Psychological Changes and Cognitive Impairments in Adolescent Heavy Drinkers

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Abstract — **Aims:** 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? **Methods:** This narrative review summarizes results of recent prospective studies that focus on causal relationships between adolescents' alcohol use, and psychological changes and cognitive impairments. **Results:** 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. **Conclusion:** 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 >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 neurodevelopmental changes that occur during adolescence have been well characterized (Giedd *et al.*, 1999; Blakemore and Choudhury, 2006), and these neurobiological alterations have been mapped to changes in motivated behavior 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 long-lasting 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 (Giedd *et al.*, 1999; Blakemore and Choudhury, 2006). Two important networks that undergo changes during adolescence are the limbic system and the prefrontal cortex (Spear, 2000b; Steinberg, 2007). The prefrontal cortex is involved in executive control and plays a significant role in regulating, organizing and controlling behavior. Executive functions include response inhibition (e.g. impulse control), working memory (WM) and attention (Gazzaniga *et al.*, 2002; Blakemore and Choudhury, 2006). 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 (Giedd *et al.*, 1999; Blakemore and Choudhury, 2006; Spear, 2013) meaning that executive functions and reward related circuits tend to mature relatively late.

It has been suggested that increased risk-taking behavior during adolescence is related to synaptic remodeling in reward circuits combined with delayed maturation of the prefrontal cortex (Spear, 2000a ; Crews *et al.*, 2007). With respect to reward and decision-making, Galvan *et al.* (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 pronounced in adolescents compared with 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 (Galvan *et al.*, 2006, 2007; Steinberg, 2007; Casey *et al.*, 2008). 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; Steinberg, 2007; Somerville and Casey, 2010).

Crone and Dahl (2012) argue that this imbalance is reflected in changes in social and affective processing during adolescence. They suggest that these neurodevelopmental changes mean that adolescents' behavior 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 rapid changing environment in which adolescents grow up. The motivational context in which adolescent's risk behavior 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, 2000b). 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 (Clark *et al.*, 2008; Castellanos-Ryan *et al.*, 2011). 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) (Sher *et al.*, 1997; Brown *et al.*, 2000), 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 with 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 *et al.* (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) 8 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, verbal learning and memory functioning compared with 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 *et al*. (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 1 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 (Duka *et al*., 2002, 2004; Crews *et al*., 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 whether 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 *et al*. (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 *et al*. (2006). Q-sort ratings of clinicians were used to assess behavioral control and resiliency from childhood (2–5 years) to early adolescence (14 years). Relatively slow development of behavioral 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 behavioral control predicts the initiation of 'first contact' with alcohol, or the development of heavy drinking.

Khurana *et al*. (2012) found that WM 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 (behavioral measure) and acting without thinking (self-report), which suggests that relatively poor WM might manifest itself through impulsive behavior, which in turn predicts alcohol use. Therefore, this study suggests that (poor) WM 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 WM and the quantity of alcohol consumed, or alcohol problems (these were not measured).

In another study, Fernie *et al*. (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 2-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 WM, 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*., 2010), 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 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 enrollment. 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 function precede the onset of alcohol involvement, and they place the individual at increased risk of 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 (Tapert *et al.*, 2002; Squeglia *et al.*, 2009; Hanson *et al.*, 2011). 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 (Wong *et al.*, 2006; Khurana *et al.*, 2012; Fernie *et al.*, 2013). 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.

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