Impact of Alcohol Use on Inhibitory Control (and Vice Versa) During Adolescence and Young Adulthood: A Review

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Abstract — Aims: Adolescence is usually the time when individuals first drink alcohol and this has been associated with relatively weak or immature inhibitory control. This review examines the changes on brain development and inhibitory function that take place during adolescence and youth as well as the relationship between inhibitory control and alcohol use at this early age. Methods: Narrative review of the chief studies related to (a) the development of inhibitory control during adolescence, (b) the deficits in the inhibitory ability in alcohol use disorders and (c) the effects of acute alcohol intake and binge drinking on inhibitory control in adolescents and young adults. Results: Inhibitory control processes are developing during adolescence and youth. Poor inhibitory functions may predispose the individual to alcohol misuse. Likewise, acute and binge alcohol drinking may impair the inhibitory control and compromise the ability to prevent or stop behaviour related to alcohol use. Conclusion: Poor inhibitory control can be both the cause and the consequence of excessive alcohol use. Adolescence and young adulthood may be a particularly vulnerable period due to (a) the weak or immature inhibitory functioning typical of this stage may contribute to the inability of the individual to control alcohol use and (b) alcohol consumption per se may alter or interrupt the proper development of inhibitory control leading to a reduced ability to regulate alcohol intake. Further longitudinal research is needed to evaluate the interaction between inhibitory control dysfunction and alcohol use in both situations.

INTRODUCTION

Adolescence is a stage of life characterized by drug experimentation and engagement in health-risky behaviours (Spear, 2000; Dahl, 2004). In Western countries, alcohol is one of the most available and used drugs at this age (Anderson and Baumberg, 2006; Johnston et al., 2009), and it currently constitutes a major public health concern (Eurobarometer, 2010; SAMHSA, 2011).

While several decades of research in adults have shown that chronic alcohol abuse is associated with major brain and cognitive impairments (e.g. Oscar-Berman and Marinovic, 2007; Harper, 2009), the relationship between alcohol consumption and neurocognitive damage during adolescence and youth is still poorly investigated. Understanding the neurocognitive consequences of alcohol on the adolescent brain is crucial, since adolescence is a period of critical brain development and the time in which alcohol use is typically initiated.

Within the various cognitive processes affected by alcohol, the inhibitory control deserves particular consideration. Indeed, the ability to inhibit a response or action may prevent alcohol misuse, but deficits in such ability might, in turn, promote excessive alcohol consumption. Recent research indicates that acute alcohol intake, as well as heavy or binge drinking during adolescence and youth, may induce anomalies in behaviour (poor decision-making, altered impulse control, etc.) and brain functioning related to inhibition (Field et al., 2007; Loeb and Duka, 2009; López-Caneda et al., 2012). Likewise, an alteration in the inhibitory control may constitute a vulnerability factor for subsequent alcohol misuse and lead to an escalation or disordered regulation of alcohol intake (Norman et al., 2011; Wetherill et al., in press).

This review will focus on the definition of inhibitory control and the main experimental paradigms used to measure it, then on the core brain circuitry involved in response inhibition and its development across adolescence and early adulthood. Finally, the role of inhibitory processes as both a determinant and a consequence of excessive alcohol use will be discussed. This review ends with some additional considerations about the relation of inhibitory control with impulsivity, as well as with other cognitive processes affected by alcohol, and with a brief discussion of the application of current knowledge to the prevention of alcohol abuse in youths.

INHIBITORY CONTROL

Inhibitory control is a core component of human behaviour. The importance of this executive function is highlighted by the broad range of psychiatric problems associated with inhibitory deficits, such as attention deficit hyperactivity disorder (Nigg, 2001), bipolar disorder (Frangou et al., 2005), obsessive-compulsive disorder (OCD) (Penades et al., 2007) and substance use disorder (Verdejo-Garcia et al., 2008). Although it is generally defined as the ability to withhold or suppress actions or thoughts that are inappropriate, inhibitory control is a heterogeneous construct which lacks of a simple operational definition, probably due to the multiple kinds of inhibitory processes underlying this executive function as well as the wide range of tasks used to measure it.

From an overall view, two different inhibitory functions can be distinguished: involuntary or automatic inhibition and voluntary or effortful inhibition (Nigg, 2000). The former one refers to the involuntary inhibition of attention that takes place to recently inspected locations or objects, which is traditionally known as inhibition of return (Klein, 2000). The effortful inhibition is frequently divided in behavioural inhibition and interference control (see Diamond, 2013, for a recent review).

Behavioural inhibition is the ability to suppress or stop responses that are ready to be emitted (prepotent responses) and it would comprise the motor inhibition measured by the Go/NoGo (GNG) and the stop-signal (SS) tasks (Logan, 1994). Interference control includes two other subtypes of
inhibition. The first one, cognitive inhibition, involves (a) the inhibition of thoughts and memories, i.e. the ability to suppress unwanted mental representations (Anderson and Levy, 2009)—usually measured by the Think/No-Think paradigm (Anderson and Green, 2001)—and (2) the inhibition of the tendency to choose smaller, immediate rewards in favour of delayed but larger rewards, also known as delayed gratification (Mischel et al., 1989), which is frequently assessed by the delay discounting task (Bickel and Marsch, 2001). The second subtype of interference control refers to the inhibition of the processing of nonpertinent or irrelevant stimuli, which can be measured, for instance, by the Stroop or the Flanker tasks (Eriksen and Eriksen, 1974; MacLeod, 1991).

For the purpose of the present review, we will focus on behavioural inhibition, which has been the type of inhibitory control more investigated in studies on the relationship between alcohol and inhibitory processes. Throughout this article, when we refer to inhibitory control, we essentially refer to behavioural or response inhibition.

Given that response inhibition is typically measured by the GNG and SS paradigms, these tasks have been widely used to examine the effects of alcohol on inhibitory processes as well as the influence of inhibitory control ability on the regulation of alcohol intake. Both tasks involve rapid, repeated responses to targets, while also demanding suppression of those prepotent responses when faced with a Stop or No-Go stimulus. The main difference between them is that while the GNG task requires that individuals respond to one type of stimuli (Go) and withhold the response to the other (No-Go), the SS task demands that individuals inhibit a response that has been already initiated when a SS is presented (Fig. 1). The commission errors or false alarms (inappropriate responses to the No-Go stimulus), for the GNG task, and the time required to stop a response once it has been initiated, for the SS task, provide the behavioural index of inhibitory control.

THE NEURAL CIRCUITRY OF RESPONSE INHIBITION

Using functional magnetic resonance imaging (fMRI), the neural substrates underlying these tasks, and therefore the inhibitory control processes, have begun to be identified. Studies in healthy population have consistently revealed a frontostral network involved in the inhibition of prepotent responses (Aron et al., 2007; Chambers et al., 2009). Within this network, the prefrontal cortex (PFC) and, particularly, the inferior frontal cortex (IFC) seem to be a critical region for successful inhibition (Konishi et al., 1999; Aron et al., 2004; Chikazoe et al., 2009). This is also supported by neuropsychological studies, which have reported impairments in inhibitory control in subjects with IFC damage (Aron et al., 2003).

Briefly, the IFC would be responsible for generating the No-Go signal which, passing through the subthalamic nucleus and the globus pallidus, would lead to the inhibition of the thalamus and, consequently, to the inhibition of motor responses in the primary motor cortex (Fig. 2) (Nambu et al., 2002; Aron and Poldrack, 2006). This is clearly a very simplified model as there are other less direct inhibitory pathways (Duann et al., 2009; Aron, 2011), as well as other regions such as anterior cingulate or parietal cortex (Durston et al., 2002; Watanabe et al., 2002) that are involved in response inhibition.

On the other hand, neuroimaging studies have found abnormal IFC functioning linked to substance use (for reviews see Volkow and Fowler, 2000; Dom et al., 2005; Feil et al., 2010), including alcohol (Pfefferbaum et al., 2001; Noël et al., 2001;...
show that inhibitory control improves with age, as already present in infancy and childhood (Diamond and Goldman-Rakic, 1989; Jones et al., 2003), it is during adolescence when this ability becomes more efficient (Tamm et al., 2002; Marsh et al., 2006; Luna, 2009). A number of studies show that inhibitory control improves with age, as demonstrated by the higher speed (reduction in reaction times) (Williams et al., 1999; Band et al., 2000), and better performance (lower commission error rates) (Casey and Trainor, 1997; Jonkman, 2006) in response inhibition across development.

This more efficient inhibitory control appears to be related to the anatomical and functional changes that take place in the PFC throughout adolescence and youth (Luna et al., 2004). Important brain maturational changes such as myelination or synaptic pruning/reorganization continue well into late adolescence and early adulthood, being the PFC the last region to reach maturity (Giedd et al., 1999; Gogtay et al., 2004; Lenroot and Giedd, 2006). Both myelination and synaptic reorganization have been associated with an improvement in neural networks functioning as well as with increased neuronal and behavioural efficiency (Casey et al., 2005; Spear, 2010).

Similarly, fMRI studies have shown that inhibitory function develops in association with changes in PFC activity. Although the relationship between behavioural performance in inhibitory tasks and greater or lesser fMRI activation is still controversial (Bunge and Wright, 2007; Luna et al., 2010), several studies have reported greater IFC activity during inhibition in children compared with adolescents, and in adolescents compared with adults. This progressive reduction in prefrontal activation has been associated with better inhibitory control performance (Casey et al., 1997; Somerville et al., 2011). These findings support the notion that an immature brain (such as the adolescent brain) displays greater and less efficient prefrontal activation as well as poorer performance related to inhibition than a mature (and, therefore, adult) brain.

The adolescent brain, and particularly the PFC, appears to be especially sensitive to the harmful effects of alcohol as compared with the adult brain (Crews et al., 2000; Spear, 2013), probably due to these maturational changes (Giedd et al., 1999; Lebel and Beaulieu, 2011). This special sensitivity along with the relative developmental delay in inhibitory control could involve, on one hand, a greater propensity to excessive alcohol consumption (due to the reduced ability to prevent or stop behaviours related to alcohol use) and, on the other, a greater vulnerability of inhibitory mechanisms to the harmful effects of alcohol (due to the alteration or interruption in the normal development of inhibitory function).

POOR INHIBITORY CONTROL AND PROPENSITY TO ALCOHOL INTAKE DURING ADOLESCENCE

The immaturity of brain functioning underlying inhibitory control during adolescence appears to be linked to the peak onset of substance abuse observed through this period (Steinberg, 2008). Adolescence constitutes a stage of special risk for drug use initiation and the development of substance dependence (Rohde et al., 2001; Hardin and Ernst, 2009), as well as for the emergence of psychiatric disorders related to disinhibitory behaviours such as conduct disorders or OCD (Zoccolillo, 1993; Pauls et al., 1995).

Ineffective response inhibition may render individuals more vulnerable to develop addictive behaviours (Perry and Carroll, 2008). In this sense, Goldstein and Volkow (2002) proposed that drug addiction is a ‘syndrome of impaired response inhibition’, in which deficits in inhibitory control, along with an increased salience of drug-related stimuli (e.g. alcoholic drinks), would contribute to the inability to control the drug...
use (Goldstein and Volkow, 2002; see also Jentsch and Taylor, 1999; Robinson and Berridge, 2003; Wiers et al., 2007).

Consistent with this hypothesis, several studies have associated a weak inhibitory control with alcohol use during adolescence and youth. For example, Henges and Marczinski (2012) observed that failures to inhibit a response, as measured by the cued GNG task (Miller et al., 1991), predicted the binge use of alcohol in young social drinkers. Other authors have reported that poor inhibitory control, as measured with the SS task, is associated with alcohol-use-related problems as well as with risk of alcohol dependence in adolescents (Nigg et al., 2006; Rubio et al., 2008).

Studies of offspring of alcoholics have shown a lower response in the inhibition performance in subjects with family history of alcohol use disorders (Nigg et al., 2004; Schweinsburg et al., 2004). Consistent with this, children and adolescents with a positive family history for alcohol use disorders also show anomalies in the anatomical and functional structure of some regions involved in inhibitory control (Schweinsburg et al., 2004; Hill et al., 2009; Heitzeg et al., 2010). These anomalies might predispose the children to develop alcohol misuse during adolescence (Norman et al., 2011). Accordingly, a recent longitudinal study conducted by Wetherill and Colleagues showed that adolescents who later became heavy drinkers displayed less activation of inhibitory circuitry during a GNG task than age-matched controls, which was indicative of neural vulnerabilities prior to the onset of alcohol use. After becoming heavy drinkers, adolescents showed more activation during response inhibition than controls, indicating that heavy drinking per se may lead to additional alterations in brain functioning related to inhibitory control (Wetherill et al., in press).

Finally, weak inhibitory control has also been proposed as a general vulnerability factor for addictive behaviours, including alcohol use disorder (Goldstein and Volkow, 2002, 2011; Brewer and Potenza, 2008).

Although reduced inhibitory ability may play a major causal role in development of alcohol misuse or heavy drinking, conversely an impairment of the inhibitory control can be directly caused by heavy alcohol consumption. As described below, alcohol might compromise brain regions responsible for successful inhibition, thus reducing the ability to withhold a response. Therefore, not only a weak response inhibition may increase or encourage alcohol consumption, but also alcohol drinking may produce a weakening of inhibitory control, leading to a lower ability to stop alcohol consumption.

CONSEQUENCES OF ALCOHOL INTAKE ON INHIBITORY CONTROL

There are two main lines of research in the study of alcohol effects on inhibitory control: (a) the study of the acute effects of alcohol on response inhibition, where subjects execute different cognitive tasks or neuropsychological testing under the influence of certain doses of alcohol and (b) the study of the consequences of heavy or binge alcohol drinking on the inhibitory ability.

Acute effects of alcohol

Studies of the acute effects of alcohol support the hypothesis that alcohol disrupts (reduces) inhibitory control ability (Reynolds et al., 2006; Ostling and Fillmore, 2010). Specifically, adolescents and youths exposed to different doses of alcohol exhibit poor performance in a variety of response inhibition tasks. For instance, using SS and GNG tasks, several studies have demonstrated that moderate to high doses of alcohol (leading to blood alcohol contents ~0.06–0.09%) impair inhibitory control in young healthy subjects (Fillmore and Vogel-Sprott, 1999; Easdon and Vogel-Sprott, 2000; Marczinski and Fillmore, 2003; Rose and Duka, 2007, 2008; Loeber and Duka, 2009). Interestingly, it has been found that although moderate doses of alcohol impair the ability to suppress a response, they do not affect the ability to execute a response, which appears to be indicative of a specific disruption of the inhibitory mechanisms (Field et al., 2010). Accordingly, the alcohol-seeking behaviour might remain intact, whereas the ability to inhibit this impulse and to control alcohol use might be compromised (Leeman et al., 2012).

Another, particularly relevant study showed that impairments in inhibitory control after a moderate dose of alcohol are most pronounced in binge drinkers than in non-binge drinker subjects (Marczinski et al., 2007). This study indicates that individuals who binge drink alcohol can be particularly sensitive to the acute alcohol effects on response inhibition, such that when they become intoxicated, they are less able to refrain from the impulse or desire to consume more alcohol, leading to further binge drinking (BD). This finding is consistent with a study conducted by Weafer and Fillmore (2008), who reported that greater impairment of inhibitory control from alcohol predicted increased ad libitum drinking in young social drinkers.

Research examining the neural correlates of acute effects of alcohol also suggests that moderate-to-high doses of alcohol induce abnormalities on brain functioning involved in inhibitory control in adults (Kiddinkholt et al., 2002; Easdon et al., 2005). However, to our knowledge, only one study has assessed the electrophysiological patterns of response inhibition during alcohol intoxication in young people (Euser and Franken, 2012). In this study, moderate doses of alcohol not only decreased performance in an emotional GNG task, but also altered the components of the event-related potentials (ERPs) related to inhibitory control (N2-NoGo and P3-NoGo) (see, e.g. Falkenstein et al., 1999; Kok et al., 2004, for information about these components). These results were interpreted as indicating that those youths under the effects of alcohol need to activate more cognitive resources during the inhibition process (Euser and Franken, 2012).

Despite the well-established view that alcohol impairs inhibitory control, to date only one fMRI study has assessed the effect of acute alcohol ingestion in young people during response inhibition (Schuckit et al., 2012). In line with other studies that considered jointly young and adult participants (Anderson et al., 2011; Nikolau et al., 2013), alcohol decreased activity of regions involved in inhibitory control (such as prefrontal and cingulate regions) during a SS task in young people, specifically in those with a low response to alcohol and, therefore, with higher risk of problem drinking (Schuckit et al., 2012). However, additional research in this field is needed to clarify the impact of acute alcohol consumption on brain functioning related to response inhibition at this young age.

Effects of heavy/binge alcohol drinking

BD or heavy episodic drinking, i.e. the consumption of large amounts of alcohol in a short time followed by periods of
higher activity in the neural circuitry involved in emotional processes in youths with a BD pattern (Townshend and Duka, 2005; Nederkoorn et al., 2009; Scaife and Duka, 2009). For instance, Townshend and Duka (2005) observed that young BD women had more difficulties to inhibit their response to alerting stimuli in a vigilance task than controls, which was interpreted as a sign of a deficit in the frontal inhibitory control. More recently, Nederkoorn et al. (2009) reported an increased SS reaction time also in young BD women, indicating again a poor response inhibition in this population. Although these data are suggestive of a greater vulnerability in females to the neurotoxic effects of alcohol on inhibitory control, which is consistent with the stronger structural and functional impairments observed in women with an alcohol use disorder (Caldwell et al., 2005; Medina et al., 2008), additional research is required to test this hypothesis.

The three electrophysiological studies that to date have examined the effects of alcohol on inhibitory processes in young binge or heavy drinkers have shown anomalies both in the latency (Petit et al., 2012) and the amplitude (López-Caneda et al., 2012; Smith and Mattick, in press) of the NoGo-P3 component of the ERPs. In the study by Petit et al. (2012), heavy social drinkers showed delayed latencies of NoGo-P3 in an alcohol-related context, which was considered as an index of prioritizing processing related to alcohol that led to poorer inhibitory performance. In a recent follow-up study by our research group (López-Caneda et al., 2012), a greater NoGo-P3 was observed in young binge drinkers, which was associated with a hyperactivation in the right IFC. These results were interpreted as indicative of the activation of additional neural resources to compensate emerging functional alterations in the regions engaged in response inhibition, which would allow binge drinkers to perform an efficient inhibitory control. Finally, the study conducted by Smith and Mattick (in press) showed longer SS reaction time in young female heavy drinkers than in female controls as well as larger P3 increase for successful compared with failed inhibition trials in female heavy drinkers. Following the authors, these results were indicative that females who regularly drink heavily needed longer time and greater cognitive effort to inhibit the response correctly.

On the other hand, to our knowledge, the only neuroimaging study examining the response inhibition in adolescent binge drinkers is the one conducted by Wetherill et al. (in press), which reported anomalies in the functioning of inhibitory circuitry before and after the onset of heavy alcohol use (see previous section). Another study in adolescents binge drinkers assessed the neural correlates of the Iowa Gambling Task (IGT), a decision-making task that can be considered a measure of cognitive inhibition (Verdejo-García et al., 2008). In this study, Xiao et al. (2013) reported that adolescents with a BD pattern displayed a poor decision-making as well as a higher activity in the neural circuitry involved in emotional and incentive-related behaviours (the amygdala and the insula). According to the authors, the hyperreactivity of this neural system could entail difficulties to inhibit the desire to consume alcohol.

Taken together, research on the effects of acute and binge alcohol drinking suggests that alcohol consumption might lead to a ‘snowball effect’ by which the acute effects of alcohol on inhibitory control would promote a continuous auto-administration of the substance which, in turn, would contribute to the deterioration of the inhibitory control system.

**ADDITIONAL CONSIDERATIONS**

**Inhibitory control and impulsivity**

Impulsivity is a psychological construct closely linked to inhibitory control. This term includes those behaviours that are risky, poorly planned, and that entail undesirable or negative consequences (e.g. Evenden, 1999; Mitchell, 2004). Within neuropsychology and cognitive neuroscience, impulsivity is often associated with disinhibition, and it is thought to arise from an impairment of inhibitory control (Enticott et al., 2006; Lawrence et al., 2009). Impulsivity, similar to inhibitory control, plays a major role in alcohol-related disorders, as is demonstrated by the fact that (a) it predicts early onset drinking age and development of heavy drinking and alcohol dependence in young adults (Ernst et al., 2006); (b) different impulsivity dimensions are positively correlated with increased alcohol use and with alcohol-related problems (Dom et al., 2006; Hittner and Swickert, 2006; Cyders et al., 2008) and (c) alcohol-dependent subjects display high scores on impulsivity measures (Whiteside and Lynam, 2003; Mitchell et al., 2005; Fox et al., 2008). In the same way, several studies have suggested that excessive alcohol consumption in adolescents and youths is linked to the increased impulsivity during this period (Carlson et al., 2010; Moreno et al., 2012). A decline in this trait that usually takes place over the 18–25 age range has been related to decrease in alcohol use (Littlefield et al., 2010).

Although impulsivity and inhibitory control are related, they can make unique contributions to alcohol use (Leeman et al., 2012) and both constructs should be taken into account in studies examining the individual’s ability to control alcohol use.

**Alcohol also affects other related cognitive processes**

Although this review is focused on the inhibitory control impairment induced by alcohol use, it is important to note that alcohol may also indirectly affect the inhibitory system. Other cognitive processes that interact with inhibitory control, such as working memory, are also affected by alcohol consumption. For instance, a study conducted by Finn et al. (1999) showed that young subjects with low working memory capacity were more susceptible to the effects of alcohol on impulsive behaviour, suggesting that alcohol reduced the ability of working memory to modulate response inhibition. Alcohol might thus affect inhibitory control via (a) weakening the inhibitory system or (b) decreasing working memory capacity (Vogel-Sprott et al., 2001).
Alcohol, inhibition and gender

Another important moderator of the relationship between alcohol and inhibitory control is the gender. In this sense, it has been observed that while men display greater disruption of inhibitory control when receiving acute doses of alcohol than women (Fillmore and Wefer, 2004), the effects of frequent or binge alcohol drinking on response inhibition appear to be greater in females compared with males (Townshend and Duka, 2005; Nederkoorn et al., 2009). However, the neurocognitive results relating to gender and alcohol consumption in non-clinical populations are still scarce and inconsistent; further research is therefore needed.

Potential clinical implications

Given that alcohol misuse is associated with deterioration of inhibitory control skills, response inhibition training could theoretically improve inhibitory control and, consequently, lead to a decrease of alcohol intake (Houben et al., 2011; Jones et al., 2011). Houben et al. (2011) demonstrated, in a recent study, that young heavy drinkers trained to withhold a response to alcohol-related stimuli during a GNG task consumed significantly less alcohol in the week following the training. This finding, although needs to be replicated and validated for longer periods, suggests that the strengthening of response inhibition may be a useful intervention strategy for reducing alcohol use. It also underlines the importance of inhibitory control mechanisms on alcohol drinking behaviour as well as the usefulness of the early detection of response inhibition problems in alcohol use disorders prevention programmes.

CONCLUSIONS

Adolescence is a stage of life frequently associated with an early onset of alcohol use. It is also characterized by a weak inhibitory control due to the immaturity of the brain circuitry supporting this executive function. These reduced inhibitory skills consequently affect the ability to control the alcohol intake. Inhibitory control processes, in particular the behavioural inhibition, may equally be the cause and the consequence of excessive alcohol use. In fact, not only a weak response inhibition may lead to alcohol consumption, but drinking alcohol, in turn, may entail a weakening of the inhibitory control, leading to a lower ability to stop alcohol consumption. In this review, we have highlighted the main studies examining the relationship between inhibitory control and alcohol use in adolescents and young adults. Nevertheless, much further research is required to clarify how the excessive alcohol consumption may induce deficits in inhibitory control or how inhibitory control disruptions may constitute a vulnerability factor for alcohol misuse. The cross-sectional nature of most of the studies exploring neurocognitive functioning in young and adolescent binge drinkers makes it difficult to establish this relationship, so longitudinal studies are needed to evaluate the extent of the interaction between the inhibitory control dysfunction and alcohol use in both directions, as a vulnerability factor and as an effect of excessive drinking. Another major challenge would be to design prevention and treatment programmes that systematically integrate this growing body of knowledge.

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