhibitie). Er wordt gesteld dat zowel snelle en automatische processen als reflectieve en doordachte processen een rol spelen bij het gebruik van alcohol. Zware drinkers vertonen meer automatisch gedrag en lijken makkelijker getriggerd te worden door alcohol stimuli middels attentie (attention bias) of automatische actie tendensen (approach/avoid tendencies). Deze relatief automatische processen kunnen worden geïnhibeerd door ons reflectieve systeem indien tijd, capaciteit en motivatie aanwezig zijn. Hiervoor zijn inhibitie en werkgeheugen nodig.

In hoofdstuk 6 en 7 hebben we bekeken of deze automatische processen ook aanwezig zijn in relatief jonge drinkers (at-risk adolescenten). Op basis van volwassen studies, voorspelden we dat verminderde impulscontrole in combinatie met sterke automatische processen, verhoogd alcohol gebruik onder adolescenten zou voorspellen. De resultaten bevestigde deze aanname; automatische actie tendensen voorspelden alcohol gebruik bij adolescenten (cross-sectioneel en prospectief) en deze relatie werd gemodereerd door response inhibitie.

Ons derde doel van deze studie was om de rol van de sociale context in de relatie tussen alcohol gebruik en automatische processen, nader te bekijken. Eerdere studies suggereren dat automatische processen worden beïnvloedt door de context waarin ze plaatsvinden. Ook de mate waarin ze alcoholgebruik voorspellen blijkt samen te hangen met de context. In hoofdstuk 8 vonden we dat de zichtbaarheid van alcohol thuis, van invloed was op de mate waarin automatische processen het drinkgedrag van jongeren 6 maanden later voorspelde. De aanwezigheid en zichtbaarheid van alcohol thuis zou alcohol cognities kunnen activeren die op hun beurt weer de mate van alcoholgebruik van jongeren kunnen beïnvloeden.

Samengevat laten de bevindingen van deze studie zien dat zowel gecontroleerde als automatische processen een belangrijke rol spelen in het drinkgedrag van adolescenten. Verminderde impulscontrole blijkt een belangrijke voorspeller te zijn voor de start van drinken bij jongeren. Langdurig gebruik van alcohol kan bijdragen aan een verslechtering van cognitieve functies die belangrijk zijn voor impulscontrole. Dit resulteert in een vicieuze cirkel waarin impulscontrole problemen, of op zichzelf of in combinatie met automatische processen, leiden tot een toename in alcoholgebruik bij adolescenten. Dit proces creëert een dubbel risico voor jongeren met impulscontrole problemen; ze zijn niet alleen gevoeliger voor problematisch drankgebruik door de vroege start van alcoholgebruik maar lopen ook een verhoogd risico op problemen in hun cognitieve ontwikkeling door het vroege en veelvuldig gebruik van alcohol. De combinatie van sterke automatische processen en verminderde impulscontrole kunnen een belangrijke rol spelen in de escalatie van drinkgedrag en verklaren mogelijk het verloop van relatieve normale drinkpatronen naar meer zwaardere vormen van drinkgedrag die ernstige gevolgen kunnen hebben voor de verdere ontwikkeling van adolescenten.



Dankwoord

Dankwoord.

Iedereen bladert altijd graag door het dankwoord. Uit nieuwsgierigheid, om te kijken of je eigen naam er tussen staat, of juist omdat het een hoofdstuk is wat iedereen begrijpt. Hoe dan ook, het Dankwoord wordt bijna altijd gelezen. Dat maakt dit hoofdstuk meteen een moeilijk hoofdstuk om te schrijven; want wat nou als ik iemand vergeet! Dus, sta je er niet tussen maar vind je wel dat je er hoort, schrijf dan een kritische review met overtuigende argumenten en misschien overweeg ik een resubmissie van mijn proefschrift.

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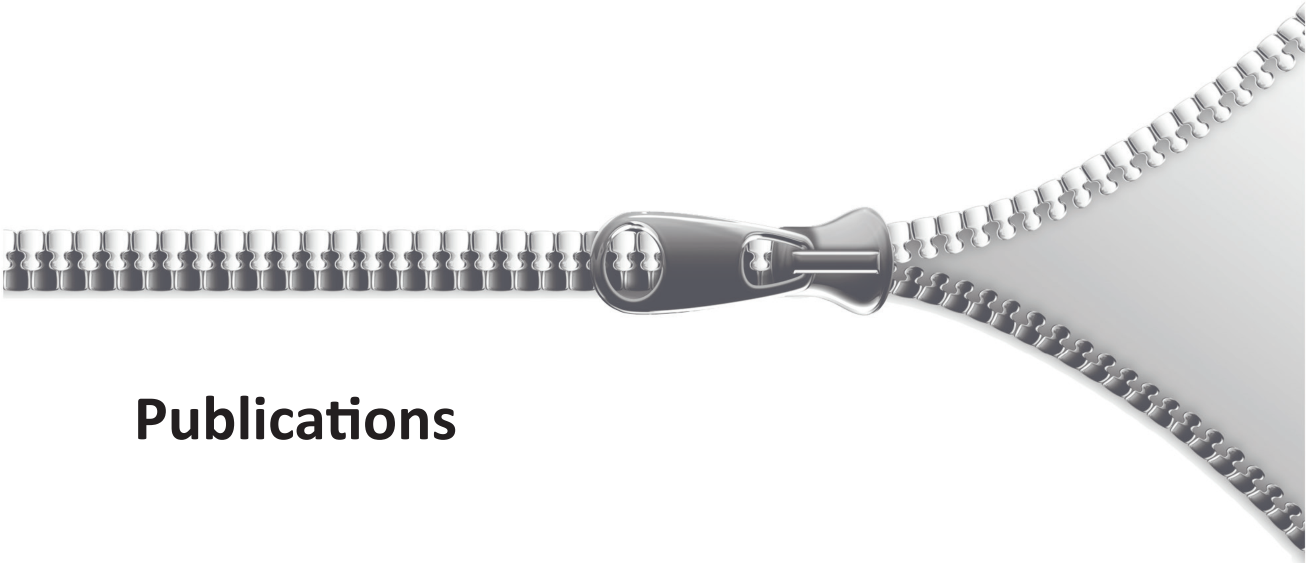

Publications

Publications in this thesis

Published or in press

Peeters, M., Monshouwer, K., Janssen, T., Wiers, R. W., & Vollbergh, W. A. M. (2014). Working memory and alcohol Use in at-risk adolescents: A 2- year follow-up. Alcoholism: Clinical and Experimental Research, 38, 1176–1183.

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Submitted

Peeters, M., Janssen, T., Monshouwer, K., Wiers, R. W. & Vollebergh, W. A. M. Weaknesses in executive functioning predict the onset of adolescents' alcohol use. Submitted.

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Other publications

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Janssen, T., Larsen, H., Peeters, M., Pronk, T., Vollebergh, W. A. M., & Wiers, R. W. Parental alcohol-specific rules and risk personalities in the prediction of adolescent alcohol use. In press.

Janssen, T., Larsen, H., Peeters, M., Boendemaker, W., Vollebergh, W. A. M., & Wiers, R. W. Do online assessed self-report and behavioral measures of impulsivity predict onset of substance use in adolescents? Submitted.

Zondervan-Zwijnenburg, M. A. J. Peeters, M., & van de Schoot, R. Pushing the limits: Sample size requirements with unbalanced subgroups in latent growth models. Submitted.

Curriculum Vitae

Curriculum Vitae

Margot Peeters (1984) received in 2007 her Bachelor degree in Educational Science at the Radboud University in Nijmegen. In the same year she started with the Research Master Behavioral Science, followed with an research internship at the department of Developmental Psychology, after which she received her master degree (Bene Meritum) in 2009 at the Radboud University. In 2009 she started her PhD project on neurocognitive processes and adolescent alcohol use, a collaboration between the University of Utrecht and the University of Amsterdam. During this period she visited the Addiction research group at the University of Liverpool and collaborated with prof. dr. Matt Field. Next to conducting research she supervised students and lectured several academic courses. Currently, she is a postdoctoral researcher at the University of Utrecht.